GSA 2024 Winter Forum Syllabus

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Perioperative Management of Implantable Cardiac Devices

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NO DISCLOSURES

CENTRAL ILLUSTRATION: An Overview of the History of Cardiac Pacing

Paradigm Shifts in Cardiac Pacemakers

1950s
AC-powered pacemakers tethered to an extension cord (Furman)

1950s
Battery-powered transistorized "wearable" pacemakers (Lillehei/Bakken)

1958
First fully implantable pacemaker (Elmqvist/ Senning)

2015
Implantable pacemaker—basic system had not evolved significantly

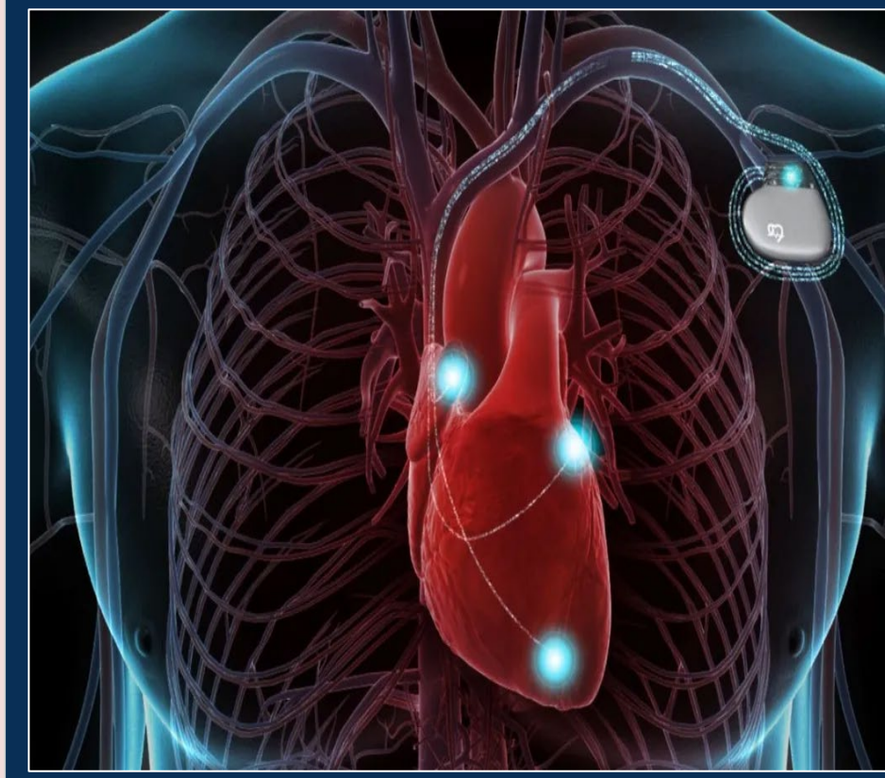
2016
Leadless pacemaker—the entire device is placed within cardiac chambers

Future
Batteryless devices, which harvest cardiac motion to power pacing circuits

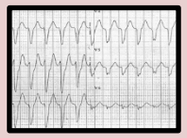
Mulpuru, S.K. et al. J Am Coll Cardiol. 2017;69(2):189-210.

Introduction to Cardiac Implantable Electronic Devices

- CIEDs monitor and/or regulate heart rhythm ensuring normal function
- 1.5 to 5% of the general population have arrhythmia
- ~3.5 million people in the US have pacemakers and about 300,000 have ICDs
- Miniaturization and increasing complexity over the years
- Several anesthesiologists have expressed discomfort in managing CIED patients
- Develop safe and effective management strategies and reduce incidence of adverse outcomes
- Practice Advisory by American Society of Anesthesiologists and Heart Rhythm Society 2011 and updated in 2020



Objectives

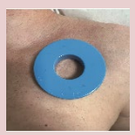


Indications for implantation

Better understanding of device function

Potential interactions

Targeted education initiative resources



Appropriate management strategies

Practice Advisory for the Perioperative Management of Patients with Cardiac Implantable Electronic Devices: Pacemakers and Implantable Cardioverter–Defibrillators 2020

*An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices**

SCAN ME

Practice advisories are systematically developed reports that are intended to assist decision-makin of patient care. Advisories provide a synth literature and analysis of expert opi ity data, open forum comments Practice advisories develope of Anesthesiologists (ASA) guidelines, or absolute re guarantee any specific modified, or rejected straints, and they are tional policies.

Practice advisories report opinions obta members. They are n same degree as stand sufficient numbers o advisories are subject t evolution of medical kn

This document upd Perioperative Managemen Electronic Devices: Pacemak Defibrillators: An Updated Rep Anesthesiologists Task Force on P Patients with Cardiac Implantable El by the ASA in 2010 and published in 201

Methodology

rdiac Implantable Electronic Devices

rdiac implantable electronic device implantable cardiac pacemaker r–defibrillator. The term car– e also refers to any cardiac

are to: (1) facilitate ement of the patient evice and (2) reduce rioperative manage– perative, postopera– where an anesthesia a care. Adverse out– table electronic device ted to, damage to the deliver pacing or shocks, anges in pacing behavior, pacing mode, and inappropri– r–defibrillator therapies.‡ comes include, but are not limited tachyarrhythmia and bradyarrhythmia,

Advisory Only
NOT
a STANDARD OF PRACTICE or GUIDELINES

This article is featured in "This Month in Anesthesiology," page 1A. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org).

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A complete bibliography used to develop this updated Advisory, arranged alphabetically by author, is available as Supplemental Digital Content 1 (http://links.lww.com/ALN/B979).

*Updated by the Committee on Standards and Practice Parameters: Jeffrey L. Apfelbaum, M.D. (Committee Chair), Chicago, Illinois; Peter M. Schulman, M.D. (Task Force Co-Chair), Portland, Oregon; Aman Mahajan, M.D., Ph.D. (Task Force Co-Chair), Pittsburgh, Pennsylvania; Richard T. Connis, Ph.D. (Chief Methodologist), Woodinville, Washington; and Madhulika Agarkar, M.P.H. (Methodologist), Schaumburg, Illinois.

†Generic pacemaker and defibrillator codes are provided in tables 1 and 2. Note that every transvenous implantable cardioverter–defibrillator includes both pacing and shock therapy capabilities for the management of bradyarrhythmias and tachyarrhythmias.

 Anesthesiology 2020; 132:225–52. DOI: 10.1097/ALN.0000000000002821

<zdoi; DOI: 10.1097/ALN.0000000000002821>

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NEWSLETTER
THE OFFICIAL JOURNAL OF THE ANESTHESIA PATIENT SAFETY FOUNDATION

CITATION: Disque D, Oliver AP, Neelankavil JP. Keeping pace: 2023 update on the perioperative management of cardiovascular implantable electronic devices (CIEDs). *APSF Newsletter.* 2024;39:25–27.

Keeping Pace: 2023 Update on the Perioperative Management of Cardiovascular Implantable Electronic Devices (CIEDs)

by Drew Disque, MD; Ashley P. Oliver, MD, MA; and Jacques P. Neelankavil, MD

Cardiovascular Implantable Electronic Device (CIED) technology continues to evolve and the global population of individuals with CIEDs is expanding. We present a focused update to the perioperative management of CIEDs since our last publication in 2020.

LEADLESS CIEDS

In our previous article in 2020, we introduced the Medtronic Micra™ leadless single-chamber ventricular pacemaker.[1] This device is inserted via the femoral vein and implanted in the right ventricular endocardium. The interest in leadless devices is driven by vascular access challenges in some patients, such as those with end-stage renal disease and multiple previous hemodialysis lines, and those with congenital heart disease with abnormal vascular anatomy. In addition, transvenous CIEDs are susceptible to infection and lead fracture. In 2023, Medtronic received approval from the Food and Drug Administration (FDA) for its newest Micra pacemakers, with two different models: the Micra AV2 and the Micra VR2. Similar to the original Micra, the Micra VR2 is intended only for ventricular sensing and pacing for patients who have atrioventricular (AV) block or atrial fibrillation. The Micra AV2 is indicated for patients with AV block, but unlike the VR2, it can provide atrial sensing and synchronous ventricular pacing. The Micra AV2 uses an accelerometer to sense the atrium and is able to pace in a VDD mode (Table 1). The key point for anesthesia professionals is that the Medtronic Micra models are not responsive to magnet application. If the patient requires asynchronous (VOO) pacing due to a risk for electromagnetic interference, the pacemaker must be reprogrammed with the programmer device.

Table 1: Generic pacemaker codes from the North American Society of Pacing and Electrophysiology and British Pacing and Electrophysiology Group.[2] Position refers to letter position in the pacemaker code (e.g., DDD, DOO, etc.).

Position	I	II	III	IV	V
	Chamber Paced	Chamber Sensed	Response to Sensing	Rate Modulation	Multisite Pacing
	O = None A = Atrium V = Ventricle D = Dual (atrium + ventricle)	O = None A = Atrium V = Ventricle D = Dual (atrium + ventricle)	O = None T = Triggered I = Inhibited D = Dual (atrium + ventricle)	O = None R = Rate modulation	O = None A = Atrium V = Ventricle D = Dual (atrium + ventricle)

The Abbott AVEIR™ VR, also a leadless device, was FDA-approved in 2022. The AVEIR VR has similar capabilities as the Micra; however, the AVEIR VR cannot perform AV sequential pacing (VDD) like the Micra AV. The AVEIR DR system, which was recently approved by the FDA, can perform dual chamber pacing. One advantage of the AVEIR devices is that they do respond to magnet placement. The magnet must be placed directly over the heart, and it will change the pacing mode to VOO at 100 beats per minute for five beats. If the battery is depleted, the magnet rate will then decrease to less than 100 depending on remaining battery life. Since the magnet

See "Update on CIEDs," Next Page

Table 2: General Recommendations for Perioperative CIED Management

Types of CIEDs

PACEMAKER

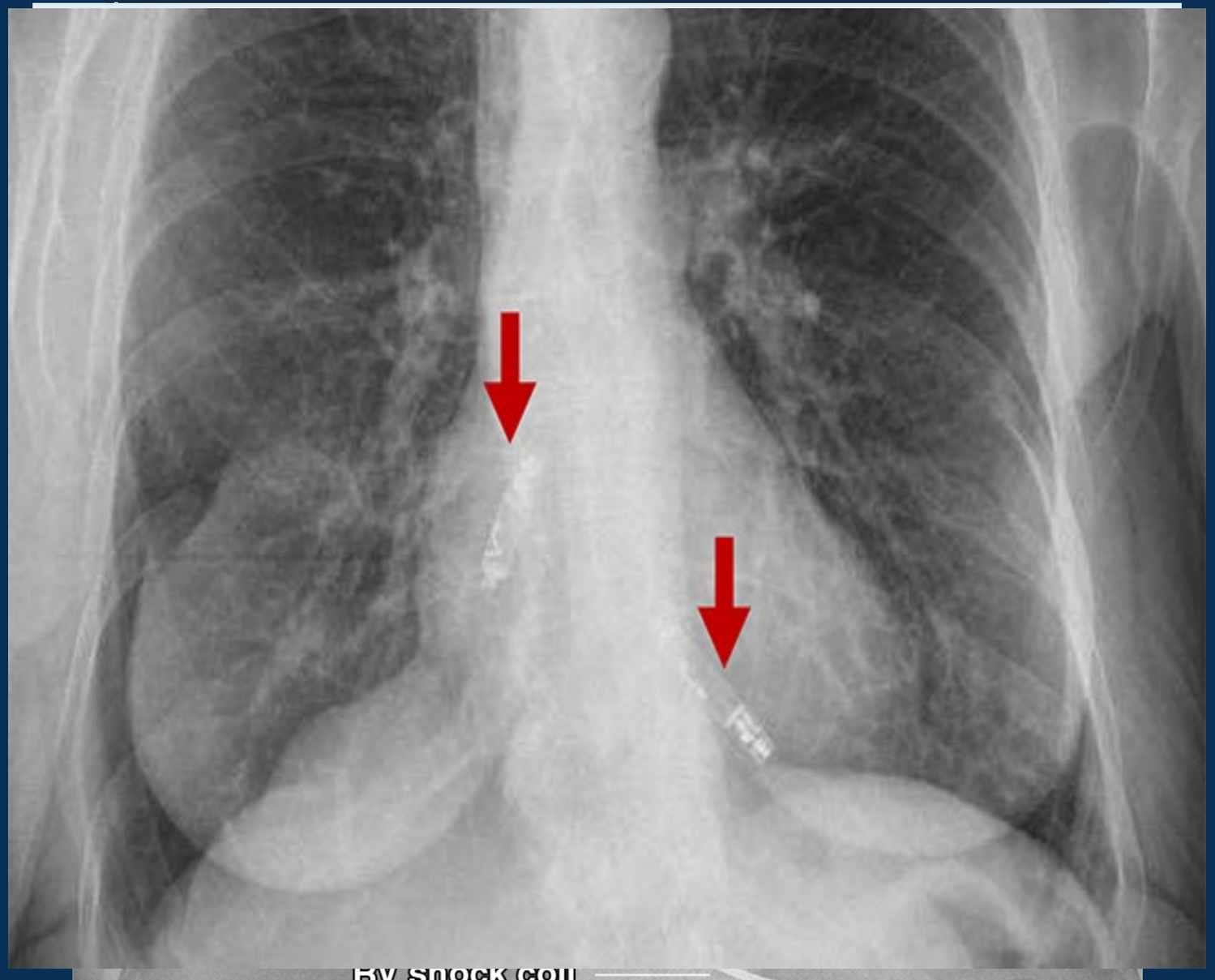
- Temporary
  - Epicardial
  - Transvenous
- Permanent
  - Dual Chamber: RA + RV
  - Single Chamber: RA or RV
  - Biventricular: RA + RV + LV (CS)
  - Leadless: Micra VR2/AV2, Nanostim and AVIER DR
  - CRT-P
  - Epicardial

CARDIAC DEFIBRILLATOR

- TV- ICD
- SC-ICD
- CRT-D

IMPLANTABLE LOOP RECORDER

Every ICD has an inbuilt pacemaker function



Leadless Pacemakers

Implantable Cardiac Defibrillator

Indications

Pacemakers

Symptomatic sinus bradycardia
Symptomatic sinus node dysfunction
Complete Heart Block
Second degree, Mobitz type 2 AV block
Symptomatic Mobitz type 1
Post-myocardial infarction

Cardiac Defibrillators

Prior MI with LVEF ≤30%
Nonischemic Cardiomyopathy with LVEF ≤35%
Prior MI, VT/VF and LVEF ≤40 during EP study
Hemodynamically unstable VT
Prior VF without any reversible cause
?HCM
Brugada syndrome
Long QT syndrome

Cardiac Resynchronization Therapy

LVEF ≤35%
QRS ≥150ms LBBB

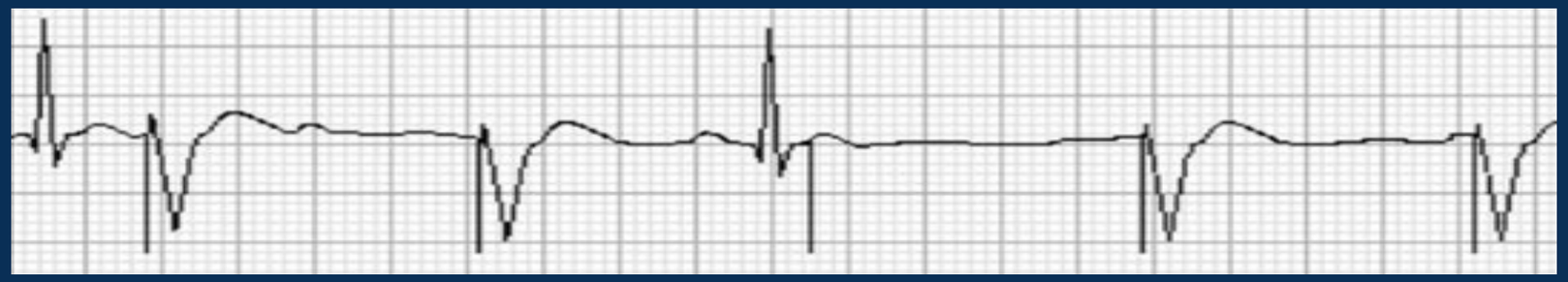
Implantable Loop Recorder

Identify asymptomatic occult arrythmia following a stroke
Assess average HR in A fib patients
Identify and assess bradycardic episodes
Screening for asymptomatic PVCs or nSVT

Modes

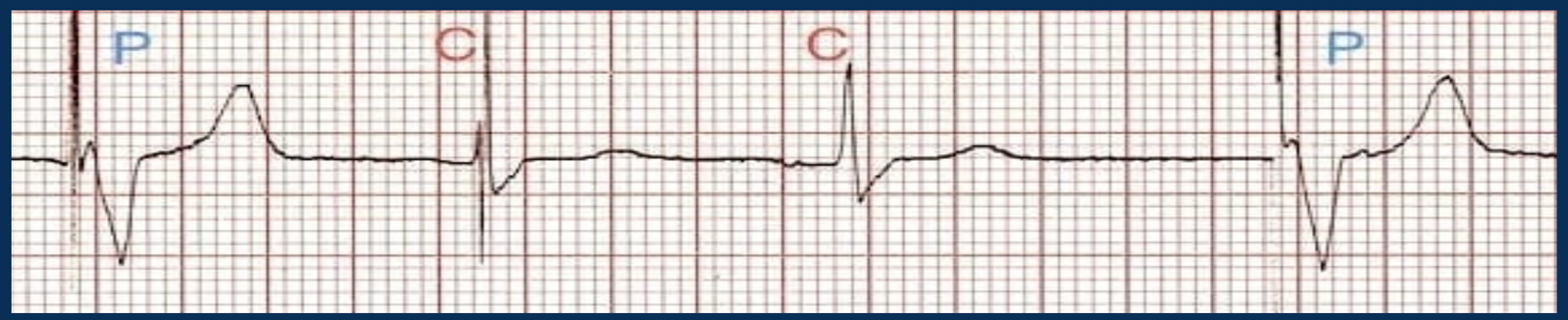
Position	Function	Response
1	Chamber paced	A- Atrium V- Ventricle D- Dual
2	Chamber sensed	A- Atrium V- Ventricle D- Dual O- None (sensing is disabled)
3	Response to sensed events	I- Inhibits pulse in response to sensed event T- Triggers pulse in response to sensed event D- Pulses can be either inhibited or triggered O- No response to sensed events
4	Rate modulation- accelerometer	O- No modulation R- Paced rate changes based on perceived physiologic need
5	Multisite pacing	O- none A- atrium V- ventricle D- Dual

V Paced
O Sensed
O Response



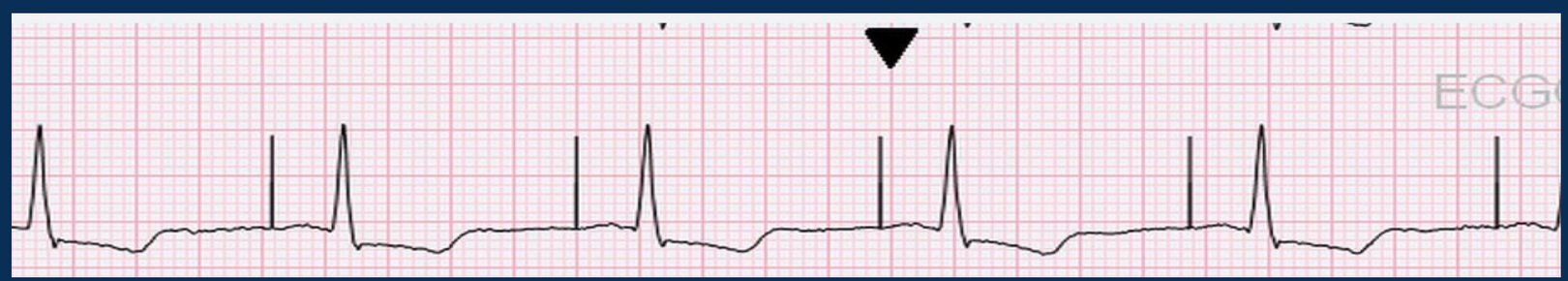
Use: Temporary during surgery due to interference from EMI. Rate modulation –
** R on T phenomenon

V Paced
V Sensed
I Response



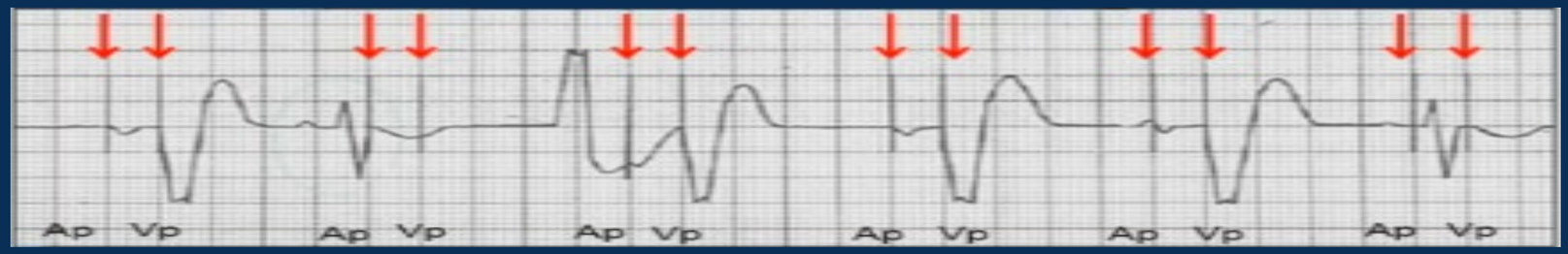
Use: If single chamber pacemaker for A fib or temporary use in the presence of intact sinus and AV node. Rate modulation +/-
** No AV node synchrony leading to pacemaker syndrome

A Paced
A Sensed
I Response



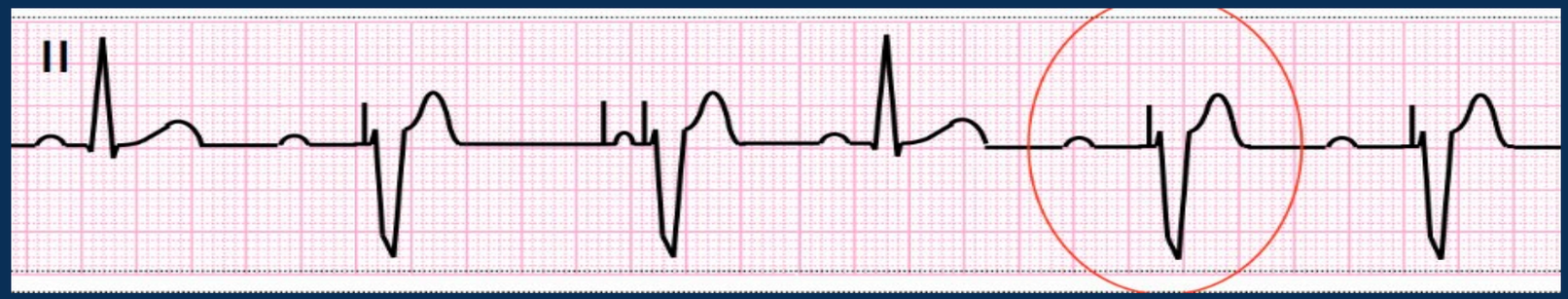
Use: Sinus node dysfunction with intact AV node. Rate modulation +/-
** Can develop AV node block later leading to bradyarrhythmias

D Paced
O Sensed
O Response



Use: Temporary during surgery due to interference from EMI. Rate modulation –
** R on T phenomenon

D Paced
D Sensed
D Response



Use: Most commonly used mode with rate modulation. AV synchrony is present. Four rhythms can be seen with normal pacemaker function-

1. normal sinus rhythm
2. Atrial pacing, normally conducted to the ventricle with a native QRS
3. AV sequential pacing
4. Atrial sensing and ventricular pacing

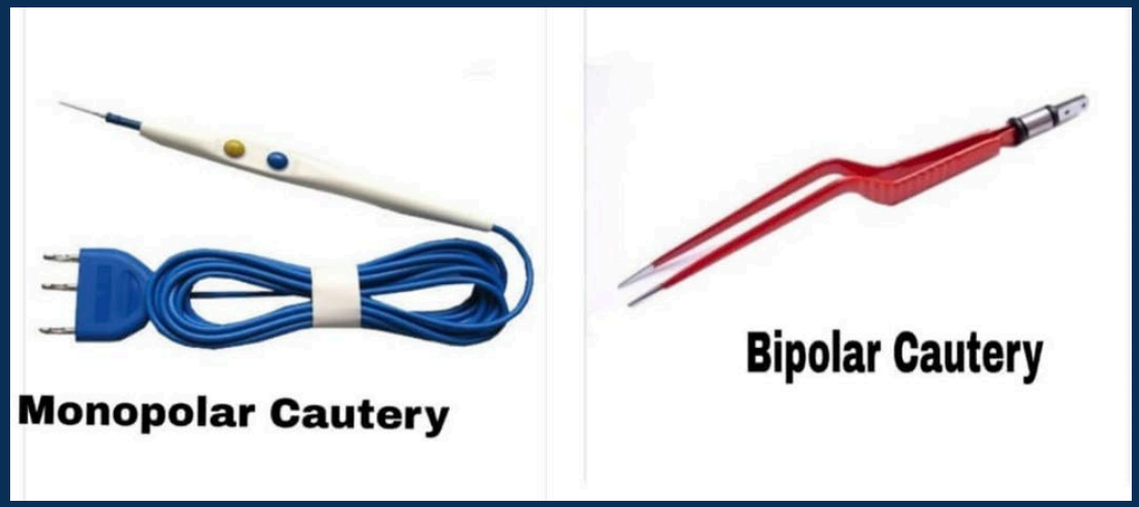
** If LV lead is not present can lead to LBBB pattern and septal dyskinesis. Can lead to dangerous bradyarrhythmia in the presence of EMI

Electromagnetic Interference

Definition- Malfunction or disruption of an electronic circuit cause by an external source with an electromagnetic field.

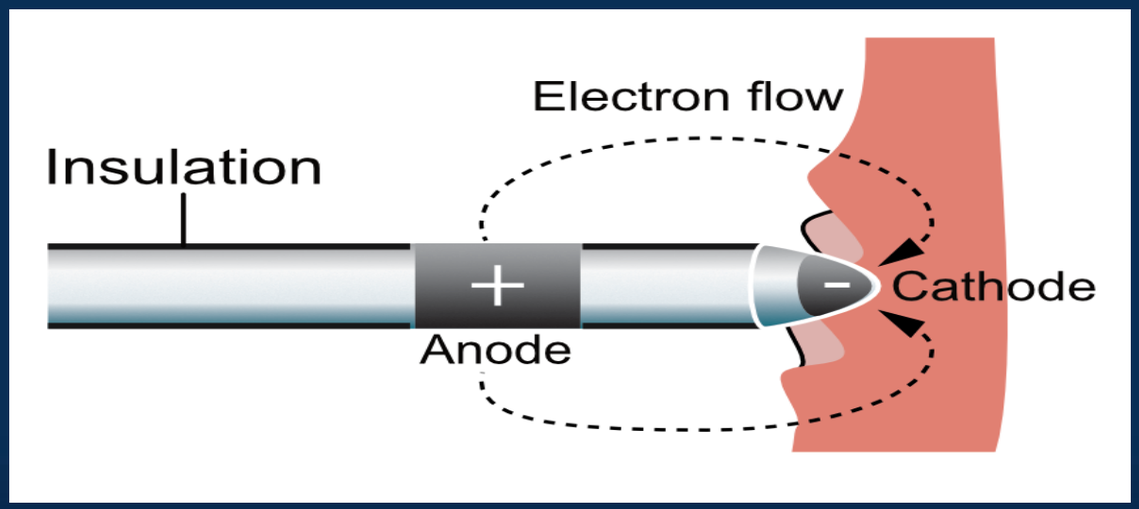
Sources of electromagnetic interference (EMI) and Mechanical interference during surgery

1. Electrosurgery Unit: Monopolar ESU > Bipolar ESU
   Coagulation mode > Cutting mode
2. Nerve stimulators, Transcutaneous electric nerve stimulation units, Lithotripsy and ECT
3. Radiofrequency Scanners and ablation devices
4. GUIDEWIRES for Central line insertion
5. Bone saws: Vibrations can cause interference



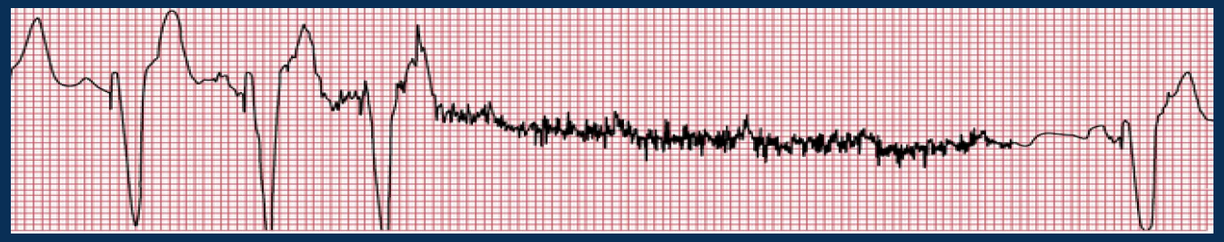
Location of interference- Above the umbilicus > Below the umbilicus

Configuration- Unipolar (lead tip- cathode and pulse generator-anode) causes more EMI than Bipolar (cathode and anode at distal tip). Intracardiac signals are sensed through electrodes

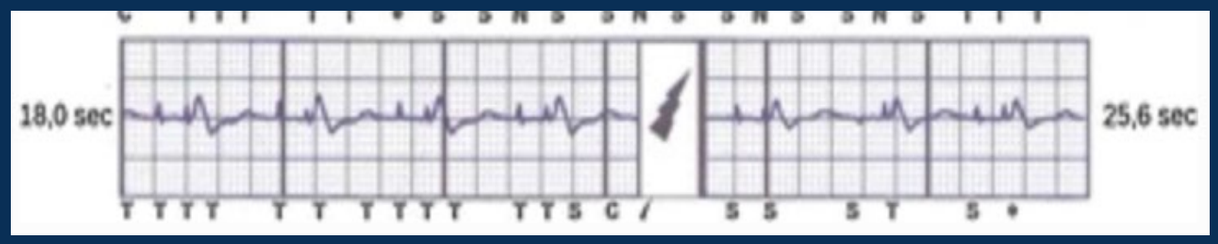


Risks of EMI and CIEDs

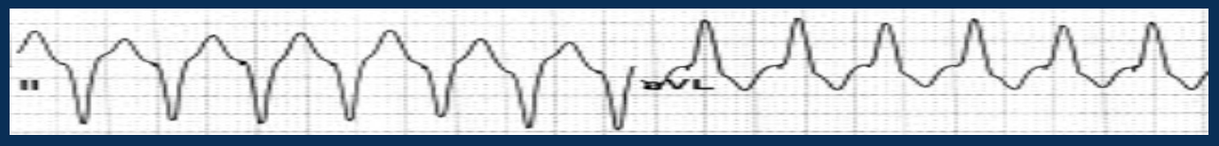
- **Underpacing** (Bradycardia or asystole)- EMI interpreted as R wave (VENTRICULAR OVERSENSING) leading to pacing inhibition



- **Shock or anti-tachycardia pacing-** EMI is misinterpreted as tachyarrhythmia with inappropriate delivery of shock



- **Direct damage** and electric short leading to generator shut down
- **Loss of data** from Implantable loop recorder
- **Overpacing** (Tachycardia)- EMI is misinterpreted as atrial signals or stimulation of rate responsive feature



- **Power on reset** mode- ICD = maximal energy shocks and VVI pacing at 60-72 beats/minute. PM = VVI at 60-72 beats/minute
- **Total device failure** with no output in older devices

Perioperative Management and Planning

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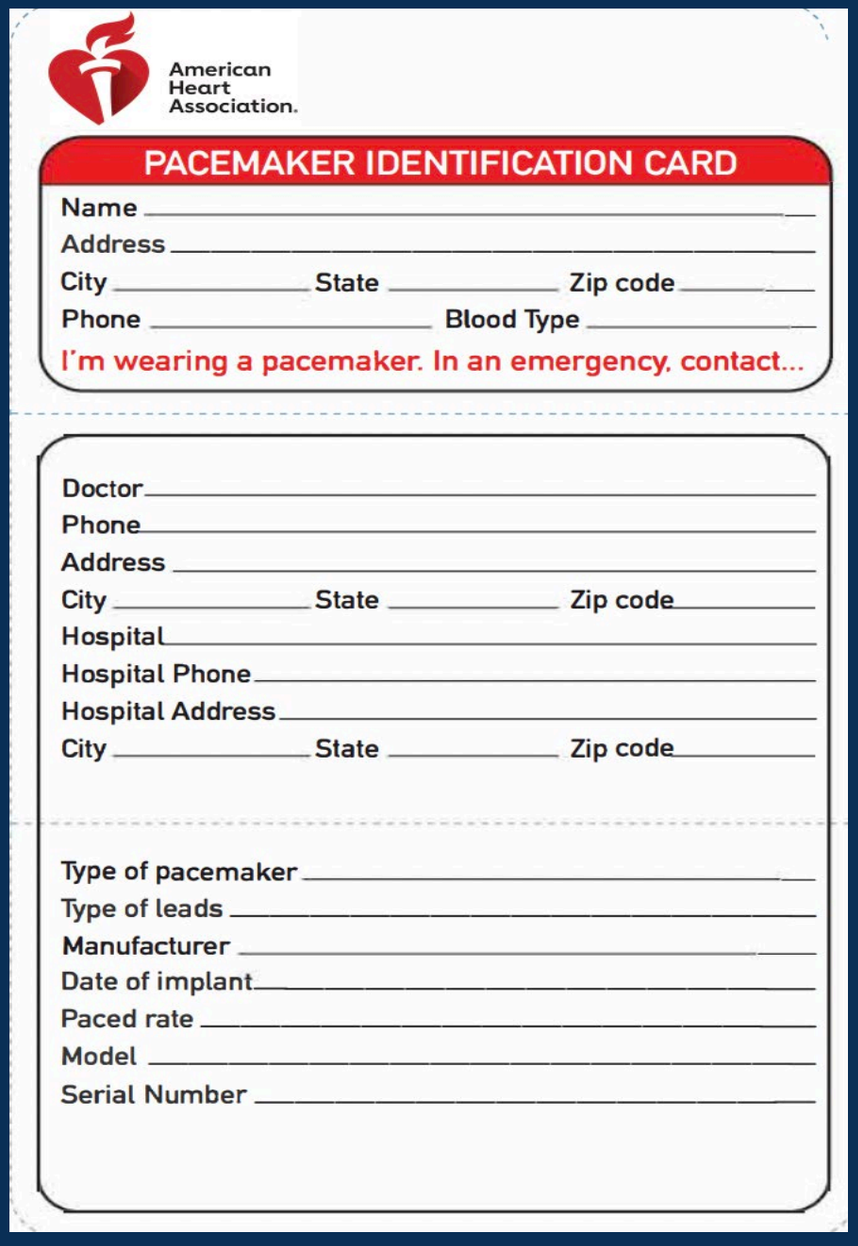
Preoperative Assessment

- Identify if a device is present
- Identify the device and indication for placement
- Is the surgery elective or an emergency?
- When was the CIED last interrogated? - settings, function and life
- Is the surgery above or below the umbilicus?
- Is the patient pacing-dependent?
- If PCM dependent or ICD- Reprogramming plan?

IDENTIFICATION



American Heart Association.

PACEMAKER IDENTIFICATION CARD

Name _____

Address _____

City _____ State _____ Zip code _____

Phone _____ Blood Type _____

I'm wearing a pacemaker. In an emergency, contact...

Doctor _____

Phone _____

Address _____

City _____ State _____ Zip code _____

Hospital _____

Hospital Phone _____

Hospital Address _____

City _____ State _____ Zip code _____

Type of pacemaker _____

Type of leads _____

Manufacturer _____

Date of implant _____

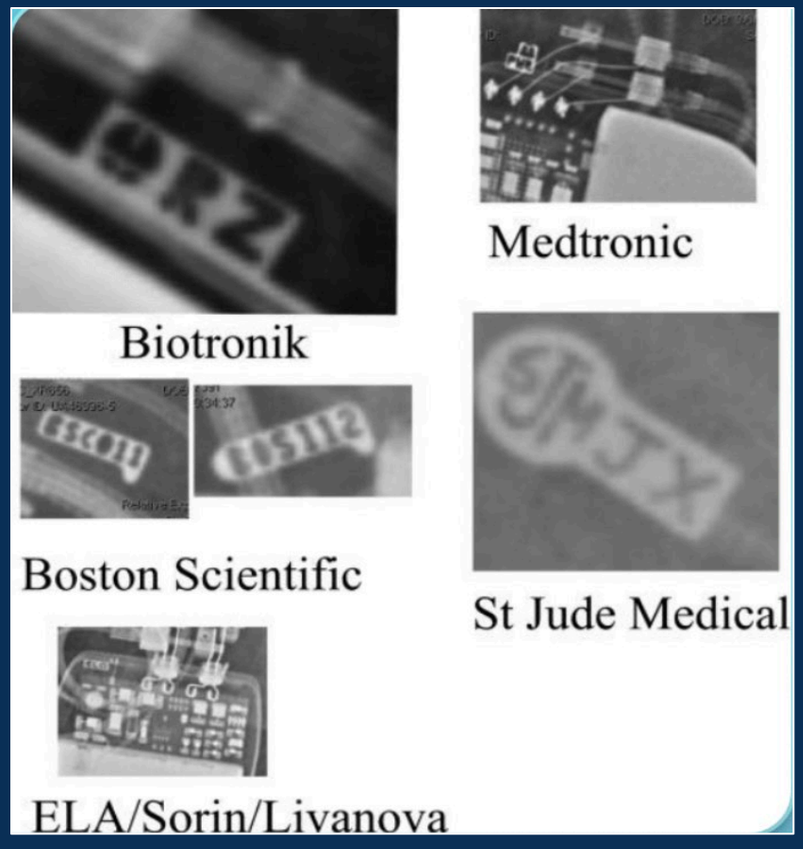
Paced rate _____

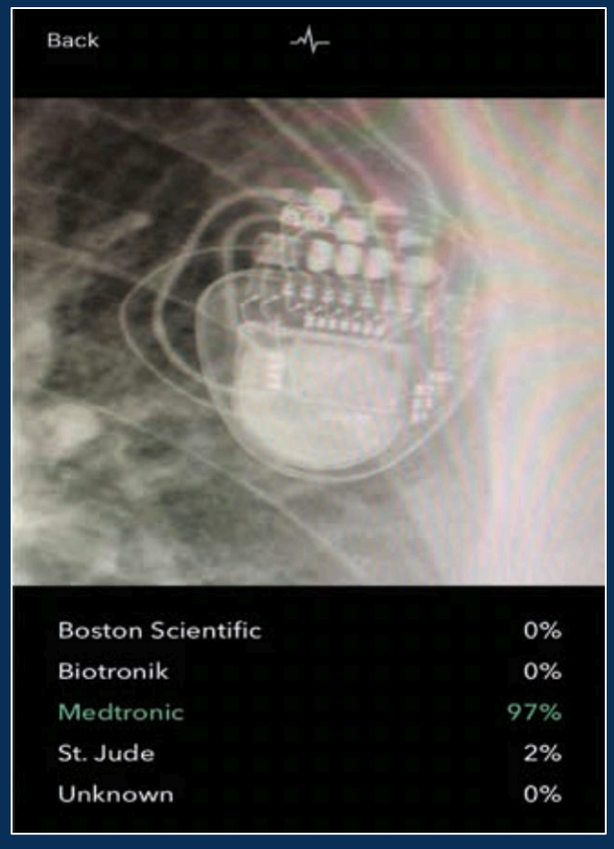
Model _____

Serial Number _____

Pulse generator company phone numbers

Biotronik	800-547-0394	Medtronic	800-505-4636
Boston Scientific	800-227-3422	St Jude Cardiac Rhythm Management	800-722-3774
ELA Medical Became (Sorin) Now LIVANOVA	877-663-7674		





Radiographic Identification
App: Pacemaker-ID

INTERROGATION OF CIED

ASA recommendation-

- 3 to 6 months for Pacemaker and ICD

Heart Rhythm Society-

- 6 months for ICD
- 1 year for Pacemaker

- Preoperative consultation with CIED care team if procedure is elective with prescription needed per HRS

SURGICAL SITE AND DISPERSION PAD

- Position the ESU and dispersive pad so the current pathway does not pass through or near the generator or leads
- Avoid proximity including waving of electrosurgery electrical field to generator and leads
- Use short, intermittent and irregular bursts of electrosurgery at the lowest feasible energy levels
- Use bipolar electrosurgery or an ultrasonic scalpel, if possible

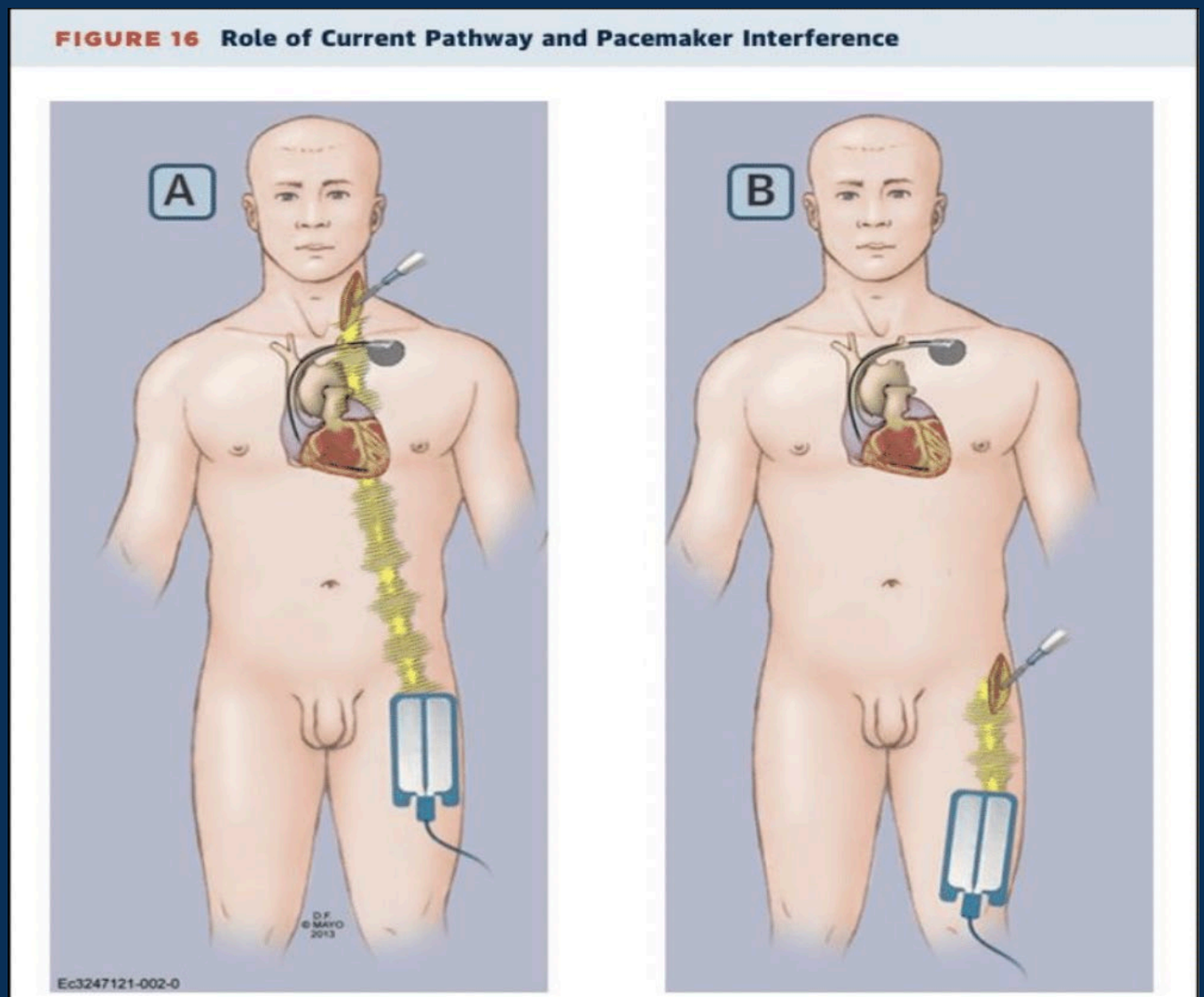


FIGURE 16 Role of Current Pathway and Pacemaker Interference

(A) High risk of interference: pre-operative reprogramming or magnet use required.
(B) Low risk of electromagnetic interference.

Mulpuru, S.K. et al. J Am Coll Cardiol. 2017;69(2):189-210.

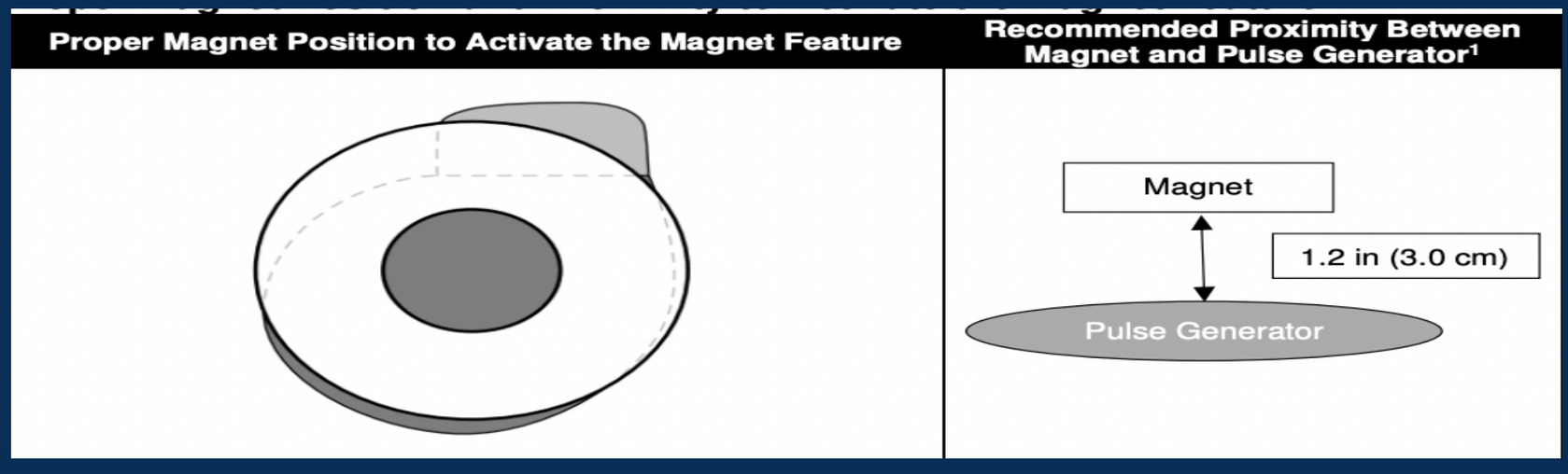
Pacemaker Dependent and/or ICD

Reprogramming Device or Magnet placement if near EMI

- Indication for pacemaker/ICD placement
- Types of device and underlying rhythm
- Devices response to magnet

ICD	•Suspends Antitachycardia therapy •** undesirable in pacer dependent patients**
Pacemaker	•Initiates asynchronous pacing with fixed AV delay •** Concern for R on T**

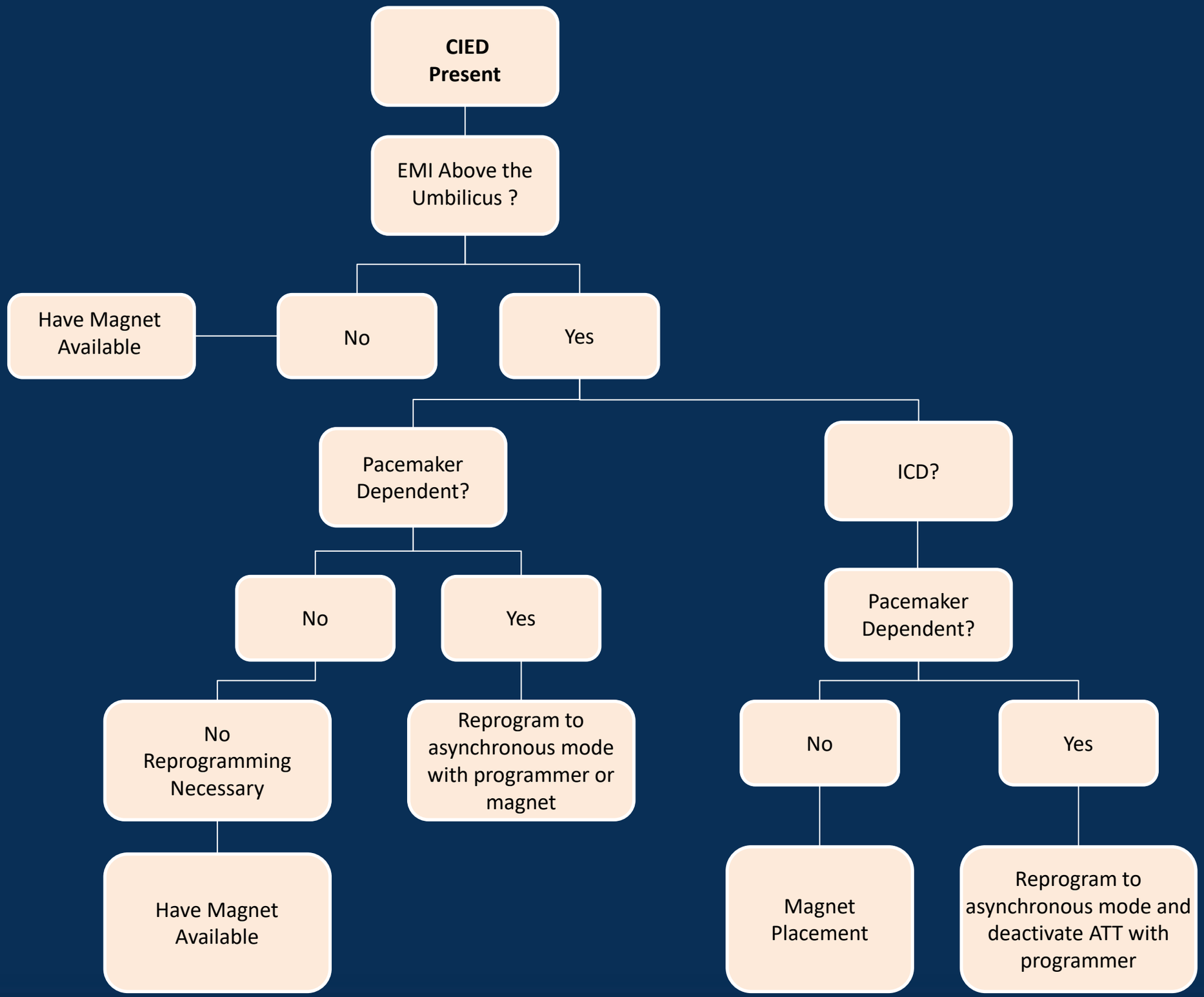
- Confirm response to magnet after placement
- Asynchronous mode with magnet
  DDD→ DOO VVI→VOO AAI→AOO



Magnet vs Reprogramming device

Magnet	Reprogramming Device
Relatively simple and placement can be confirmed easily	Needs expertise for reprogramming
Best use for emergency situations and no delay	Best used for elective situations or when in house electrophysiology staff is present
Pacer dependent ICDs and leadless pacemakers (Micra) cannot be reprogrammed	ICDs, CRT and leadless pacemakers can be programmed to prevent EMI
Biotronik, Boston Scientific and St Jude devices can have magnet function disabled	Devices can be checked and required settings can be appropriately set (15-20 bpm above native heart rate if pacer dependent)
Changes reversible immediately after magnet removal	Will need reprogramming again after EMI is removed
Apply only if access to magnet is adequate	Can be used if patient is prone or generator is inaccessible

***Patient must be monitored with EKG, pulse oximetry and transcutaneous pacing/defibrillation pads until the post operative reprogramming or magnet removal and confirmation of appropriate return of CIED function and hemodynamic stability


CIED Present
EMI Above the Umbilicus ?
Have Magnet Available
No
Yes
Pacemaker Dependent?
ICD?
No
Yes
Pacemaker Dependent?
No Reprogramming Necessary
Reprogram to asynchronous mode with programmer or magnet
No
Yes
Have Magnet Available
Magnet Placement
Reprogram to asynchronous mode and deactivate ATT with programmer

Response to Magnet

Medtronic

Boston Scientific

St Jude

- Boston Scientific: Transvenous= continuous beeping every second Subcutaneous= beeping 60 secs
- Medtronic: tone only upon initiation for 10 to 30 seconds
- St Jude: do not emit any sound

CIED Intraoperative Management when EMI is present

- Continuous electrocardiographic (ECG) and pulse oximetry or arterial pressure waveform monitoring.
- Preparation for the possibility of urgent cardioversion, defibrillation, or transcutaneous pacing especially when anti-tachycardia therapy is deactivated or pacer is in asynchronous mode.
- Always have defibrillation and pacing device readily available
- Do not place pads directly over CIED
- Place dispersive pad and nerve stimulators away from electrical path of CIED generator or leads
- May consider suspending ICD function during CVC guidewire insertion
- If intraoperative emergency arises ask the EMI to be stopped, remove magnet before cardioversion. If no resolution→ external cardioversion according to ACLS
- If unanticipated cardiac implantable electronic device interactions occur, temporarily suspend the procedure until the source of EMI can be identified and managed

Radiofrequency ablation

- Keep radiofrequency current path (electrode tip to current return pad) as far away from generator and leads as possible
- Avoid direct contact between ablation catheter and generator and leads

Lithotripsy

- Avoiding focus of lithotripsy beam near generator

Magnetic Resonance Imaging

- Is the MRI absolutely necessary and the only imaging modality that is available?
- Remove the patient from the MRI area when use of external defibrillator/monitor, programming system, or any other MRI unsafe equipment is required
- ? An individual capable of programming the CIED remain available during the MRI
- MRI-conditional CIEDs- interrogate prior to imaging, program to **MRI mode**, suspend ATT/ program to asynchronous mode, reinterrogate after and restore its permanent settings
- MRI nonconditional CIEDs- interrogate prior to imaging, if pacing dependent reprogram to asynchronous mode, suspend ATT/defibrillation if ICD, reinterrogate after and restory its permanent settings.

Radiofrequency Identification Devices

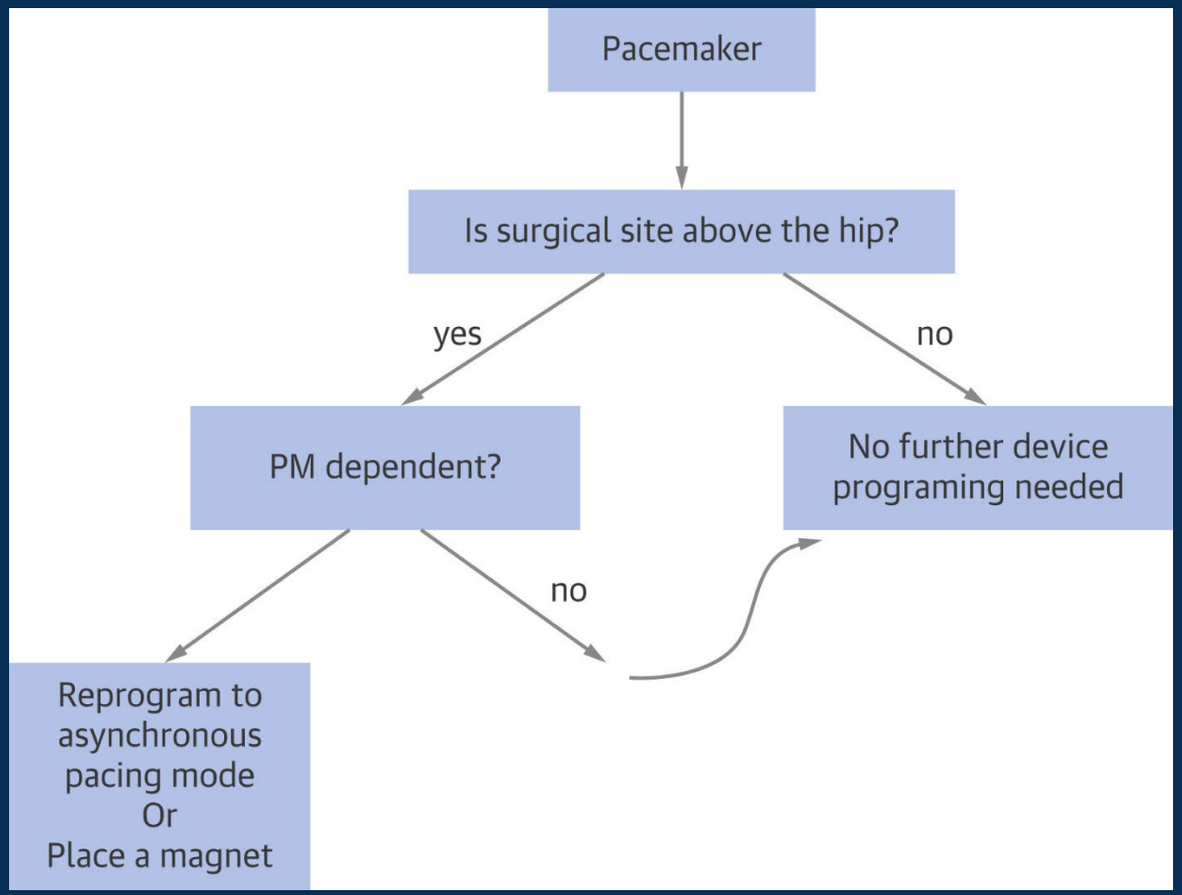
- Avoid use of these devices in close proximity to a CIED

Electroconvulsive Therapy

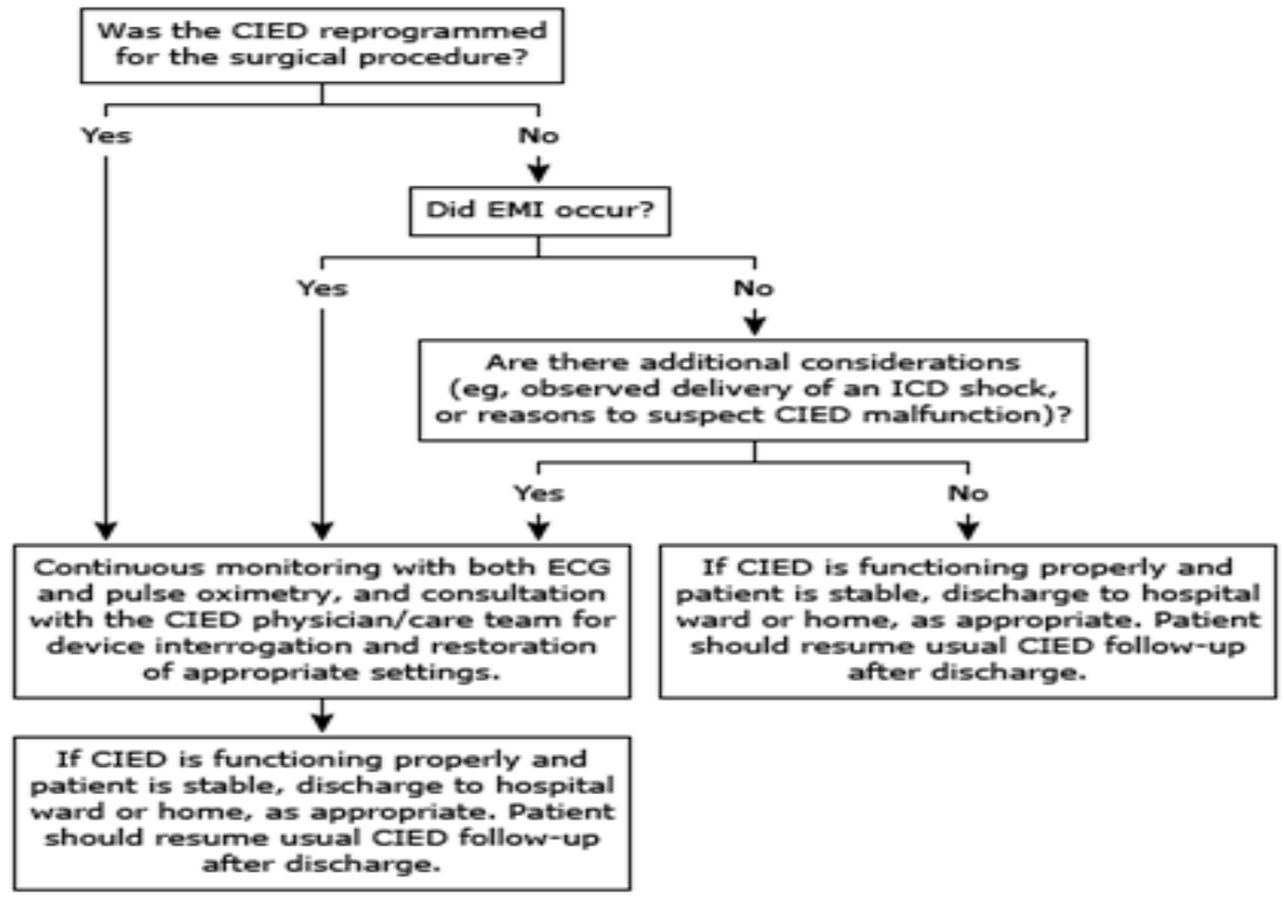
- Pacing dependent patients- asynchronous pacing, ICD- suspend ATT and defibrillation function
- Monitor for and be prepared to manage postconvulsive sinus tachycardia
- Monitor for and treat ventricular arrhythmias

EMERGENCY SURGERY

- Conduct a focused history and physical examination
- Review medical record and obtain most recent interrogation report if available
- Determine the type of CIED with manufacturer card or Chest Xray
- Obtain a 12 lead EKG
- Determine if patient is pacemaker dependent
- If EMI is to occur and surgical site is above umbilicus then develop a plan depending on the type of CIED (magnet vs reprogramming device vs temporary pacemaker)



Postoperative management of patients with a pacemaker or implantable cardioverter-defibrillator*



CIED: cardiac implantable electronic device; EMI: electromagnetic interference; PACU: post-anesthesia care unit; ICD: implantable cardioverter-defibrillator; ECG: electrocardiography.

* Refer to UpToDate topics addressing perioperative management of patients with a pacemaker or implantable cardioverter-defibrillator.

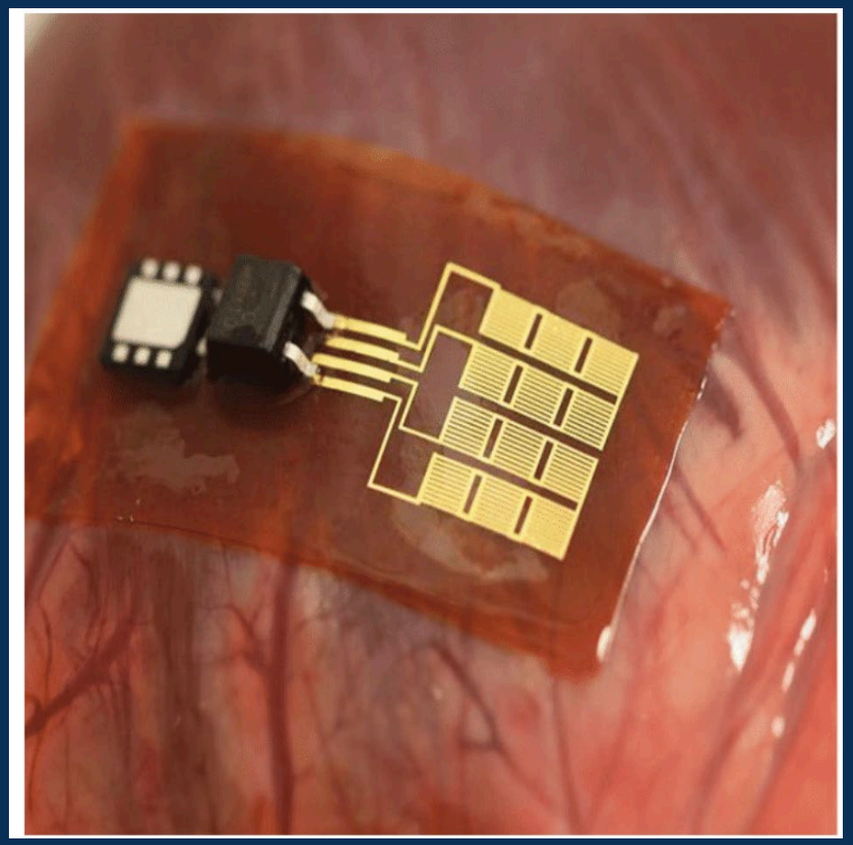
ASA advisory-

- Monitor EKG, pulse oximetry and blood pressure throughout the immediate postoperative period and until settings are restored
- If the device was reprogrammed- Ensure transcutaneous pacing and cardioversion equipment are available until device's appropriate settings are restored
- Interrogation may not be needed in low risk situations
- Interrogation is needed for – emergency surgery without appropriate preoperative evaluation, delivery of antitachycardia therapy was observed or suspected, concern of malfunction
- Check device within 30 days after surgery if not performed in the immediate post operative period

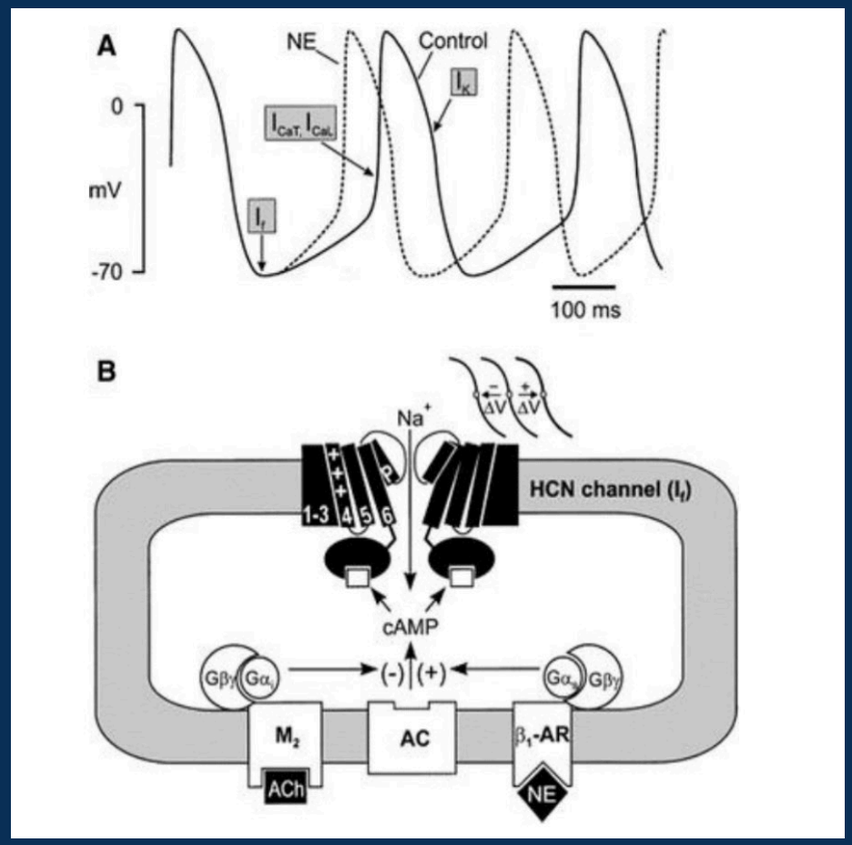
HRS advisory-

- For most cases involving EMI, interrogation can take place within one month
- For reprogrammed CIEDs, hemodynamically challenging cases, cardiothoracic surgery, RFA and external cardioversion, interrogate prior to transfer from cardiac telemetry

RECENT ADVANCES



Battery less pacing



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Questions??

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Thank You!

Focused Update on The Pre-Operative Management of Diabetes

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Disclosures

- I have no financial disclosures or conflicts of interest to declare.

Roadmap For Today

- Disease Background
- Update on Pre-Op Testing/Surveillance
- Update on Pre-Op Medication Management
- Parting Thoughts

60yo male, BMI 42, who presents to the PAT clinic prior to undergoing an elective FESS.

- Med Hx: T2DM, obesity, OSA, HTN, and CAD (PCI 2013, no symptoms).
- > 4 METS, doesn't smoke/drink, and no anesthetic complications in the past.
- Meds: Amlodipine, prandial Aspart, 50 units Glargine BID, Carvedilol, and 81mg ASA.
- The remainder of his pre-op is uneventful. Labs are uneventful, outside of HgBA1C of 7.8.

A little history…

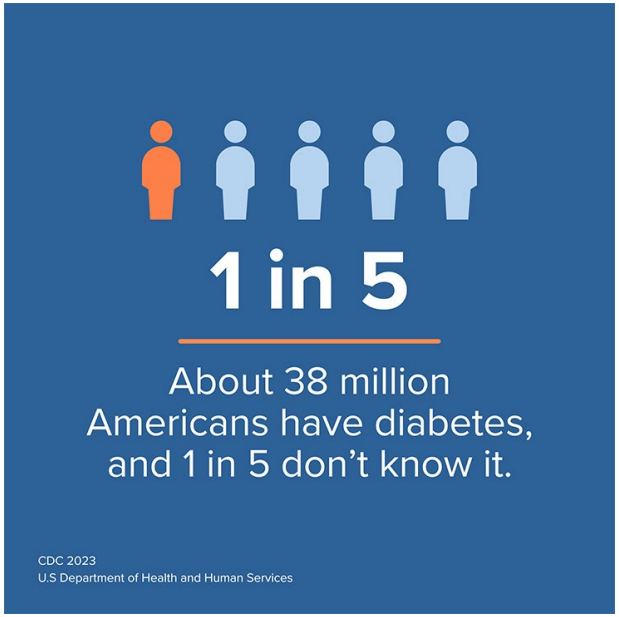
- 2nd Century AD: Aretaeus of Cappadocia:
  - Coined the term diabetes.
    - Greek for “siphon” or “to pass through.”
  - Noted in Greek, Chinese, and Egyptian literature.
- 1600s: Thomas Willis
  - Added the term “mellitus.”
    - From Greek work for “honey” or “sweet.”
- 1889: Minkowski and von Mering
  - Proved the pancreas was integral in the disease process.
- 1921: Banting and Best
  - Isolated insulin from pancreatic islet cells to treat Type 1 DM.

Current Definition/Diagnosis

- W.H.O. Definition:
  - A chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves.
  - Type 1 DM: Young/adolescents, relative lack of insulin
  - Type 2 DM: Middle aged adults with concomitant disease, relative insulin resistance.
- Diagnosis:
  - Laboratory Exam:
    - DM: HgB A1C > 6.5
    - Pre-DM 5.7-6.4
    - RBS> 126
    - 2 Hr OGTT > 200

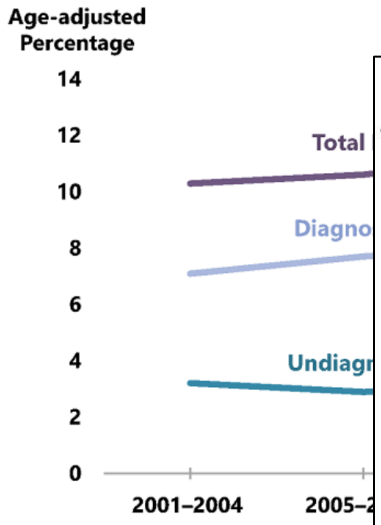
How common is DM in the US?

- As of 2021:
  - 38.4mil (11.6%) Americans of all ages have the dx of diabetes.
  - 38.1mil of those were adults over the age of 18.
  - ~23% of adults over 18 are undiagnosed.
- With age comes…diabetes.
  - ~30% of adults over the age of 65 had the dx of DM.
- 97.6mil people over 18yo have pre-diabetes.
- 1.2 mil new dx of diabetes/year.



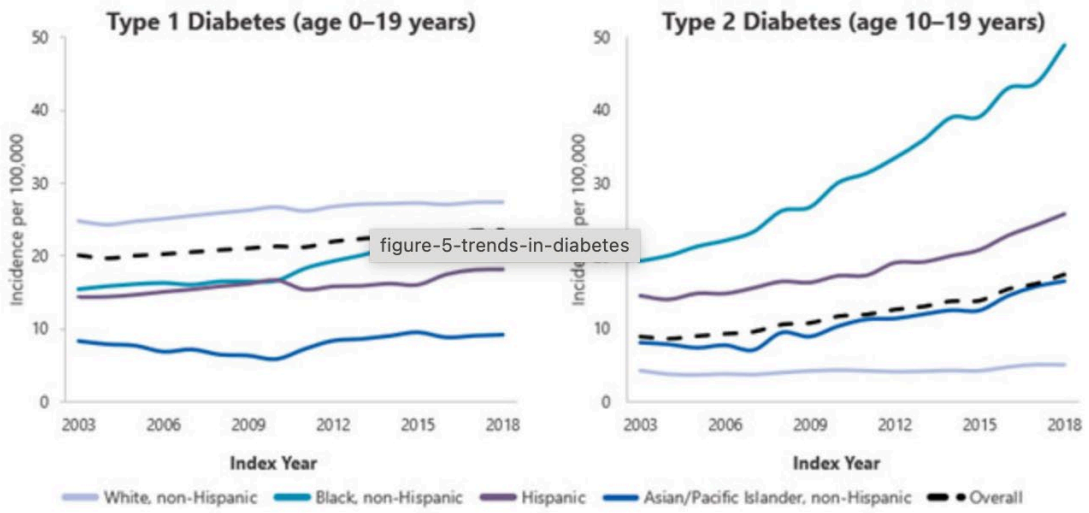
It doesn't seem to be going anywhere!

Figure 1. Trends in age-adjusted prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 2001–2020



Notes: Diagnosed diabetes was based on self-r
A1C levels among people self-reporting no diab
only.
Data sources: 2001–March 2020 National Healt

Figure 5. Trends in incidence of type 1 and type 2 diabetes in children and adolescents, overall and by race and ethnicity, 2002–2018



Note: Adapted from Wagenknecht LE et al.[1] Data are model-adjusted incidence estimates (see Appendix B: Detailed Methods and Data Sources).
Data source: SEARCH for Diabetes in Youth study.

Why isn't it getting any better?

- Poor diet, lack of access to quality food, lack of education, and lack of free time.
- Concomitant disease and behaviors make DM more likely:
  - Smoking:
    - 22% are smokers, 36% were former smokers.
  - Obesity:
    - 90% of those surveyed with DM were obese (BMI greater than 25)
    - 74% had a BMI between 25-40.
  - Decrease in physical activity
    - 32% reported low physical activity.

DM care is expensive!!

- The total estimated costs of diagnosed diabetes in the United States in 2022 was $413 billion.
  - Total direct estimated costs of diagnosed diabetes increased from $227 billion in 2012 to $307 billion in 2022 (2022 dollars).
  - Total indirect costs increased from $89 billion to $106 billion in the same period (2022 dollars).
- From 2012 to 2022, excess medical costs per person associated with diabetes increased from $10,179 to $12,022 (2022 dollars).

Diabetes is common perioperatively!

CLINICAL PRACTICE

Diabetes mellitus and perioperative outcomes: a scoping review of the literature

Daniel J. Drayton[1,*], Rebecca J. Birch[2], Carlota D'Souza-Ferrer[2], Michael Ayres[1], Simon J. Howell[1] and Ramzi A. Ajjan[3]

[1]Leeds Institute of Medical Research, University of Leeds, UK, [2]Leeds Institute for Data Analytics, University of Leeds, UK and [3]Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, UK

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- Estimated 15% of surgical patients will carry the DM (Type 1 or 2) diagnosis.
- ~ 50% of diabetic patients will require surgical procedure in their lifetime.
- As well, in multiple studies, DM carries an increased risk of peri-operative complications: such as infection, increased length of stay, etc…

Diabetes impacts surgical outcomes!

The Impact of Diabetes on Morbidity and Mortality Following Thyroidectomy

Roshan V. Patel, BS; Avneet Randhawa, BS; Karandeep S. Randhawa, BS; Owais M. Aftab, BS; Imran M. Khawaja, BA; Michael Hegazin, DO; Jean Anderson Eloy, MD, FACS, FARS; Christina H. Fang, MD

Laryngoscope, 133:3628–3632, 2023

- Retrospective cohort of pts w/w/o DM diagnosis using NSQUIP database.
- Total of ~51k pts,
- ~4300 of which were DM undergoing thyroidectomy.
- Findings:
  - Increased risk of adverse post-operative outcomes:
    - AKI, poor wound closure, and increased LOS.

TABLE III.
Chi-square Analysis of Adverse Outcomes in Non-DM versus DM Thyroidectomy Patients.

	Non-DM (%)	DM (%)	*p*-Value
Ventilation >48 h	N/A	N/A	N/A
Progressive renal insufficiency	0.0	0.0	0.376
Intraoperative/postoperative transfusions	0.1	0.6	**<0.001**
Stroke/cardiovascular accident	0.0	0.1	**0.024**
Cardiac arrest requiring CPR	0.1	0.4	**<0.001**
Myocardial infarction	0.1	0.3	**0.007**
Superficial incisional SSI	0.4	0.2	0.201
Organ/space SSI	0.1	0.2	**0.015**
Urinary tract infection	0.2	0.8	**<0.001**
Septic shock	0.0	0.1	0.118
Sepsis	0.1	0.5	**<0.001**
Pneumonia	0.2	0.8	**<0.001**
Wound disruption	0.0	0.2	**0.007**
Pulmonary embolism	0.1	0.1	0.389
Acute renal failure	0.0	0.2	**<0.001**
Deep incisional SSI	0.1	0.2	0.103
Unplanned intubation	0.3	1.0	**<0.001**
DVT requiring therapy	0.1	0.0	1.000
Any surgical complication	0.6	1.2	**0.003**
Any medical complication	0.9	2.8	**<0.001**
Any complication	1.4	3.5	**<0.001**
Death	0.1	0.5	**<0.001**
Extended LOS	12.3	19.4	**<0.001**
Extended operation time	9.9	11.4	**0.019**
Unplanned reoperation	1.2	2.0	**<0.001**
Unplanned readmission	2.3	4.5	**<0.001**

Note: Bold value signifies *p*-values.
CPR = cardiopulmonary resuscitation; DM = diabetes mellitus; DVT = deep vein thrombosis; LOS = length of stay; SSI = surgical site infection.

TABLE IV.
Binary Logistic Regression Analysis of Adverse Outcomes in Diabetes Mellitus (DM) versus Non-DM Thyroidectomy Patients.

Outcome	Odds Ratio	95% Confidence Interval	*p*-Value
Acute renal failure	5.836	1.060–32.134	**0.043**
Wound disruption occurrences	6.194	1.752–21.900	**0.005**
Unplanned readmission	1.380	1.096–1.737	**0.006**
Superficial incisional surgical Site infection	0.240	0.058–0.995	**0.049**
Urinary tract infection	2.173	1.186–3.980	**0.012**
Occurrences			
Organ space surgical site	3.322	1.016–10.864	**0.047**
Infection occurrences			
Pneumonia occurrences	2.091	1.125–3.884	**0.020**
Any medical complication	1.697	1.246–2.313	**0.001**
Any complication	1.495	1.136–1.968	**0.004**
Mortality	1.429	0.589–3.469	0.430

Note: Bold value signifies *p*-values.
LOS = length of stay.

Postoperative Morbidity and Mortality in Diabetic Patients After Fast-Track Hip and Knee Arthroplasty: A Prospective Follow-up Cohort of 36,762 Procedures

Milla Ortved, MD,* Pelle B. Petersen, MD, PhD,* Christoffer C. Jørgensen, MD,*† and Henrik Kehlet, PhD,*† on behalf of the Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement Collaborative Group

July 2021 • Volume 133 • Number 1

- Multicenter prospective of 37k non-diabetics, diabetics on insulin, and diabetics on oral meds.
- Primarily looking at length of stay and other complications.
- Findings:
  - Pts with pharmacologically treated DM were at increased odds for LOS >4.
  - While rates were low, DM pts were also at increased odds of other complications.

What can we do as anesthesiologists to help patients with DM?

- Offer yet another pre-operative touch point for patients.
- Leverage the pre-operative process to achieve optimal glucose management.
  - Testing/Surveillance
  - Medication Management
  - Collaboration

58yo male, BMI 42, who presents to the PAT clinic prior to undergoing an elective UPP.

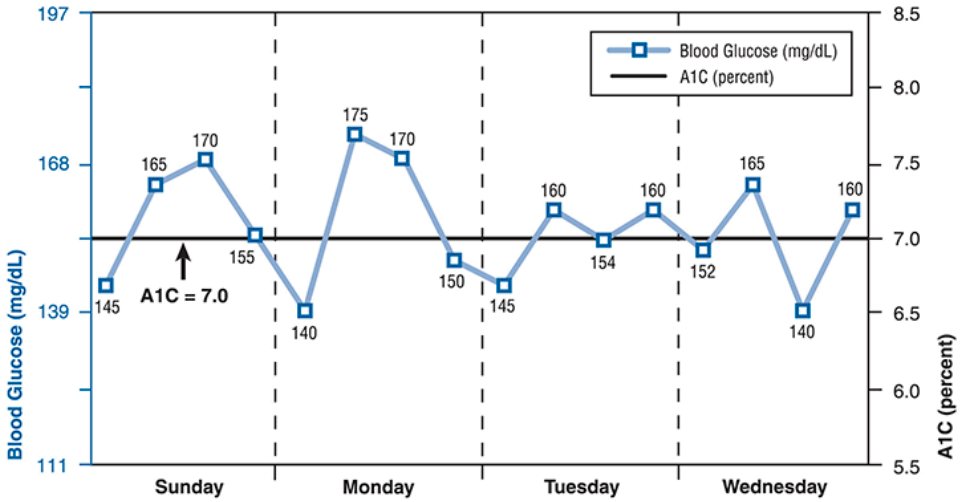
- Med Hx: DM2, obesity, HTN, and gout.
- Social Hx: He achieves > 4 METS, doesn't smoke/drink, and has no anesthetic history that he knows of.
- Meds: amlodipine, carvedilol, aspart with meals, 60 units glargine qhs, and semaglutide qday.

His pre-op is uneventful, but you notice his Hgb A1C is 7.2. He states that his most blood sugars over the last 2 wks have been 130-140, so he isn't sure why his A1C is still high.

A closer look at Hemglobin A1C

- Routine test for the presence of DM or Pre-DM.
- 3mo avg of the level of glycosylated HgB.
  - Note: Accuracy falls in anemia
- Pre-DM → 5.7% DM →6.5%.
  - WHO: Hgb A1C of >7% is considered to have uncontrolled DM.

Caution needs to be used, as it is only an average.



Source: https://www.niddk.nih.gov/health-information/diagnostic-tests/a1c-test

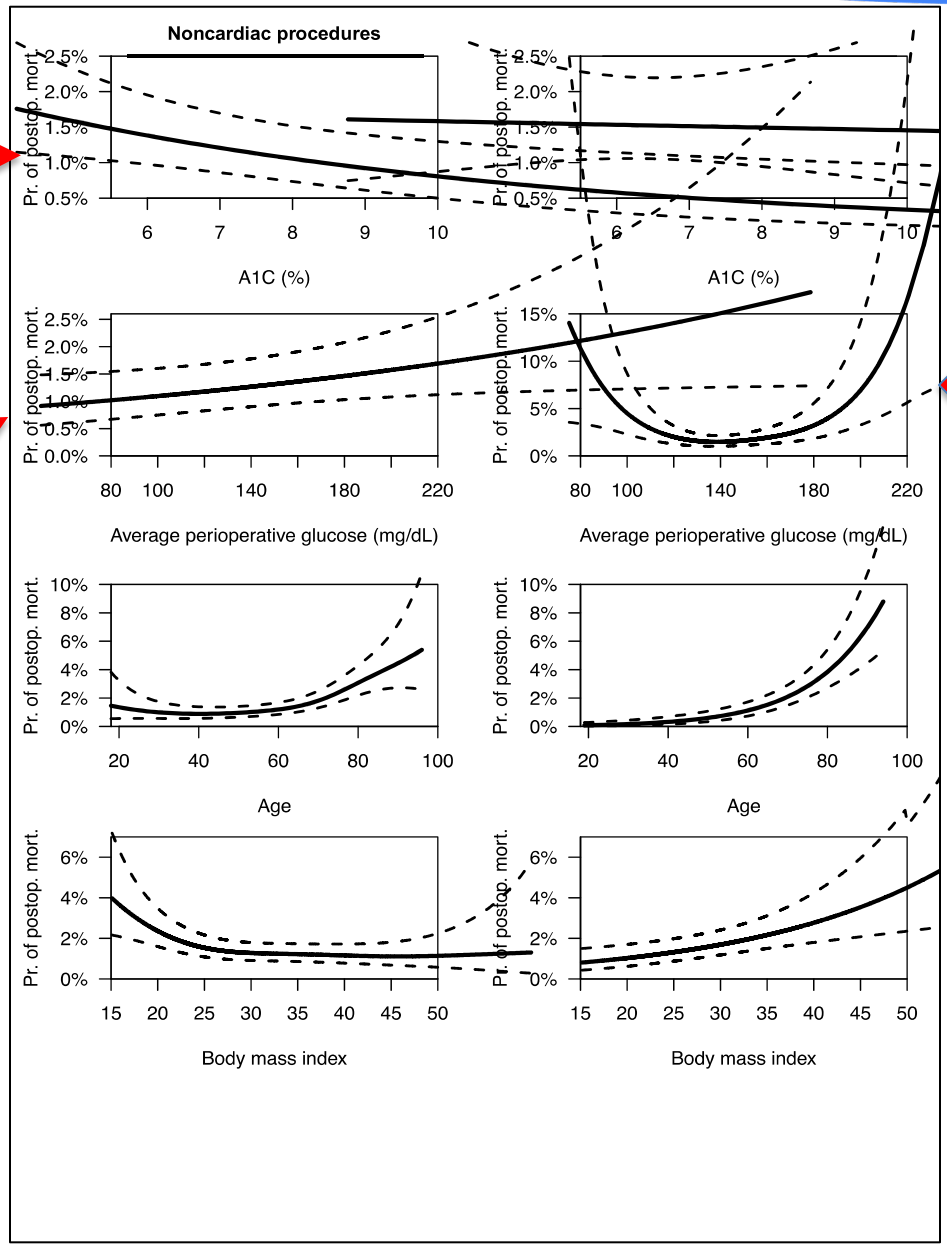
Effect of A1C and Glucose on Postoperative Mortality in Noncardiac and Cardiac Surgeries

Diabetes Care 2018;41:782–788 | https://doi.org/10.2337/dc17-2232

- Retrospective review of >400,000pts at Duke University Health.
- ~6600 non-cardiac pts and ~6400 cardiac surgery patients.
- Elevated A1C predicts a pre-operative glucose level, but…
  - No association between elevated A1C and post-operative M/M in non-cardiac surgical patients.
  - Perioperative glucose had correlation to 30d mortality, but not A1C.
  - Small signal for A1C in cardiac patients, but statistically insignificant.
- Overall:
  - A1C is not a predictor of post-operative complications and outcomes.

Negative correlation between A1C and post-op mortaility.

Positive correlation between peri-op hypergylcemia and post-op mortality.



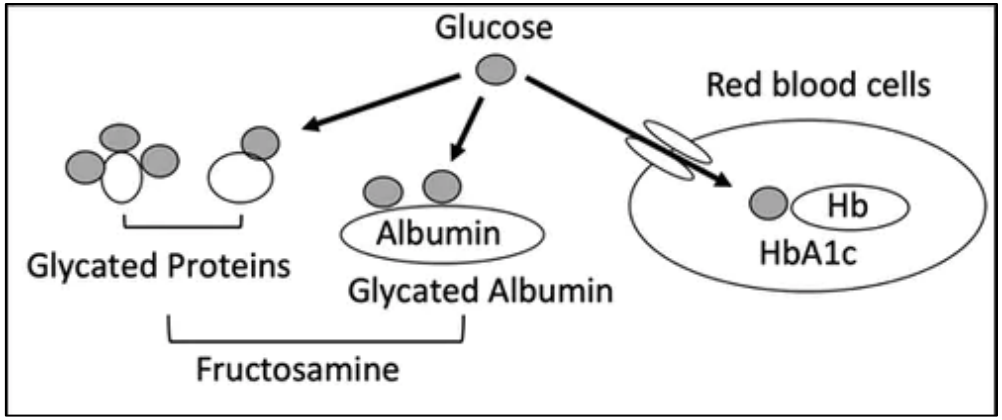
U-Shaped curve in cardiac patients showing tight control affords no benefit.

(Re) Enter Fructosamine

- Fructosamine:
  - Measures level of glycated proteins, primarily albumin.
  - Reflects a 2-3wk time period of control.
  - Caveats:
    - Can be inaccurate in patients with low albumin.
    - Send-out lab in some institutions.

Glucose (mg/dl)	A1c (%)	Fructosamine (µmol)
90	5	212.5
120	6	250
150	7	287.5
180	8	325
210	9	362.5
240	10	400
270	11	437.5
300	12	475
330	13	512.5
360	14	550
390	15	587.5

Source: https://www.preopevalguide.com/diabetes-mellitus



Multicenter Study > Bone Joint J. 2019 Jul;101-B(7_Supple_C):3-9.
doi: 10.1302/0301-620X.101B7.BJJ-2018-1418.R1.

2019 John Insall Award: Fructosamine is a better glycaemic marker compared with glycated haemoglobin (HbA1C) in predicting adverse outcomes following total knee arthroplasty: a prospective multicentre study

N Shohat [1 2], M Tarabichi [1], T L Tan [1], K Goswami [1], M Kheir [1], A L Malkani [3], R P Shah [4], Ran Schwarzkopf [5], J Parvizi [1]

- Prospective multicenter look at 1200 joint surgery patients
- Findings:
  - Positive correlation between fructosamine >293 and M/M, but no such signal in the A1C group
  - Pts with elevated fructosamine were:
    - 11.5x more likely to develop infection.
    - 4 and 4.5 times more likely to be re-operated on or re-admitted.

Variable	PJI		Re-admission		Re-operation	
	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Preoperative fructosamine (≥ 293)	16.26 (4.1 to 64.4)	< 0.001*	4.62 (1.78 to 11.93)	0.01*	4.37 (1.36 to 14.02)	0.03*
Operative time (mins)	1.02 (1.0 to 1.03)	0.13	1.01 (1.00 to 1.02)	0.17	1.01 (1.00 to 1.03)	0.14
Length of stay (days)	1.52 (1.03 to 2.25)	0.03*	1.29 (1.02 to 1.63)	0.04*	1.37 (1.06 to 1.77)	0.01*
Body mass index (kg/m²)	0.95 (0.84 to 1.08)	0.43	1.01 (0.95 to 1.08)	0.68	0.98 (0.90 to 1.06)	0.65
Elixhauser comorbidity index	0.67 (0.35 to 1.27)	0.22	0.95 (0.69 to 1.29)	0.74	1.01 (0.71 to 1.44)	0.95
ASA grade	1.25 (0.41 to 3.80)	0.69	1.07 (0.57 to 2.0)	0.83	1.86 (0.84 to 4.11)	0.13

*Statistically significant
OR, odds ratio; CI, confidence interval; ASA, American Society of Anesthesiologists

Table III. Adverse outcomes in patients with high and low fructosamine and glycated haemoglobin (HbA1c) levels

Outcome	Fructosamine			HbA1c								
	Low < 293 µmol/l (n = 1059)	High ≥ 293 µmol/l (n = 60)	p-value*	Low < 5.9% (n = 699)	High ≥ 5.9% (n = 420)	p-value*	Low < 7% (n = 1050)	High ≥ 7% (n = 69)	p-value*	Low < 7.5% (n = 1080)	High ≥ 7.5% (n = 39)	p-value*
Prosthetic joint infection, n (%)	6 (*0.6*)	4 (*6.7*)	0.001†	4 (*0.6*)	6 (*1.4*)	0.2	8 (*0.8*)	2 (*2.9*)	0.1	10 (*0.9*)	0 (*0.0*)	1.0
Wound complication, n (%)	8 (*0.8*)	0 (*0.0*)	1.0	5 (*0.7*)	3 (*0.7*)	1.0	8 (*0.8*)	0 (*0.0*)	1.0	8 (*0.7*)	0 (*0.0*)	1.0
Re-admission, n (%)	25 (*2.4*)	6 (*10.0*)	0.005†	17 (*2.4*)	14 (*3.3*)	0.45	27 (*2.6*)	4 (*5.8*)	0.1	31 (*2.9*)	0 (*0.0*)	0.6
Re-operation, n (%)	16 (*1.5*)	4 (*6.7*)	0.02†	10 (*1.4*)	10 (*2.4*)	0.25	18 (*1.7*)	2 (*2.9*)	0.4	20 (*1.9*)	0 (*0.0*)	1.0
Mortality, n (%)	1 (*0.1*)	1 (*1.7*)	0.1	1 (*0.1*)	1 (*0.2*)	1.0	2 (*0.2*)	0 (*0.0*)	1.0	2 (*0.2*)	0 (*0.0*)	1.0

*Fisher's exact test
†Statistically significant

Shohat Th

Published online 2021 Jan 26. doi: 10.1038/s41598-021-81803-6 PMID: 33500515

Fructosamine is a valuable marker for glycemic control and predicting adverse outcomes following total hip arthroplasty: a prospective multi-institutional investigation

Noam Shohat,[1,2] Karan Goswami,[1] Leigham Breckenridge,[1] Michael B. Held,[3] Arthur L. Malkani,[4] Roshan P. Shah,[3] Ran Schwarzkopf,[5] and Javad Parvizi[1]

- Prospective multi-center study of 1220 pts over one year.
- Primary Outcome: Presence of joint infections.
- Secondary Outcome: Superficial infections, readmissions, and death.
- Findings:
  - Pts with fructosamine >293 were 6.7x more likely to suffer a peri-prosthetic joint infection.
  - When compared to non-DM patients, elevated risk of readmissions and death

Complications	Total cohort (n = 1212)			Fasting plasma glucose ≥ 100 mg/dL (n = 423)		
	Normal fructosamine (n = 1158)	High fructosamine (n = 54)	p value	Normal fructosamine (n = 391)	High fructosamine (n = 32)	p value
PJI	16 (1.4%)	5 (9.3%)	0.002	6 (1.5%)	4 (12.5%)	0.004
Wound complication	29 (2.5%)	2 (3.7%)	0.645	14 (3.6%)	2 (6.3%)	0.345
Readmission	51 (4.4%)	9 (16.7%)	0.001	16 (4.1%)	7 (21.9%)	0.001
Mortality	7 (0.6%)	2 (3.7%)	0.057	4 (1.0%)	1 (3.1%)	0.327

Table 2. Adverse outcomes in patients with high (≥ 293 µmol/L) and low (< 293 µmol/L) fructosamine levels in the entire cohort and in a subgroup who had glucose levels above 100 mg/dL. *PJI* periprosthetic joint infection.

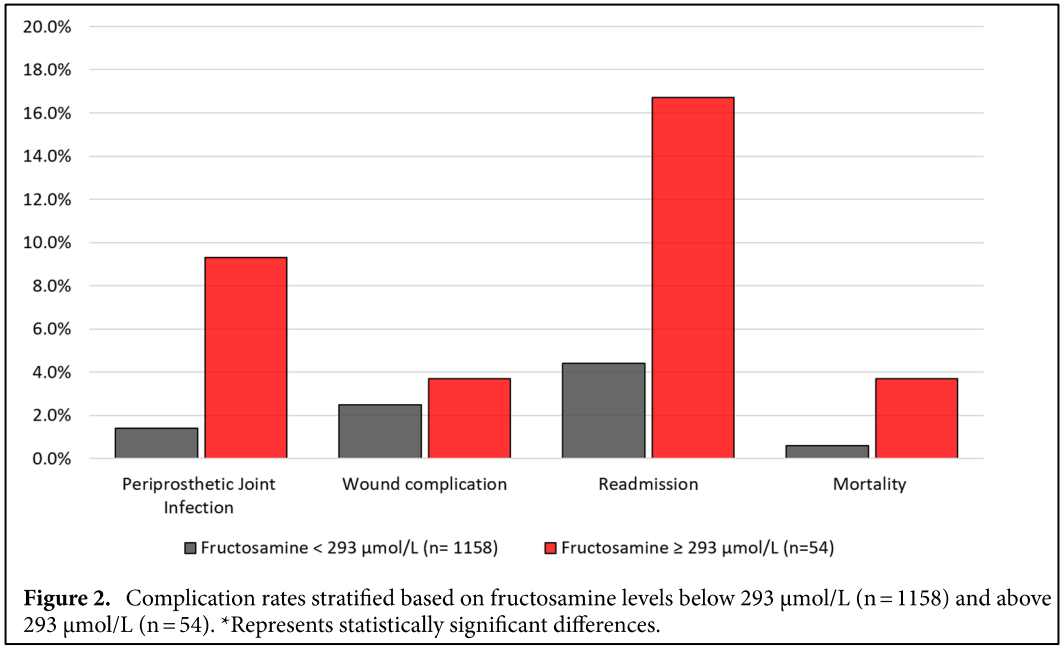


Figure 2. Complication rates stratified based on fructosamine levels below 293 µmol/L (n = 1158) and above 293 µmol/L (n = 54). *Represents statistically significant differences.

HgbA1C vs. Fructosamine

- HgBA1C:
  - little predictive value in relationship to perioperative outcomes.
  - Not good reflection of recent glycemic control.
- Fructosamine:
  - Good reflection of glycemic control over 2-3 weeks.
  - Idea of control closer to their surgical date, especially if changes have or will be made.
  - Time frame allows for return to the OR much sooner.

65yo female, BMI 33, who presents to PAT prior to an elective hernia repair.

- Med Hx: DM2, obesity, OSA, HTN, HLD, and CAD.
- Social Hx: > 4 METS, doesn't smoke/drink, no anesthetic issues.
- Meds: carvedilol, lisinopril, ASA 81mg, metformin, ertugliflozin, and Lantus 40u qhs.

The remainder of her pre-op is uneventful.

Medication Management in DM

Preoperative Management of Endocrine, Hormonal, and Urologic Medications: Society for Perioperative Assessment and Quality Improvement (SPAQI) Consensus Statement

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- Explosion of therapeutics both oral and injectables.
- Often prescribed in combinations.
- Some are easier to manage than others.
- Management is often a moving target.

Pre-op Insulin Management

TABLE 1. Summary of Recommendations for the Preoperative Management of Insulins

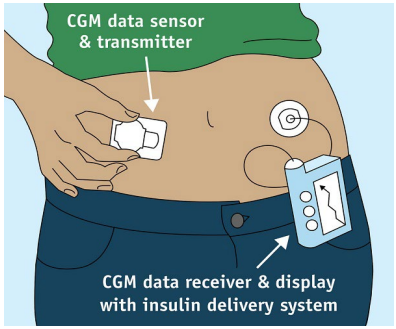
Medication class	Examples	Administration before day of surgery	Administration on morning of surgery	Additional Considerations
Insulin, intermediate-acting	NPH[a]	Continue[b]	Continue[b]	Decrease dose by 50% on morning of surgery and consider 25% dose reduction on evening before surgery
Insulin, long-acting	Glargine, detemir, degludec	Continue[b]	Continue[b]	Administer 60%-80% of usual dose the evening before surgery (or the morning of surgery, if normally taken in the morning) in those with type 2 diabetes and those prone to hypoglycemia
Insulin, premixed	Human NPH/regular 70/30; insulin lispro protamine/lispro 75/25	Continue	Continue[b]	If fasting hyperglycemia (>200 mg/dL), use half the usual dose of premixed insulin on the morning of surgery; otherwise, do not administer and give half the dose of the intermediate- or long-acting component as intermediate- or long-acting insulin
Insulin, pump		Continue	Continue[b]	Continue basal infusion at 60%-80% of usual rate and do not provide boluses
Insulin, short-/rapid-acting	Regular, aspart, lispro, glulisine	Continue	Hold	May use on the morning of surgery for urgent treatment of hyperglycemia
Insulin, U-500		Continue	Continue	Reduce dose on morning of surgery based on patient's blood glucose and risk factors for hypoglycemia

[a]NPH, neutral protamine Hagedorn.
[b]See additional considerations.

Source: https://www.mayoclinicproceedings.org/action/showPdf?pii=S0025-6196%2820%2931129-0

Pre-op Management of Insulin Pumps

- Acceptable to continue in the perioperative setting.
  - Basal rate at 60-80% of normal.
- Almost always short acting formulations.
- If the needle isn't in the surgical field, leave it on during the case.
- Get a primer on device fxn.



Oral DM Medications

- Secretagogues
  - Stimulate endogenous insulin secretion outside of meals.
- Biguanides
  - Suppress hepatic gluconeogenesis.
- Dipeptidyl peptidase-4 Inhibitors (DPP-4)
  - Decrease enzymatic breakdown of GLP-1 and increase insulin production.
  - Work only in the gut and with meals.
- Thiazolidinediones (TZDS)
  - Increase insulin sensitivity, and directly stimulate peripheral receptors to increase uptake of glucose
- Glucagon Like Peptide -1 Agonists (GLP-1)
  - Increase insulin production and suppress glucagon effects.
- Sodium Glucose Co-Transportor-2 Inhibition (SGLT-2)
  - Increase glucose excretion from the proximal convoluted tubules.

Pre-op Management of Oral Medications

TABLE 2. Summary of Recommendations for the Preoperative Management of Non-Insulin Diabetes Medications

Medication class	Examples	Administration before day of surgery	Administration on morning of surgery	Additional considerations
Alpha-glucosidase inhibitors	Acarbose, Miglitol	Continue	Hold	—
Biguanides	Metformin	Continue	Hold	In patients without contraindications and with preserved renal function (GFR[a] >50 mL/min) undergoing ambulatory surgeries for which no more than one meal is expected to be omitted, non-interruption may be acceptable.
DPP-4 inhibitors	Vildagliptin, sitagliptin, saxagliptin, linagliptin,	Continue	Hold	For patients undergoing ambulatory surgeries for which no more than one meal is expected to be omitted, non-
GLP-1 agonists	Liraglutide, lixisenatide, semaglutide, dulaglutide	Continue[b]	Hold	Before day of surgery: For GI surgeries or when concern for nausea, vomiting, or gut dysfunction, consider holding weekly dose within 7 days before surgery. Day of surgery: If weekly dose is due on morning of surgery, delay until later in day after surgery is complete
Insulin secretogogues (sulfonylureas, glinides)	Glipizide, glyburide, glimepiride, repaglinide, nateglinide	Continue	Hold	—
SGLT-2 inhibitors	Dapagliflozin, canagliflozin, empagliflozin, ertugliflozin	Hold	Hold	Canagliflozin, dapagliflozin, and empagliflozin should each be discontinued at least three days before scheduled surgery. Ertugliflozin should be discontinued at least four days before scheduled surgery.

[a]DPP-4, dipeptidyl peptidase-4; GFR, glomerular filtration rate; GLP-1, glucagon-like peptide-1; SGLT-2, sodium glucose co-transporter 2.
[b]See additional considerations.

Source: https://www.mayoclinicproceedings.org/action/showPdf?pii=S0025-6196%2820%2931129-0

What are SGLT-2 Agonists and why are they popular?

- Na/Glucose Co-Transporter Agonists that block reuptake of glucose (subsequently Na) in the proximal convoluted tubule.
- DECREASE A1C and daily RBS.
- Have nephro and cardioprotective properties.
  - Popular choice in DM w/atherosclerotic disease.
- Promote weight loss and decrease insulin use.

What is the problem with SGLT-2?

Study name	Age, years	Type of DM	Sex	SGLT-2 inhibitor	Blood analysis	Arterial blood gas	Basal metabolic panel	Renal function tests
Mistry and Eschler (2021) [12]	47	T2DM	Female	Empagliflozin	HbA1C: 13.6%	pH: 7.24. Serum bicarbonate: 11 mmol/L, β-hydroxybutyrate: 6.78 mmol/L	Plasma glucose: 187 mg/dL, anion gap: 22 mmol/L	Not reported
	34	T2DM	Male	Canagliflozin	HbA1C: 8.2%	pH: 7.27, serum bicarbonate: 12 mmol/L, β-hydroxybutyrate: 5 mmol/L	Serum glucose: 251 mg/dL, anion gap: 24 mmol/L	Not reported
Brown and McColl (2018) [13]	53	T2DM	Male	Dapagliflozin	WBC count: 12 × 10^3 µL	pH: 7.24, β-hydroxybutyrate: 6.2 mmol/L	Blood glucose: 162 mg/dL, lactate: 4.5 mmol/L, anion gap: 30	Not reported
Chou et al. (2018) [14]	61	T2DM	Female	Dapagliflozin	Not reported	pH: 6.986, CO_2: 20.9mmHg, serum bicarbonate: 7.0 mEq/L	Blood glucose: 180 mg/dL, blood ketones: 8.0 mmol/L, urine ketones: positive, serum lactate: 9.0 mg/dL, anion gap: 20 mEq/L	Blood urea nitrogen: 25mg/dL, serum creatinine: 0.8mg/dL
Diaz-Ramos et al. (2019) [15]	44	T2DM	Female	Canagliflozin	Not reported	pH: 7.27, PCO_2: 29 mm/Hg	Serum glucose: 163 mg/dL, serum bicarbonate: 14 mmol/L, anion gap: 18 mmol/L, urinary ketones: positive, serum acetone: positive	Not reported
Gajjar and Luthra (2019) [16]	28	T2DM	Female	Dapagliflozin	HbA1c: 10%	pH: 7.27, bicarbonate: 18 mmol/L, β-hydroxybutyrate: 5.29 mmol/L	Serum glucose: 111 mg/dL, anion gap: 20	Creatinine: 0.4 mg/dL
Lee and Ahn					WBC count: 11,800/µL, Hb: 13g/dL, platelet count:	pH: 6.904, pCO_2: 12.0 mmHg,	Serum glucose: 410 mg/dL, insulin, 3.3 µlU/mL, anion	Blood urea nitrogen:

Euglycemic Diabetic Ketoacidosis (eDKA)

- Diagnosed with widening anion gap and normoglycemia.
- Almost always in the setting of decreased insulin production.
  - Fasting for surgery, acute illness, inflammation, etc…
- Rates est. between .2-.6% per 1000 patients on these meds.
- 2X more likely to develop eDKA, than those on other DM meds.
- 73 cases noted by FDA between 2013-2015.

SGLT2 Inhibitor–Induced Euglycemic Diabetic Ketoacidosis: A Case Report

Katherine M. Wang and Robert T. Isom

- 40yo female underwent cerebral reperfusion procedure for Moya Moya dz.
- Post-op developed slurred speech.
- Found to have a left infarct, acidosis, 2+ urine glucose, and 4+ urine ketones.
- Stopped SGLT2 the day before her procedure.
- With the anion-gap and normal BS and SGLT-2 use immediately thought eDKA.
- Tx initiated to close the gap.

Table 1. Inpatient Laboratory Values

	Admission	POD0	POD1	POD2
Hematocrit, %	30.9		31.5	30.4
Sodium, mmol/L	139	140	138	136
Potassium, mmol/L	4.0	4.0	3.8	4.7
Chloride, mmol/L	102	111	107	112
Serum CO_2, mmol/L	27		14	<5
Urea nitrogen, mg/dL	18		8	17
Creatinine, mg/dL	0.57		0.42	0.48
Calcium, mg/dL	9.1		8.1	8.2
Albumin, g/dL				4.4
Glucose, mg/dL	146	133-164	149	160-167
Anion gap	10		17	27
pH		7.36	7.01	7.30
P_{CO_2}, mm Hg		38.2	11.5	12.3
Lactate, mmol/L			1.0	
β-hydroxybutyrate, mmol			7.7	3.5

Note: Conversion factors for units: creatinine in mg/dL to μmol/L, ×88.4; calcium in mg/dL to mmol/L, ×0.2495; lactate in mmol/L to mg/dL, ×9.01; glucose in mg/dL to mmol/L, ×0.05551; urea nitrogen in mg/dL to mmol/L, ×0.357.
Abbreviations: CO_2, carbon dioxide; POD, postoperative day.

CASE REPORT Open Access

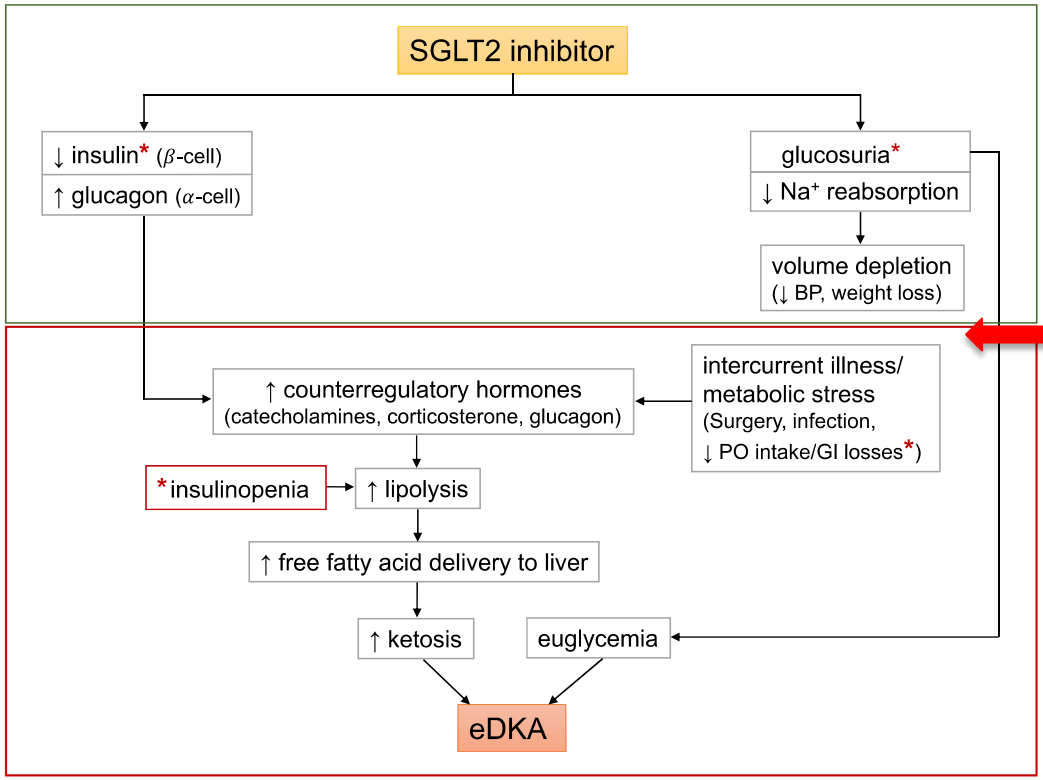
Euglycemic diabetic ketoacidosis induced by sodium-glucose cotransporter 2 inhibitor in the setting of prolonged fasting: a case report

- 51 year old male presented with 3 days of N/V, SOB, and abdominal pain.
- Med Hx of DM2 on metformin and dapagliflozin.
- Had been fasting 14+ hrs daily for 30 days during Ramadan.
- HAGMA with RBS of 243.
- eDKA noted and treated and patient released 4 days later.

Table 1 Metabolic panel

Labs	Reference range	ED	Day 1	Day 2
Random blood glucose	3.9–6.1 mmol/L (70.2–109.8 mg/dL)	13.5 (243)	6.4 115.2	9.2 165
Sodium	136–145 mmol/L	143	142	136
Potassium	3.4–5.1 mmol/L	4.4	3.7	3.6
Chloride	98–107 mmol/L	109	110	109
Venous blood gas				
pH		6.92	7.2	7.3
$PaCO_2$	35.0–45.0 mmHg	20.4	24.7	41.1
HCO_3	35.0–40.0 mmol/L	4	11	25
Anion gap	8–16 mEq/L	30	21	2
Serum lactate	0.5–2.2 mmol/L	2.50	0.7	0.6

Why this occurs?



Not just surgery!

Figure 1. Proposed role of sodium-glucose cotransporter 2 (SGLT2) inhibition in euglycemic diabetic ketoacidosis (eDKA). Classic DKA results from insulin deficiency (absolute or relative) and concurrent increase in counter-regulatory hormones leading to ketosis, hyperglycemia, and osmotic diuresis. In contrast, SGLT2 inhibitor therapy in a well-compensated individual at baseline causes glucosuria, mild volume depletion, and lower serum glucose levels, associated with decreased insulin secretion (green box). During times of intercurrent illness and/or metabolic stress (eg, surgery or gastrointestinal illness), decreased carbohydrate intake coupled with lower serum glucose levels can further depress insulin secretion. This can ultimately lead to eDKA (red box).*Possible pathways of carbohydrate deficiency and causes of insulinopenia. Abbreviations: BP, blood pressure; PO, oral.

Source: Katherine M. Wang, Robert T. Isom. SGLT2 Inhibitor–Induced Euglycemic Diabetic Ketoacidosis: A Case Report. Kidney Medicine, Volume 2, Issue 2, 2020, Pages 218-221, ISSN 2590-0595, https://doi.org/10.1016/j.xkme.2019.12.006.

- Bottom Line:
  - Stop these meds at least 3 days in advance.
  - Ertugliflozin needs to be stopped at least 4 days in advance of any surgical procedure.
- If not stopped DOS:
  - Hospital:
    - consider the surgery, the patient, and discuss, discuss, discuss.
  - Ambulatory setting:
    - consider rescheduling and delaying any non-urgent/emergent cases.

52yo female presents to pre-op holding for an elective THA in the hospital.

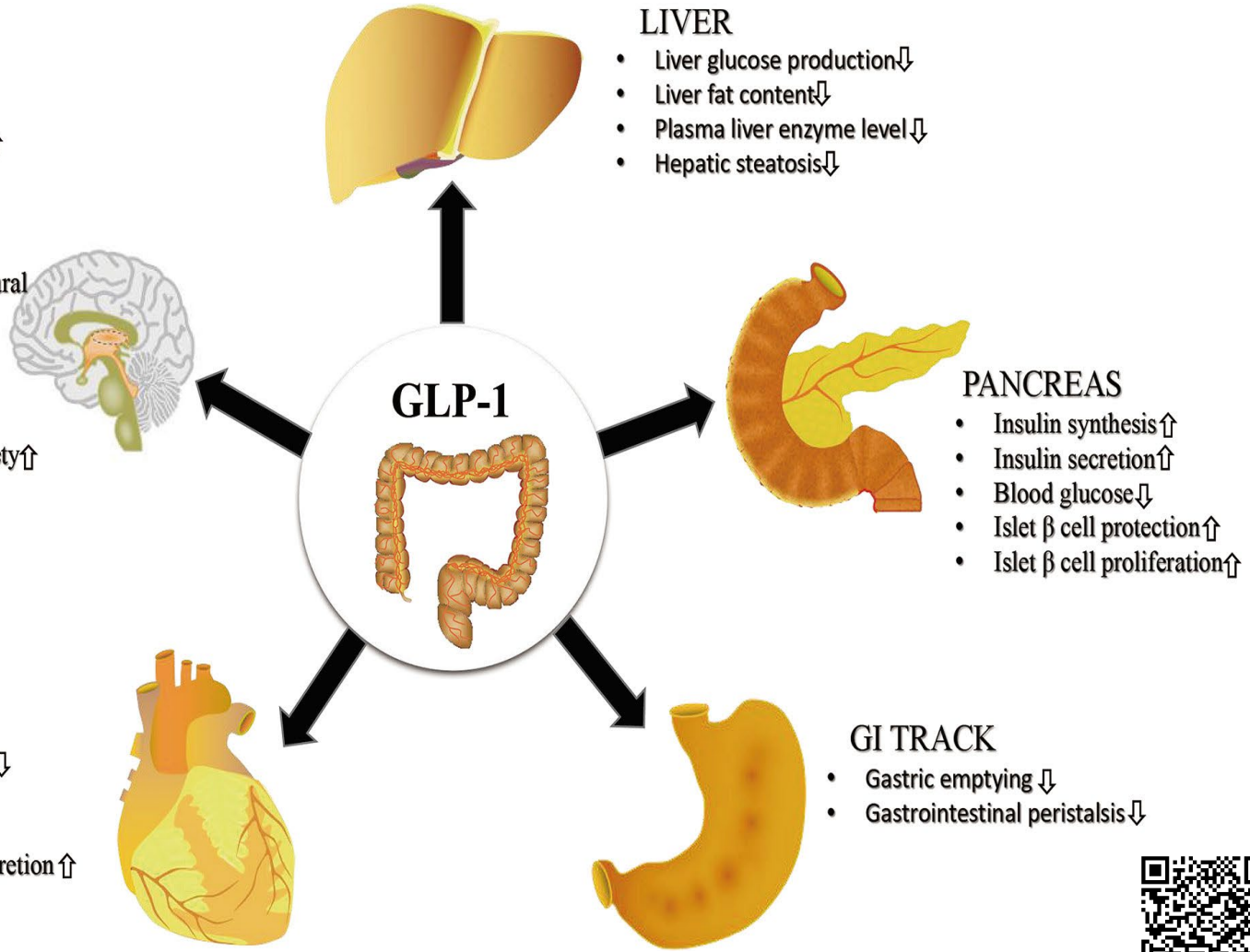
- Med Hx: DM2, obesity, OSA, HTN, and CAD.
- Meds: Took her metoprolol this a.m., stopped her Trulicity yesterday.
- Social Hx: Denies smoking/drinking, METS>4, no anesthetic complications in her hx.

She states that since beginning the Trulicity 2 mos ago, she has some early satiety, bloating, and off and on N/V, but nothing like that for at least the last 8hrs. She states that feels fine and hasn't had anything PO for 12hrs.

What are GLP-1 Receptor Agonists?

- Exogenous GLP-1 hormone that slows gastric emptying, increases insulin production/secretion, and decreases in glucagon production.
- Current Indications:
  - DM2: (Especially with concomitant CAD, obesity, and PVD):
    - liraglutide (Victoza), lixisenatide (Lyxumia), semaglutide (Ozempic, Rybelsus), and dulaglutide (Trulicity)
  - Weightloss:
    - semaglutide (Wegovy), liraglutide (Saxenda)

Why are they so popular?



CASE REPORTS / CASE SERIES

Regurgitation under anesthesia in a fasted patient prescribed semaglutide for weight loss: a case report

Emerging Anesthesia Risks with Semaglutide

Reed Fezza, MS; Brenton Rains, CRNA; Tyler Fezza, BS; John Paul Fezza, MD

Anesthesia Considerations for a Patient on Semaglutide and Delayed Gastric Emptying

Erina Fujino [1], Kathryn W. Cobb [1], Jay Schoenherr [1], Lindsey Gouker [1], Elisa Lund [1]

1. Anesthesiology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, USA

Why are they so problematic?

- GLP-1 hormone slows gastric emptying.
- Delayed gastric emptying theoretically predisposes patients to pulmonary aspiration.
- Not a lot of this in the literature.

Do all patients have this issue?

Journal of Clinical Anesthesia 87 (2023) 111091

- Retrospective observational study of 404 pts undergoing upper endoscopy, 33 of which were on GLP-1.
- 27 pts had residual gastric contents, 8 of them on GLP-1.
- Findings
  - There was a prevalence ratio (PR) of 5.15 for RGC in pts on GLP-1.
  - PR increased to 16.5 in presence of GI symptoms and GLP-1 use.
- Note: small study, underpowered, and doses and durations of medications were not reported.

REPORTS OF ORIGINAL INVESTIGATIONS

Influence of semaglutide use on the presence of residual gastric solids on gastric ultrasound: a prospective observational study in volunteers without obesity recently started on semaglutide

- Small prospective study of 20 adults
- 10 pts on semaglutide and 10 pts not taking the drug.
- Gastric ultrasound used to compare stomach contents in these groups after:
  - a standardized overnight fast of at least 10hrs.
  - 2hrs after ingestion of clear liquids.
- Findings:
  - Supine 70% of GLP1 pts had gastric contents vs 10% for the non-GLP group.
  - Lateral, 90% of GLP1 pts had gastric contents vs. 20% in the non-GLP1 group
  - No difference in liquid volumes at 2hrs post ingestion.
  - GLP1 medications could be associated with risk of RGC.

Hot off the presses…

EDITORIAL

Perioperative management of long-acting glucagon-like peptide-1 (GLP-1) receptor agonists: concerns for delayed gastric emptying and pulmonary aspiration

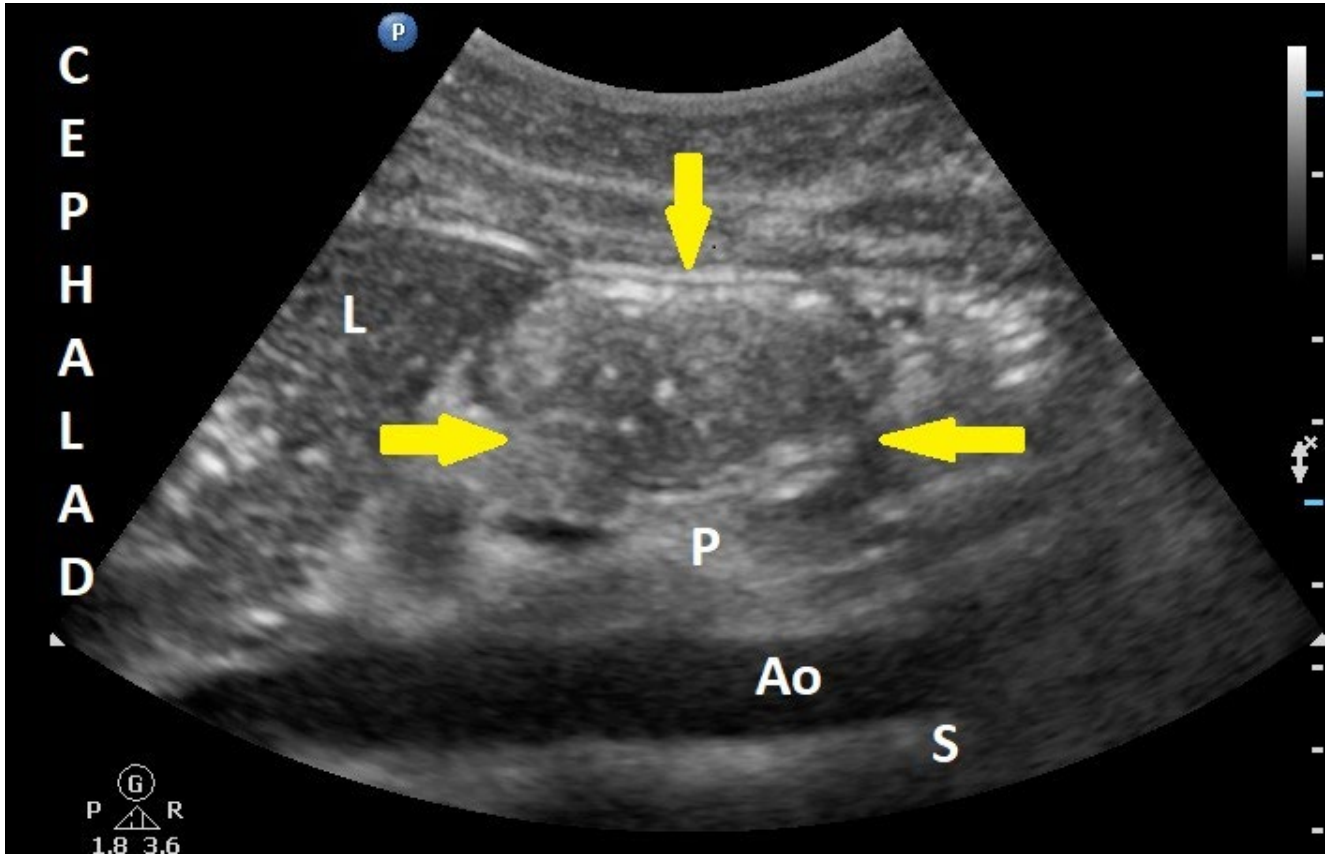
Mark L. van Zuylen[1,2], Sarah E. Siegelaar[3,4], Mark P. Plummer[6], Adam M. Deane[5], Jeroen Hermanides[1] and Abraham H. Hulst[1,4,*]

- Scoping review of current evidence and literature (previous studies included!)
- Suggest:
  - Tachyphylaxis to delayed gastric emptying with therapy of 8-12wks.
  - Scant evidence linking GLP-1 A and pulmonary aspiration directly.
- Bottom Line:
  - GLP-1 A therapy less than 8-12 weeks, caution should be exercised in the peri-operative setting.
  - GLP-1 A therapy more than 8-12 wks, hold times should be sufficient.
  - Longer hold times require consultation with prescribing provider.

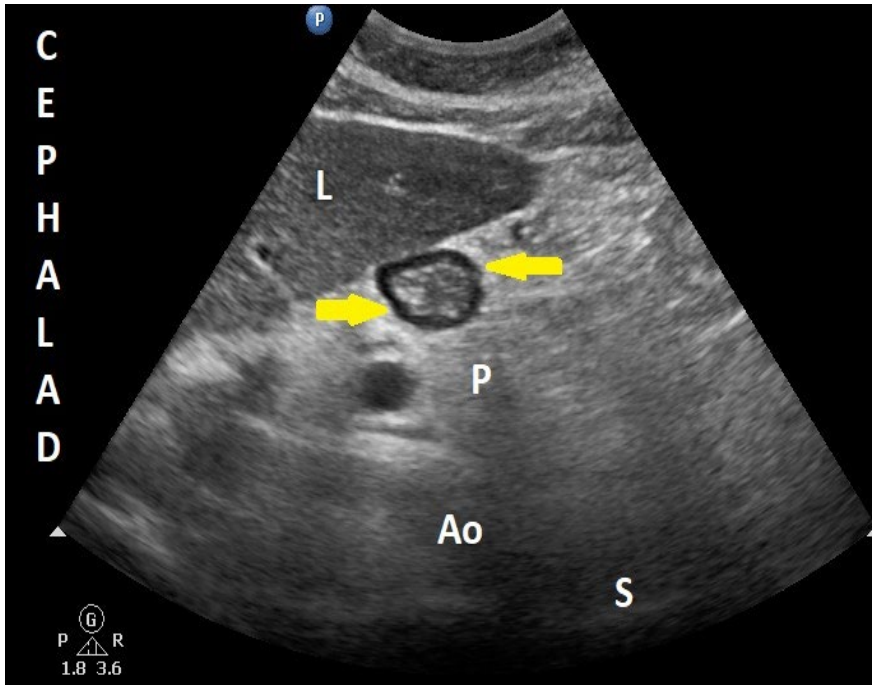
What then does the ASA say?

- Once daily dosing, hold GLP-1 agonists on the day of the procedure/surgery.
- Once weekly dosing, hold GLP-1A the week prior to the procedure/surgery.
- Hold times are irrespective of the indication, dose, or the type of procedure/surgery.
- If GLP-1 agonists prescribed for diabetes management are held for longer than the dosing schedule, consider consulting an endocrinologist for bridging the antidiabetic therapy to avoid hyperglycemia.

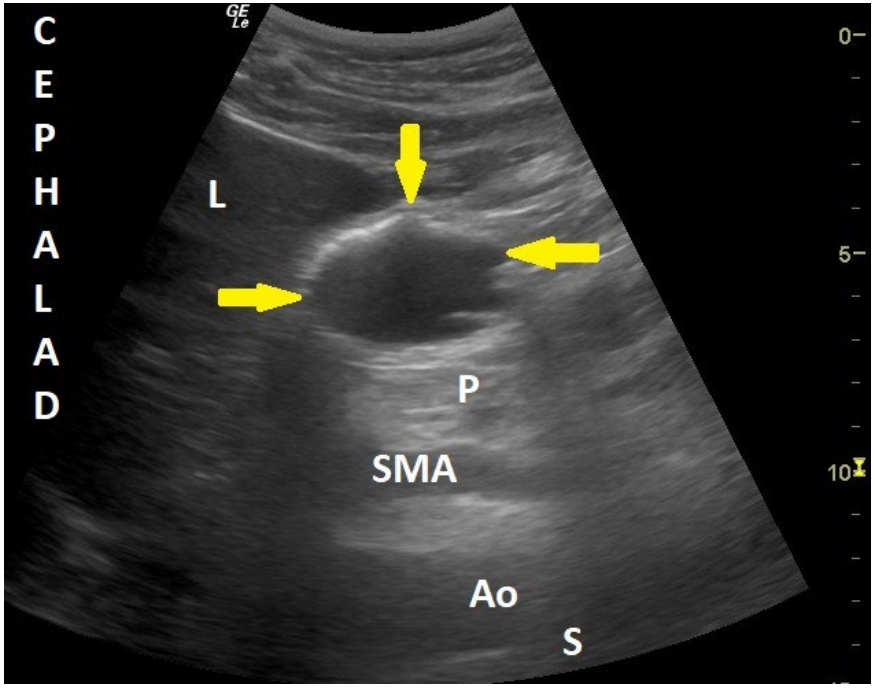
Source: https://www.smithsonianmag.com/innovation/a-brief-history-of-the-sonogram180978732/#:~:text=In%201963%2C%20they%20produced%20the,Glasgow%27s%20industrial%20factories%20and%20shipyards.



Source: https://www.asra.com/news-publications/asra-newsletter/newsletter-item/asra-news/2021/11/01/pocus-spotlight-gastric-ultrasound



Ultrasound image of an empty gastric antrum.



Ultrasound image of gastric antrum with clear fluid.

Source: https://www.asra.com/news-publications/asra-newsletter/newsletter-item/asra-news/2021/11/01/pocus-spotlight-gastric-ultrasound


Don't Mind
Me
quickmeme.com

What does the ASA recommend?

- If GI symptoms are present regardless of hold times:
  - Consider delaying elective procedure.
  - Discuss concerns of potential risks of proceeding with the proceduralist/surgeon and the patient.
- No GI symptoms and the GLP-1 agonists have been held as advised:
  - Proceed as usual.
- No GI symptoms but the GLP-1 agonists were not held as advised:
  - Proceed with 'full stomach' precautions or consider evaluating gastric volume by ultrasound, if possible and if proficient with the technique.
    - If the stomach is empty, proceed as usual.
    - If the stomach is full or if gastric ultrasound inconclusive or not possible, consider delaying the procedure or treat the patient as 'full stomach' and manage accordingly.
  - Discuss the concerns of potential risk of regurgitation and pulmonary aspiration of gastric contents with the proceduralist/surgeon and the patient.

Source: ASA Task Force on Pre-Operative Fasting

What to do in ”real” life!?

- Hospital:
  - Follow the ASA guidelines and any DOS algorithm that your system develops for these meds.
  - Elective vs. Emergent/Urgent/Time Sensitive Cases
  - Error on the side of caution if unsure.
- Ambulatory:
  - Discretion is the better part of valor!
    - Appropriate hold times and no GI symptoms.

      → Proceed with full stomach precautions.
    - If any GI symptoms regardless of GLP-1 hold times.

      → Postpone/Reschedule
- Utilize ultrasound!

In Summary

- Diabetes is common, impacts outcomes, and not going anywhere!
- HgBA1C is good, but fructosamine is a more useful pre-operative marker of glycemic control!
- Stop SGLT-2 agonists at least 3 days prior to any elective/non-urgent procedure.
  - Ertugliflozin needs to be stopped at least 4 days in advance of an elective

Summary cont…

- Current evidence suggests that stopping GLP-1 agonists 1 day or week prior to procedures is sufficient.
  - If longer, involve prescribing provider.
- DOS GLP-1 A's decision making is complicated!
  - Use the ASA guidelines as a framework!
  - Develop an institutional protocol that everyone follows!
  - Ambulatory setting is ok with resources.
- Learn gastric ultrasound and POCUS!

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EMORY
HEALTHCARE

Perioperative Management of Buprenorphine and Methadone in Opioid Naïve and Tolerant patients

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Objectives

- **A)**
- B)
- C)
- D)

EMORY HEALTHCARE

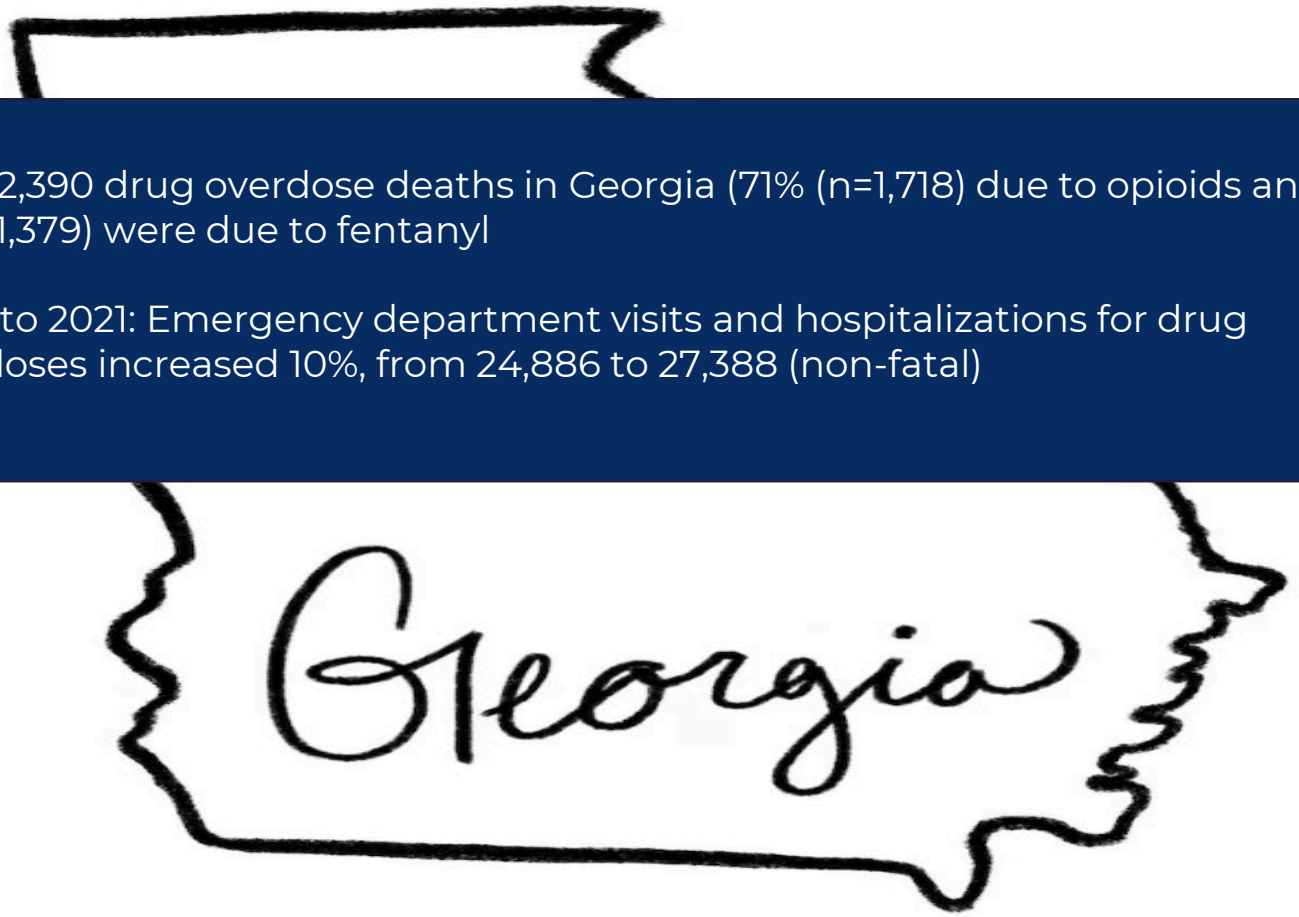
Public health crisis

- Opioid use disorder (OUD)
  - Prescription opioid medications
  - Illicit opioids
- 2.5 million people in the USA have OUD
- 1999: >1 million people have died from drug overdose
- 2021: >80,000 overdose death with >80% due to synthetic opioids (fentanyl)

EMORY HEALTHCARE

2021: 2,390 drug overdose deaths in Georgia (71% (n=1,718) due to opioids and 57% (1,379) were due to fentanyl

2019 to 2021: Emergency department visits and hospitalizations for drug overdoses increased 10%, from 24,886 to 27,388 (non-fatal)



GEORGIA DEPARTMENT OF PUBLIC HEALTH

GEORGIA DEPARTMENT *of* PUBLIC HEALTH

Public health crisis

- FDA approved medications approved for OUD
  - **Methadone** (full MOR agonist)
  - **Buprenorphine** (partial MOR agonist, κ-opioid receptor [KOR] antagonist, and nociceptor receptor agonist)
  - **Naltrexone** (MOR and KOR antagonist)

13

J Clin Invest. 2020 Jan 2; 130(1): 10–

EMORY HEALTHCARE

Public health crisis

Opioid Prescriptions 1	Prescription Drug Monitoring Program (PDMP) 2	Medication for Opioid Use Disorder (MOUD) 3
2011-2020: 44.4% decrease in opioid Rx 2019-2020: ↓ 6.9%	2019: 750 million times 2020: 910 million times	2017: ~70,000 more professionals certified to prescribed Buprenorphine
		↓ Buprenorphine prescriptions for OUD Approx. 2x

Section 1262 of the Consolidated Appropriations Act, 2023 (also known as Omnibus bill)

- Removes the federal requirement
  - Special waiver prior to prescribe **buprenorphine** for OUD
  - Discipline restrictions
  - Patient limits
  - Certification related to provision of counseling

EMORY HEALTHCARE

Buprenorphine in the perioperative period

- Increase in use of buprenorphine for OUD
- Perioperative period is a vulnerable time
- Fear of relapse
- Fear inadequate pain relief
- Fear experiencing opioids withdrawal symptoms
- Fear they will be treated unfairly or judged

Am J Addict. Author manuscript; available in PMC 2020 Oct 1.
Published in final edited form as:
Am J Addict. 2020 Jul; 29(4): 295–304.
Published online 2020 Mar 22. doi: 10.1111/ajad.13022

PMCID: PMC7416726
NIHMSID: NIHMS1608103
PMID: 32202000

Incidence of Postoperative Opioid Overdose and New Diagnosis of Opioid Use Disorder Among US Veterans

Jonathan Siglin, BS,[1,2] John D. Sorkin, MD, PhD,[1,3,4] and Khodadad Namiranian, MD, PhD[1,5,6]

Discussion and Conclusions

The postoperative period is strongly associated with opioid overdose, but only weakly associated with new diagnosis of OUD. This is likely due to the difficulty of diagnosing OUD in the postoperative period.

EMORY HEALTHCARE

Journal of Substance Abuse Treatment
Volume 109, February 2020, Pages 8-13

Postoperative opioid misuse in patients with opioid use disorders maintained on opioid agonist treatment ☆

Khodadad Namiranian MD, PhD [a b], Jonathan Siglin [c 1], John David Sorkin MD, PhD [d e 2], Edward J. Norris MD [a b], Minu Aghevli PhD [a], Edward C. Covington MD [f]

In conclusion, for patients with opioid use disorders in remission through stable OAT participation, surgery is associated with increased odds of opioid misuse. Further and more detailed research is needed to validate these findings and to identify the responsible factors for postoperative relapse to opioids. Meanwhile, our health care system should recognize that patients with OUD-in-remission are susceptible to relapse in the postoperative period and should furnish every effort to decrease this potentially fatal consequence.

EMORY HEALTHCARE

Namiranian et al…

- Chronic relapsing disease
- Loss of physiologic tolerance to opioids → fatal overdose
- Exposure to a previously used drug → resumption of use
- Loss of coping mechanism
  - Stress of surgery
  - Sedation
- Perioperative pain management
  - Denial of appropriate opioid medication → illicit drug use
  - Over prescribing of opioid medication

Namiranian et al…

Increase in opioid use and overdoses, even among individuals without OUD

1 in 1000 inpatients suffer an in-hospital postoperative opioid overdose

Highest risks of overdose and continued opioid use are seen

- Patients with history of substance use disorder

Cureus. 2022 Mar; 14(3): e23385.
Published online 2022 Mar 22. doi: 10.7759/cureus.23385
PMCID: PMC9033510
PMID: 35481308

Continuation Versus Discontinuation of Buprenorphine in the Perioperative Setting: A Retrospective Study

Monitoring Editor: Alexander Muacevic and John R Adler

Braden Schuster,[1] Brooke Bell,[1] Anthony Massoll,[1] and Seth White[2]

The use of buprenorphine perioperatively was associated with significantly reduced oral morphine equivalent (OME) requirements postoperatively. Further research is needed to give definitive recommendations for whether to continue or discontinue buprenorphine prior to surgery.

EMORY HEALTHCARE

Buprenorphine

- Long-acting, mixed opioid agonist and antagonist
  - partial MOR agonist and κ-opioid receptor [KOR] antagonist

EMORY HEALTHCARE

Buprenorphine

- High affinity for the mu-opioid receptor
- Displaces full mu-opioid agonists
- Long half-life (24–42 hours for sublingual or buccal administration; 26 hours for transdermal administration and 43–60 days for slow-release subcutaneous injection)
- Highly lipophilic and slowly dissociates from the receptor
- Oral buprenorphine takes 2–3 days to be eliminated from the body.
- Peak plasma concentrations increase with buprenorphine dose, the increase is not in direct proportion which results in a 'leveling off' of opioid effects, even with further dose increases
- Buprenorphine is metabolized completely by the liver to norbuprenorphine, an active metabolite with some weak analgesic activity.

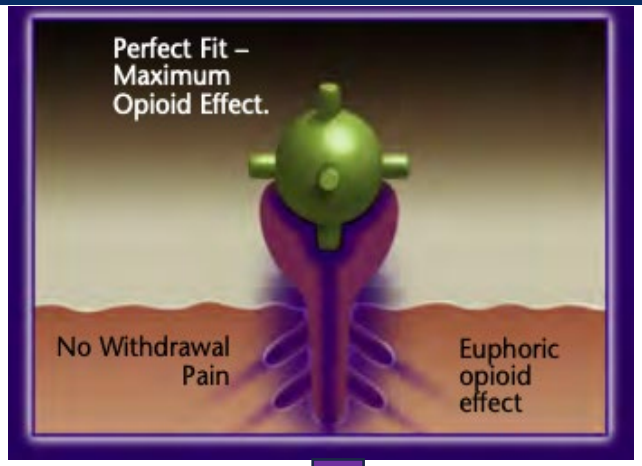
EMORY HEALTHCARE

Buprenorphine

- Benefits
  - Lowers potential for misuse of opioids
  - Diminishes withdrawal symptoms
  - Reduces cravings
  - Offers protection in overdose situations

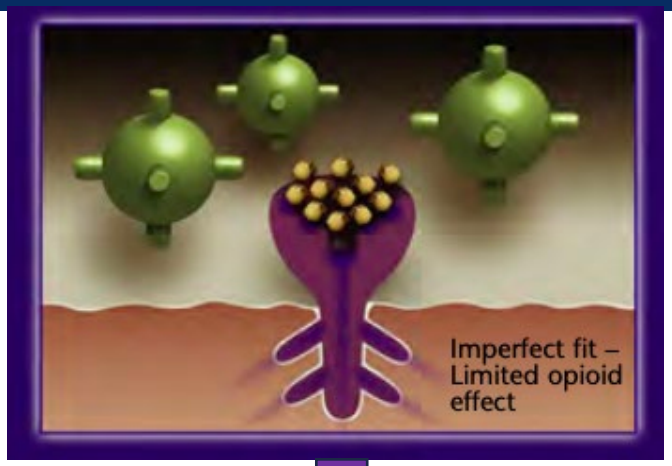
EMORY HEALTHCARE

FULL MU OPIOID



Analgesia
Euphoria
Sedation
Constipation
Respiratory depression

BUPRENORPHINE

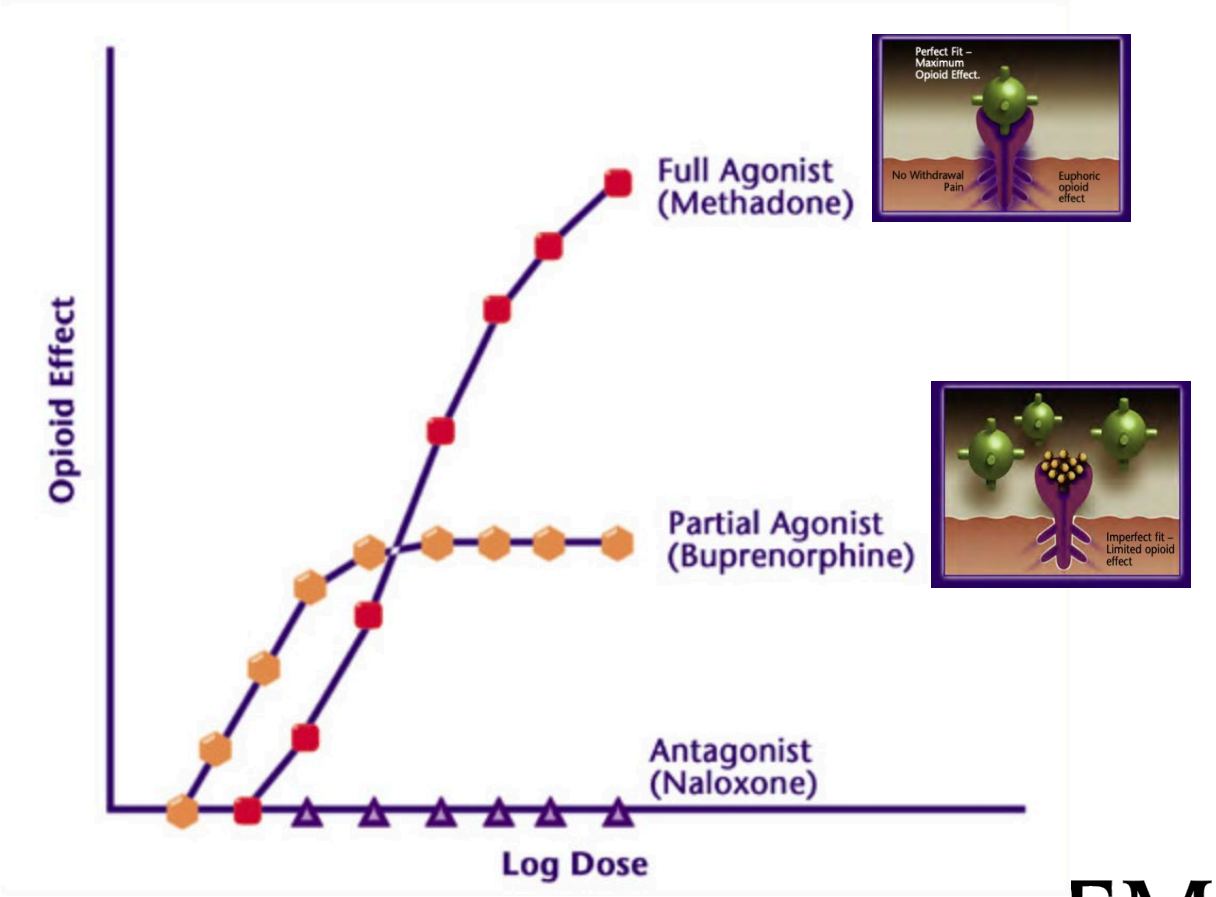


Competes with full agonist
Higher affinity for receptor
Partial activation of receptor
Limited opioid effect

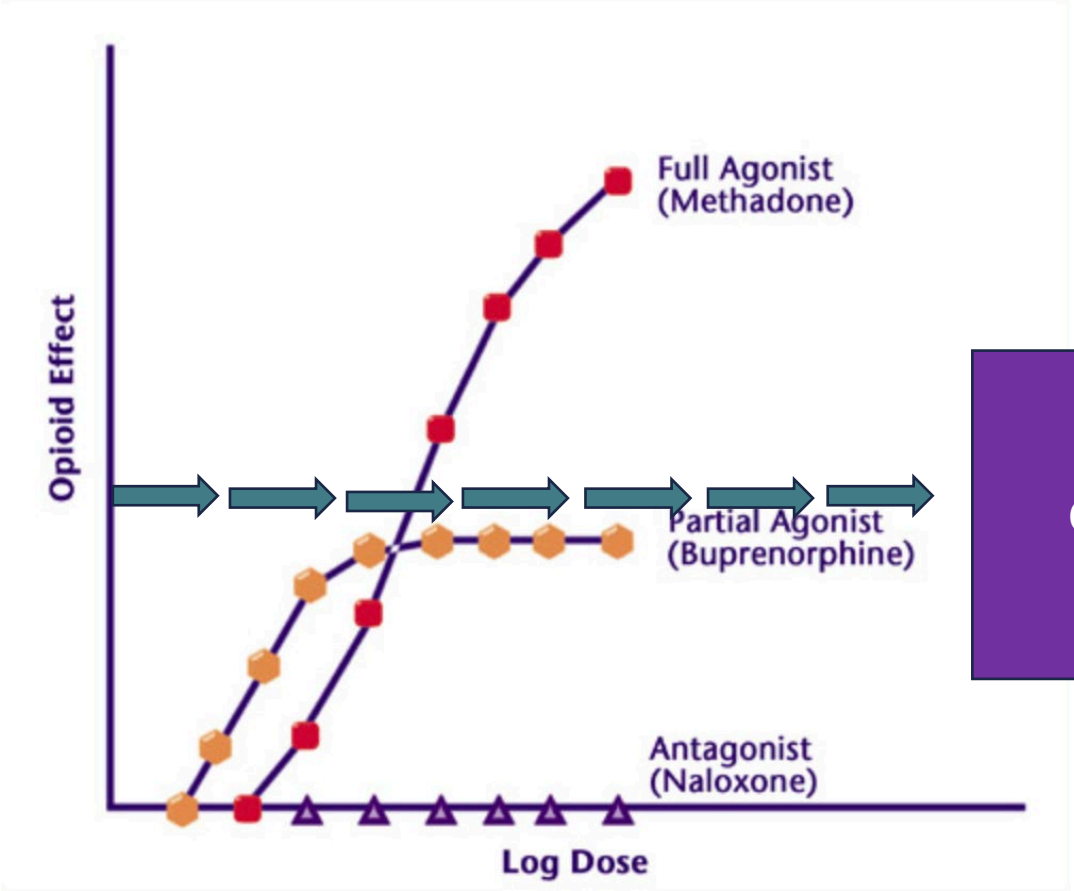
The National Alliance of Advocates for Buprenorphine Treatment

EMORY HEALTHCARE

Buprenorphine



Buprenorphine

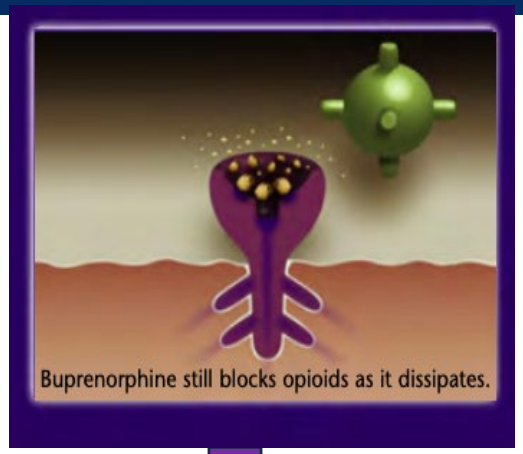


Ceiling effect*

? Ceiling effect

EMORY HEALTHCARE

Buprenorphine



Long half life
Slow dissipation from receptor

Receptor availability study

Buprenorphine dose	Available mu receptors
1mg	71-85%
2mg	53%–72%
4mg	36%–55%
8mg	20%–35%
12mg	13%–24%
16mg	9%–20%
24 mg	4-15%
32 mg	2%–12%

EMORY HEALTHCARE

Buprenorphine Formulations

MILLIgram dosing
(OUD)

a)Sublingual Buprenorphine
(+/- naloxone)

b)Buccal Buprenorphine
(+/- naloxone)

c)Injectable Buprenorphine

**contains naloxone*

Naloxone reduces the abuse potential if intravenous use attempted

MICROgram dosing
(Pain Management)

a)Parenteral Buprenorphine
(IV/IM)
0.3 mg IM/IV every six hours

b)Transdermal Buprenorphine
5 mcg/h to 20 mcg/h

c) Buccal Buprenorphine
75 to 900 mcg ; BID dosing

EMORY HEALTHCARE

Buprenorphine in the perioperative period

Anesthesiology. Author manuscript; available in PMC 2020 Feb 25.
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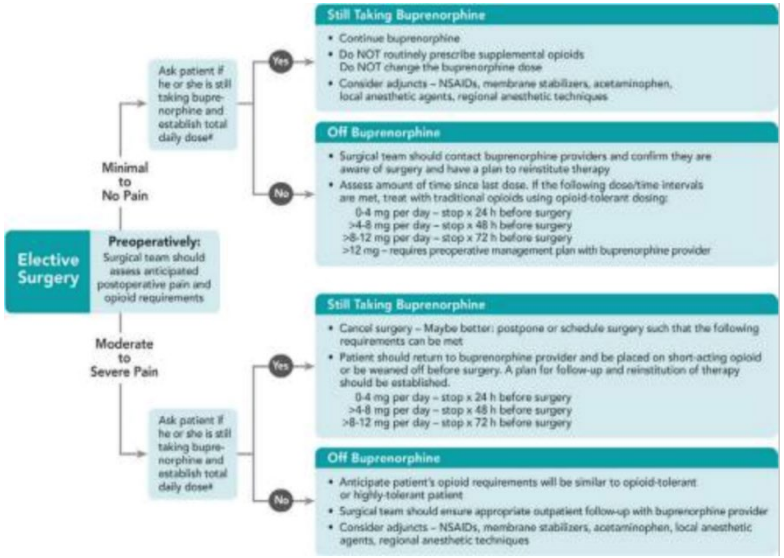
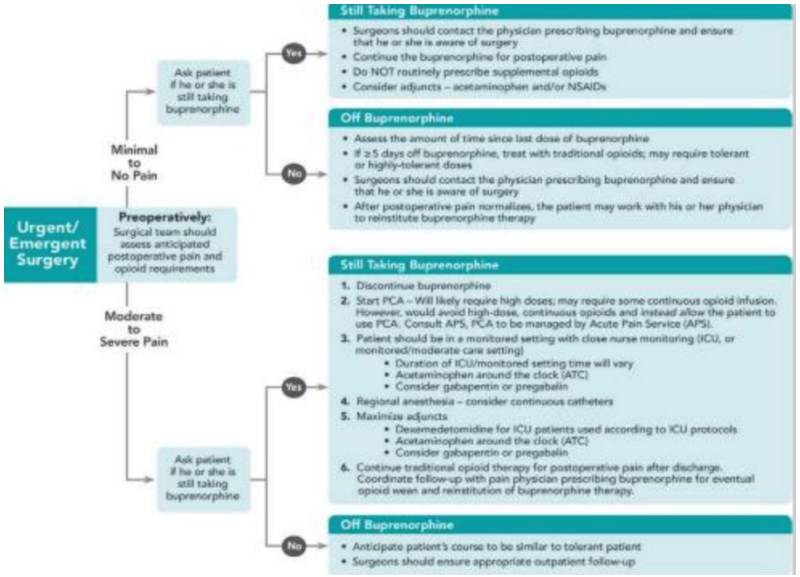
doi: 10.1097/ALN.0000000000001633

PMCID: PMC7041233
NIHMSID: NIHMS1014047
PMID: 28511196

To Stop or Not, That Is the Question: Acute Pain Management for the Patient on Chronic Buprenorphine

T. Anthony Anderson, Ph.D., M.D., Aurora N. A. Quaye, M.D., E. Nalan Ward, M.D., Timothy E. Wilens, M.D., Paul E. Hilliard, M.D., and Chad M. Brummett, M.D.

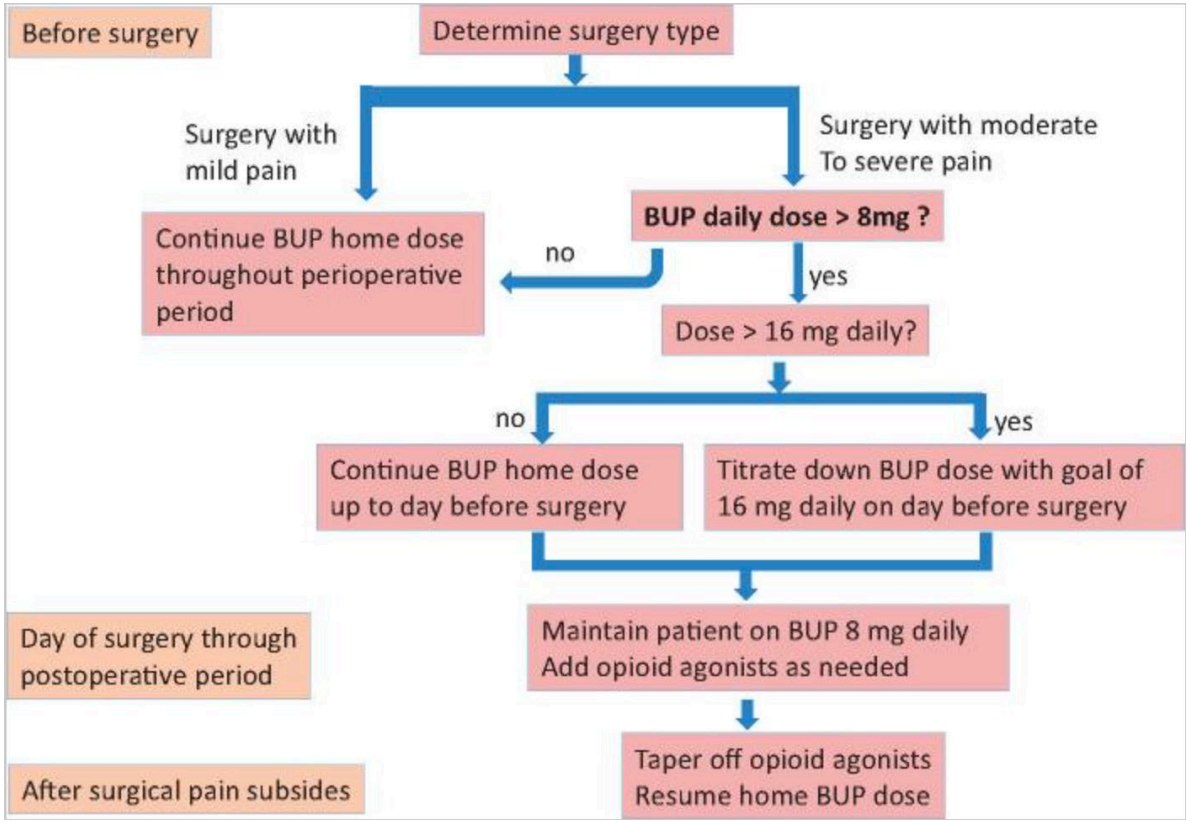




Pain Med. 2019 Jul; 20(7): 1395–1408.
Published online 2018 Nov 30. doi: 10.1093/pm/pny217
PMCID: PMC7963209
PMID: 30500943

Perioperative Management of Buprenorphine: Solving the Conundrum

Aurora Naa-Afoley Quaye, MD and Yi Zhang, MD, PhD



EMORY HEALTHCARE

Buprenorphine in the perioperative period

- Vulnerable time
- Concern for withdrawal
  - Weaning dose and discontinuation
- Relapse of OUD
- Inadequate pain management
- Judgement

EMORY HEALTHCARE

Buprenorphine management in the perioperative period: educational review and recommendations from a multisociety expert panel

Lynn Kohan [1], Sudheer Potru [2,3], Antje M Barreveld [4], Michael Sprintz,[5] Olabisi Lane,[6] Anuj Aryal,[7] Trent Emerick,[8] Anna Dopp,[9] Sophia Chhay,[9] Eugene Viscusi [10]

Perioperative Management of a Patient on Buprenorphine for OUD

Preoperative Planning

Grade B, Moderate Level of Certainty

- Buprenorphine should not be routinely discontinued preoperatively
- Discontinuing Buprenorphine can increase risk of OUR or harm
- In most cases, avoid tapering buprenorphine prior to surgery

Intraoperative and Postoperative Planning

Grade B, Moderate Level of Certainty

- Multimodal analgesia, including adjunctive medications and regional techniques should be utilized whenever possible
- Consider administration of full mu agonists with high affinity for the mu receptor if needed to achieve adequate analgesia

Grade C, Low level of Certainty

- Consider increasing and/or dividing dosing of buprenorphine to achieve adequate analgesia

Buprenorphine management in the perioperative period: educational review and recommendations from a multisociety expert panel

Lynn Kohan [1], Sudheer Potru [2,3], Antje M Barreveld [4], Michael Sprintz,[5] Olabisi Lane,[6] Anuj Aryal,[7] Trent Emerick,[8] Anna Dopp,[9] Sophia Chhay,[9] Eugene Viscusi [10]

Discharge planning

Grade A, moderate level of certainty

- If a full mu agonist is initiated or if buprenorphine is increased during the perioperative period, a post-discharge plan to taper off the full mu agonist or return to the preoperative dose of buprenorphine is recommended.

- Engage in collaboration with the patient's outpatient buprenorphine prescriber if possible.

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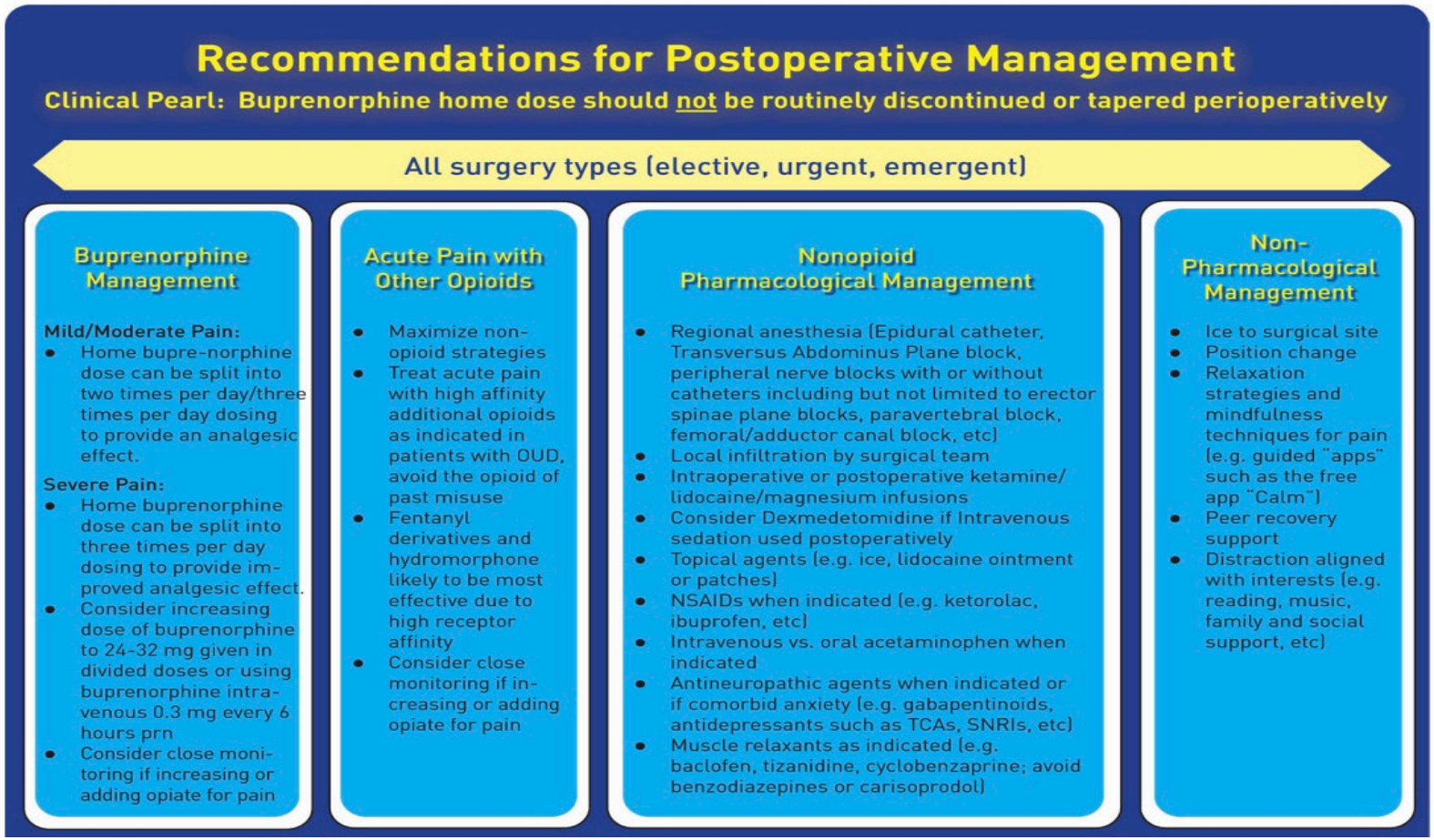

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Buprenorphine in the perioperative period

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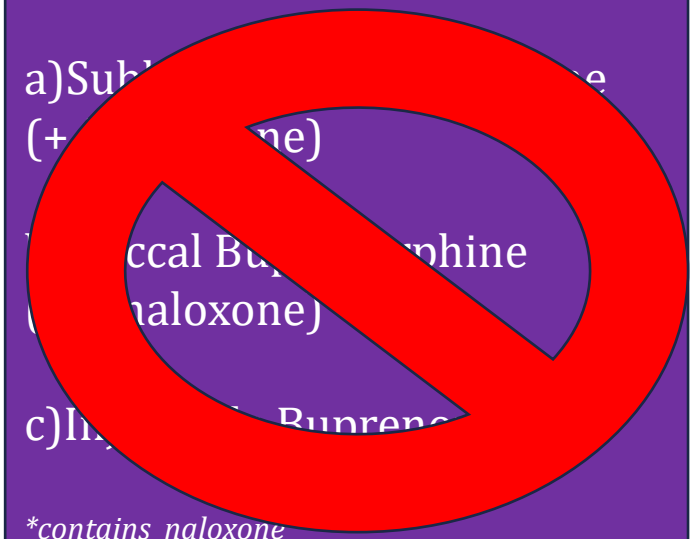
HEALTHCARE

Perioperative Management of Buprenorphine and Methadone in Opioid Naïve and Tolerant patients

Buprenorphine Formulations

MILLIgram dosing
(OUD)



**contains naloxone*

MICROgram dosing
(Pain Management)

a)Parenteral Buprenorphine
(IV/IM)
0.3 mg IM/IV every six hours

b)Transdermal Buprenorphine
5 mcg/h to 20 mcg/h

c) Buccal Buprenorphine
75 to 900 mcg ; BID dosing

Naloxone reduces the abuse potential if intravenous use attempted

EMORY HEALTHCARE

Buprenoprhine for chronic pain

Transdermal (TD) 5-20mcg/hr

Opioid analgesic daily dose Oral Morphine Equivalent (OME)	Recommended Transdermal Buprenorphine starting dose
<30mg or *Opioid naive	5mcg/hr
30-80mg	10mcg/hr

Taper existing OME to no more than 30 OME prior to initiating TD	May use short acting analgesics PRN for breakthrough pain	>80 OME may not achieve adequate analgesia with 20mcg/hr

EMORY HEALTHCARE

Buprenoprhine for chronic pain

- Buccal Buprenorphine

Opioid analgesic daily dose Oral Morphine Equivalent (OME)	Recommended Buccal Buprenorphine starting dose
<30mg or *Opioid naive	75 mcg once daily or every 12 hours
30-89 mg	150 mcg BELBUCA every 12
90-160 mg	300 mcg BELBUCA every 12 hours
>160mg	consider alternate analgesic

Taper existing OME to no more than 30 OME prior to initiating medication

EMORY HEALTHCARE

Buprenorphine HCL

- Buprenorphine hydrochloride
- Injection (intravenous or intramuscular)
- 0.3mg approx. equivalent to 10 mg morphine sulfate
  - Analgesic and respiratory depressant effects
- Indications and usage: “Pain severe enough to require an opioid analgesic and for which alternate treatments are inadequate”

EMORY HEALTHCARE

Buprenorphine HCL

- 0.3mg/ml
- 0.3mg (1ml) via deep intramuscular OR slow (over ~2 minutes) intravenous injection
- May repeat every 6 hours as needed

EMORY HEALTHCARE

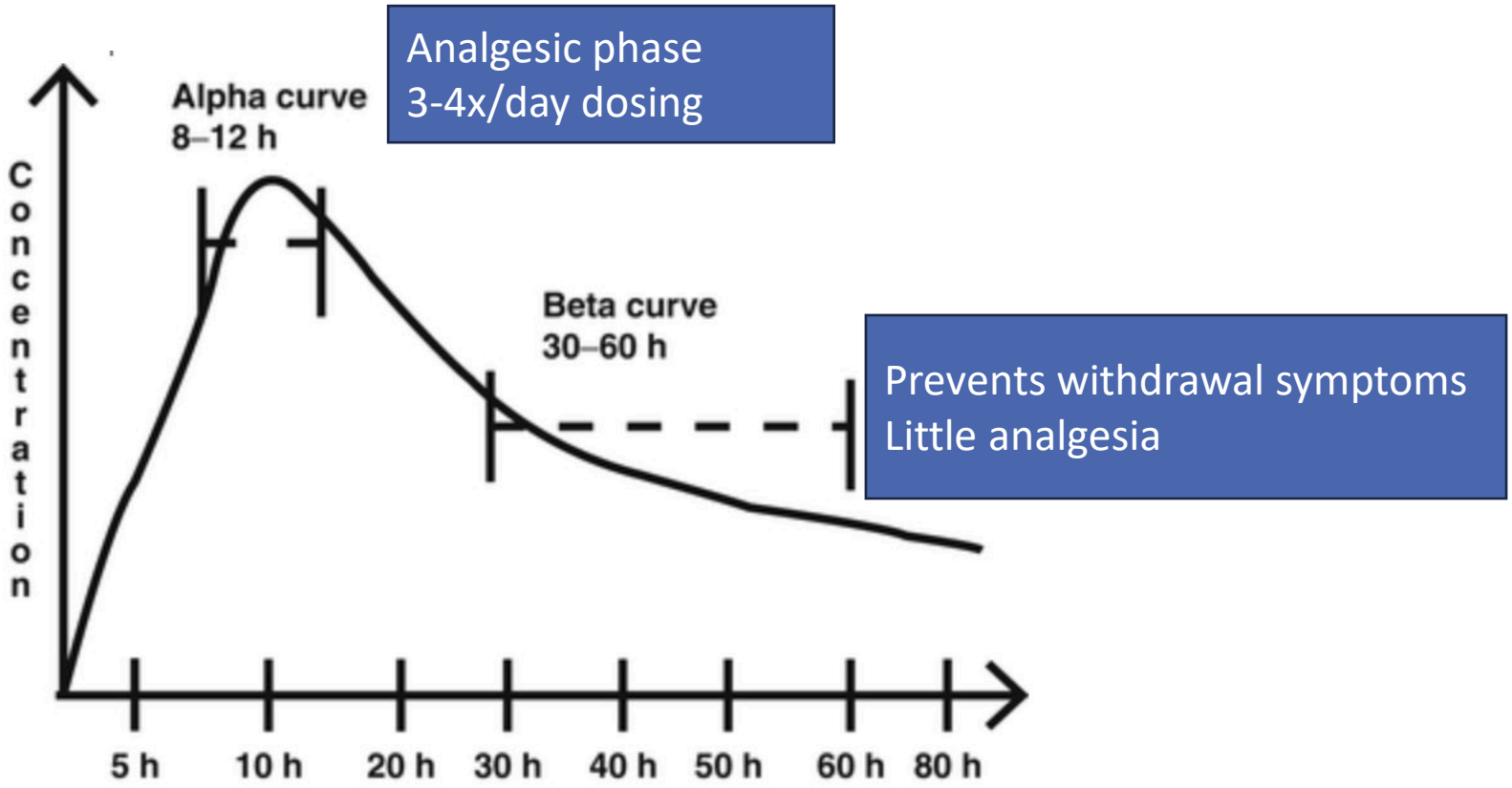
Perioperative Management of Methadone

Long-acting synthetic full mu receptor agonist	N-methyl-D-aspartate (NMDA) receptor antagonist	Decrease reuptake of serotonin and norepinephrine in the brain
	• Anti-hyperalgesic • Anti-allodynic properties • Inhibit the development of tolerance • Neuropathic pain	• Mood-elevating

Perioperative Management of Methadone

- Methadone has no ceiling effect
- Variable half-life (15 to 55 hours)
- Treatment for severe pain and OUD
- Typical daily dose for OUD between 60 and 120 mg/d

Biphasic Elimination



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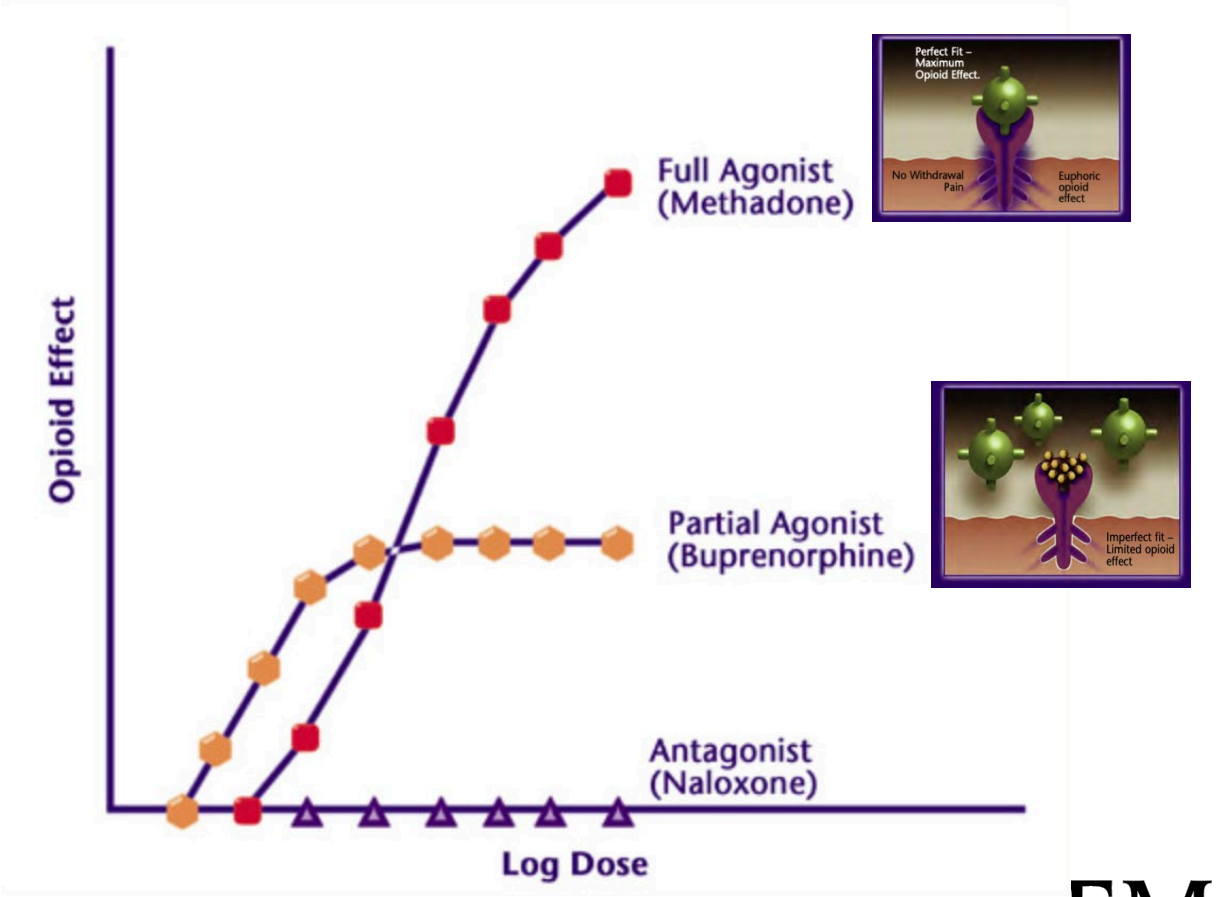
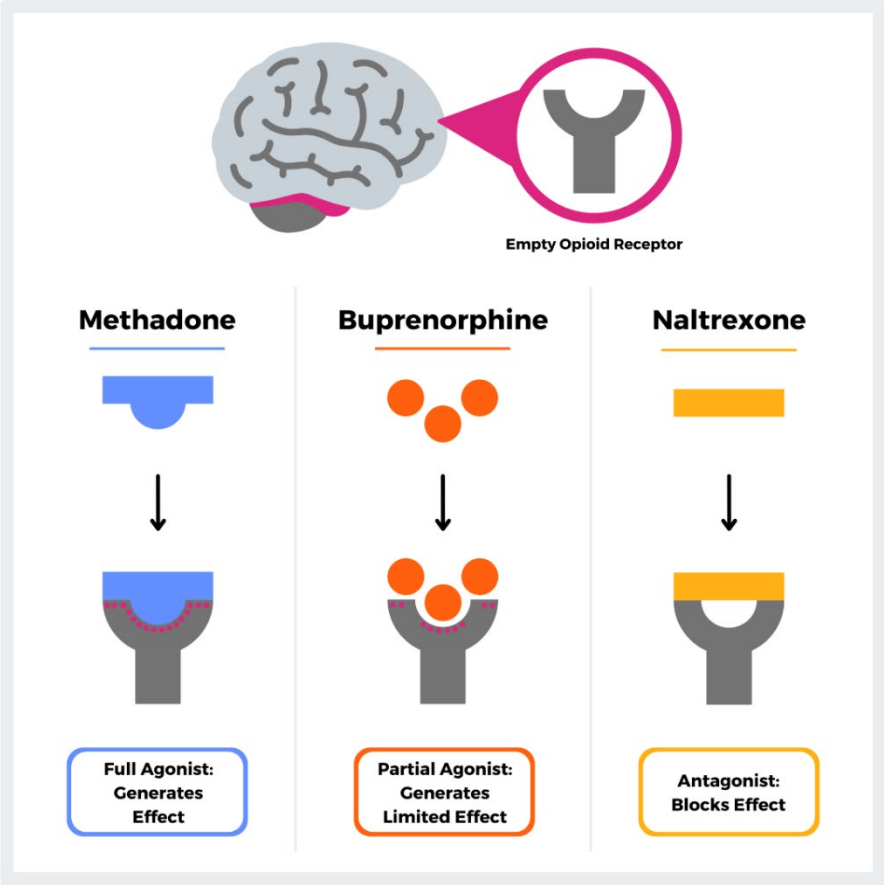
Perioperative Management of Methadone



EMORY HEALTHCARE

MOUD



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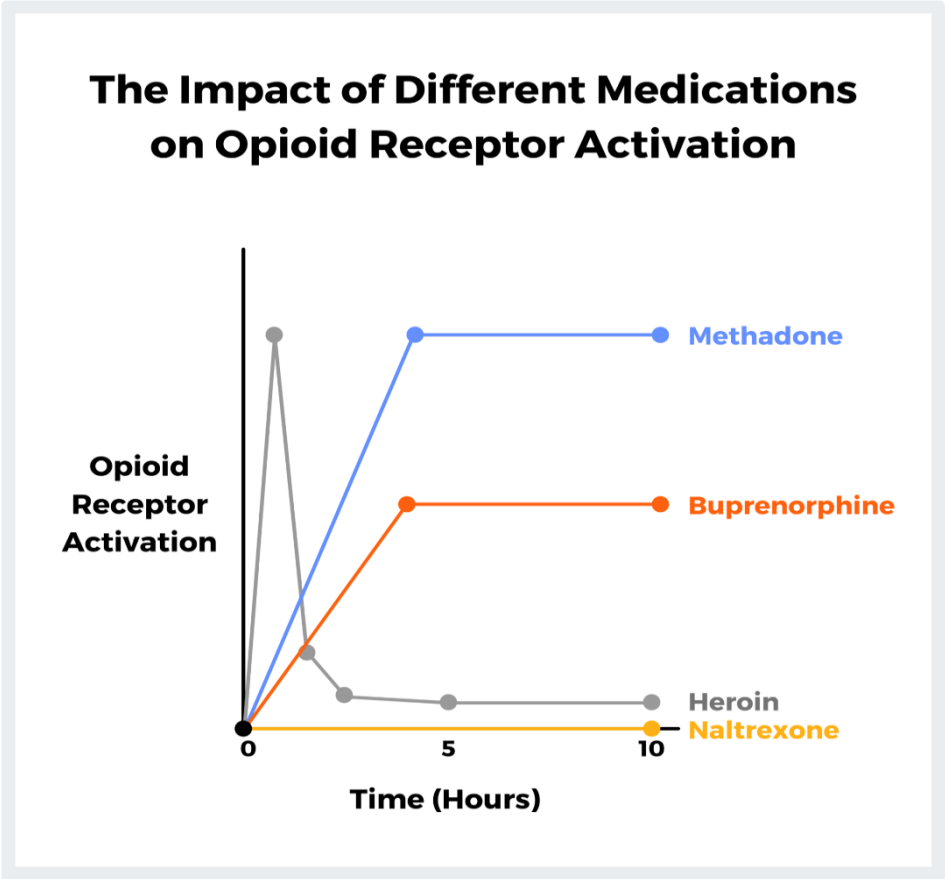
MOUD



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Perioperative Management of Methadone

EMORY HEALTHCARE

Perioperative Management of Methadone

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Cases

EMORY HEALTHCARE

Perioperative Management of Buprenorphine and Methadone

EMORY HEALTHCARE

GEORGIA ALLIANCE FOR PATIENT PROTECTION

GAPP Membership

Georgia Alliance for Patient Protection (GAPP) is a grassroots organization of physicians, other healthcare professionals, and patients who are dedicated to ensuring physician-led, team-based care for all Georgia patients and to advocating for truth and transparency regarding healthcare practitioners.

- Physician Member -- $99
- Patient Advocate Member -- $35 (Patients, Advocates, Interested Citizens)
- Physician Practice Group (5 or fewer personnel) -- $250
- Physician Practice Group (10 or fewer personnel) -- $650
- Physician Practice Group (11 or more personnel) -- $1000
- Silver Level Members/Groups (includes Committee position of responsibility) -- $1,500
- Platinum Level Members/Groups (includes Board position of responsibility) -- $2,500
- Medical Specialty Society Membership --
  $2,500 – Patron Member
  $5,000 – Partner Member
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plural

Find Your State Legislator

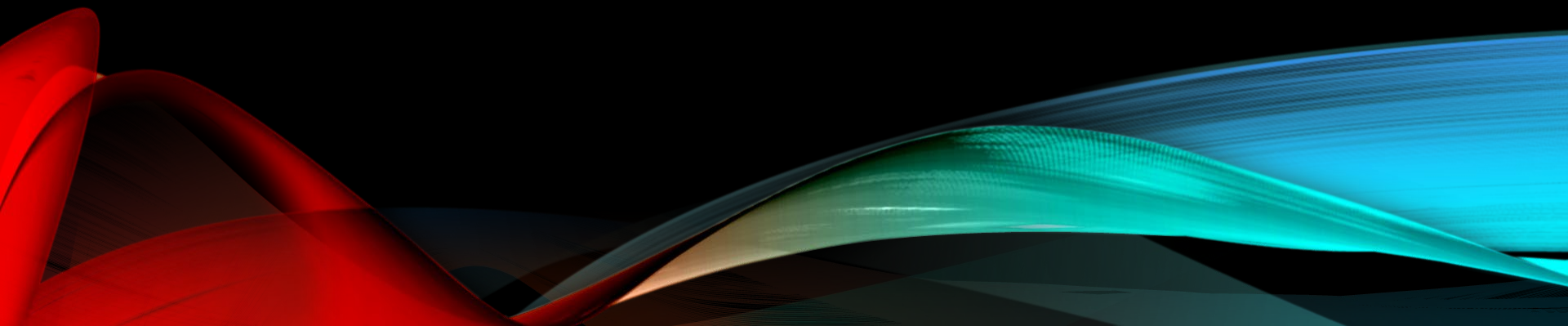
PERIOPERATIVE MANAGEMENT OF THE ADULT PATIENT WITH CONGENITAL HEART DISEASE

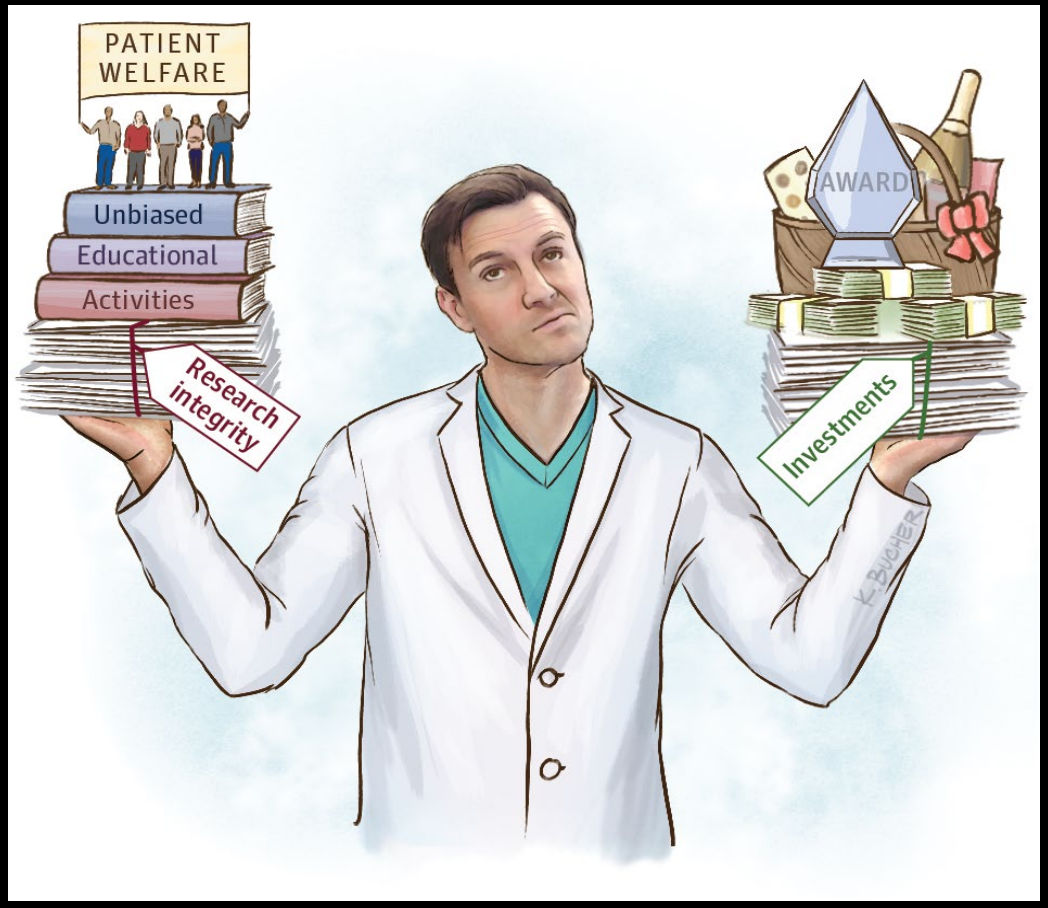
Anne Elisa Cossu, MD, MS, FASA

Assistant Professor of Anesthesiology

Children's Healthcare of Atlanta

Emory University School of Medicine

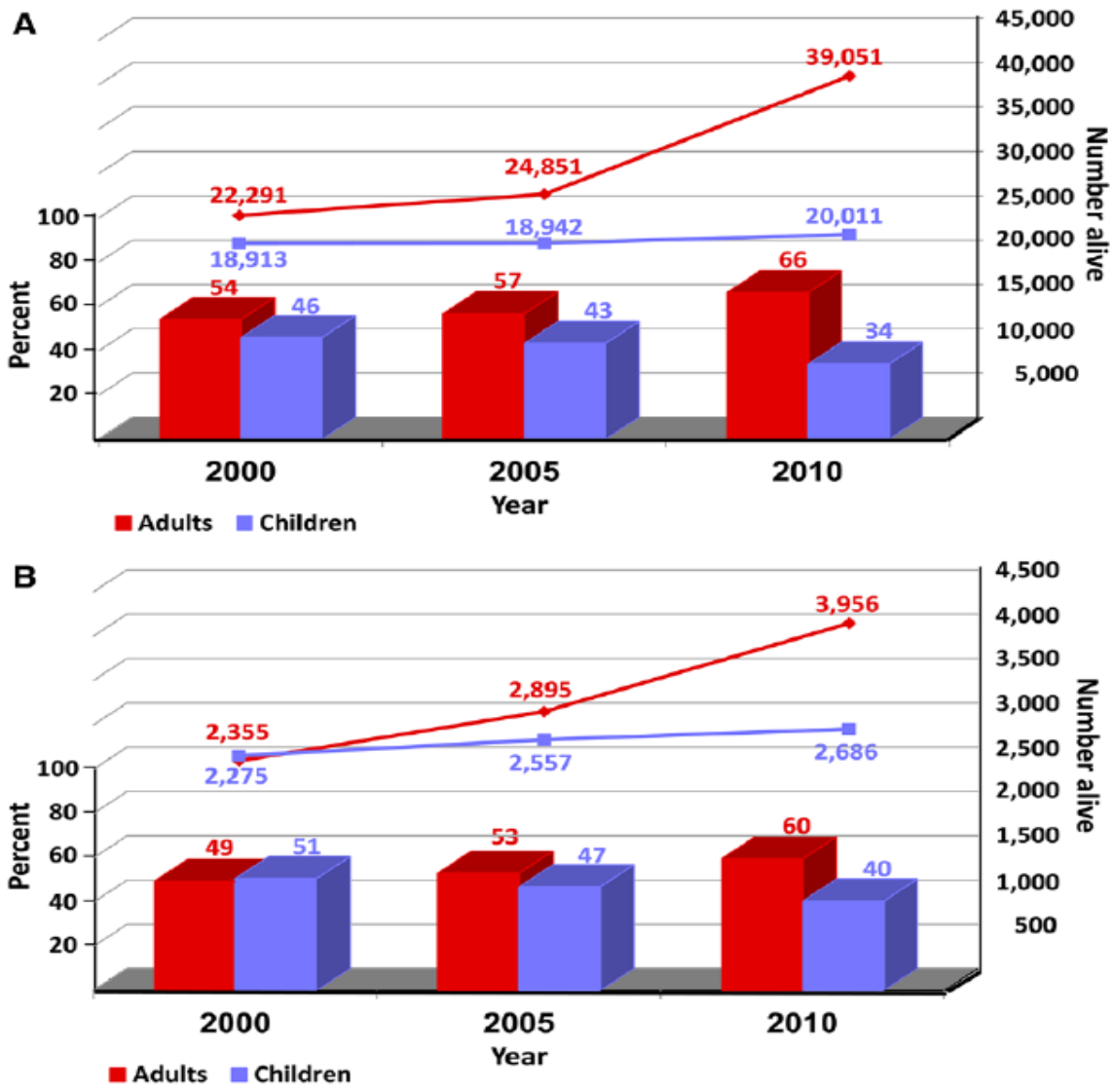




NOTHING TO DISCLOSE, NO CONFLICT OF INTEREST

OR SCHEDULE

ENT/Dental	Ortho	Gen Surg	Ophthal	Ob/Gyn
23 yo, Trisomy 21 s/p CAVC repair, T & A	32 yo, dTGA s/p ASO, ORIF humerus fx	23 yo,HLHS with Fontan, lap appy	30 yo, Marfan's syndrome, detached retina	41 yo, Coarct Aorta, C section
19 yo, Heterotaxy with single ventricle/systemic RV, wisdom tooth extraction	27 yo, TOF, Hardware removal femur	45 yo, HLHS s/p OHT, ex lap bowel obstruction	6 yo, Williams syndrome, strabismus surgery	50 yo s/p Mustard, robotic hysterectomy



Prevalence of CHD from 2000 to 2010:

↑ 11% in Children
↑ 57 % in Adults

Figure 3. The numbers and proportions of adults and children in Quebec, Canada, with all (**A**) and severe (**B**) congenital heart disease over time in 2000, 2005, and 2010.

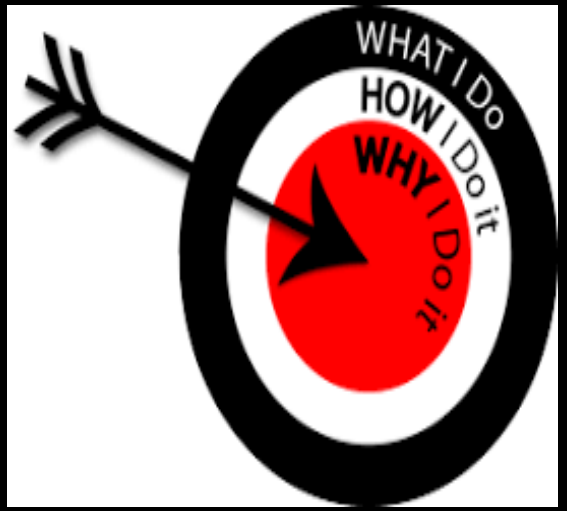
Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime prevalence of congenital heart disease in the general population from 2000 to 2010. Circulation. 2014;130(9):749-56

Category and Age Group	CHD Severity/Race-Ethnicity	Estimated US Prevalence per 1000 (95% Confidence Interval), %	Estimated No. of Individuals (95% Confidence Interval)*
CHD severity			
All ages	Overall	7.85 (7.79–7.92)	2 425 000 (2 405 000–2 444 000)
	Severe	0.92 (0.90–0.94)	283 000 (277 000–290 000)
Children	Overall	13.21 (13.03–13.39)	980 000 (966 000–993 000)
	Severe	1.66 (1.60–1.73)	123 000 (119 000–128 000)
Adults	Overall	6.16 (6.10–6.22)	1 444 500 (1 431 000–1 459 000)
	Severe	0.68 (0.66–0.70)	160 000 (155 000–165 000)
Race-ethnicity			
Children	Non-Hispanic white	13.31 (13.12–13.49)	620 000 (612 000–629 000)
	Non-Hispanic black	12.69 (12.50–12.88)	133 000 (131 000–135 000)
	Hispanic	13.26 (13.08–13.45)	227 000 (224 000–230 000)
Adults	Non-Hispanic white	6.36 (6.29–6.42)	1 104 000 (1 094 000–1 115 000)
	Non-Hispanic black	5.63 (5.56–5.69)	155 000 (153 000–156 000)
	Hispanic	5.58 (5.52–5.65)	186 000 (184 000–188 000)

Gilboa SM, Devine OJ, Kucik JE, Oster ME, Riehle-Colarusso T, Nembhard WN, Xu P, Correa A, Jenkins K, Marelli A. Congenital Heart Defects in the US. Circulation. 2016;134:101–109.

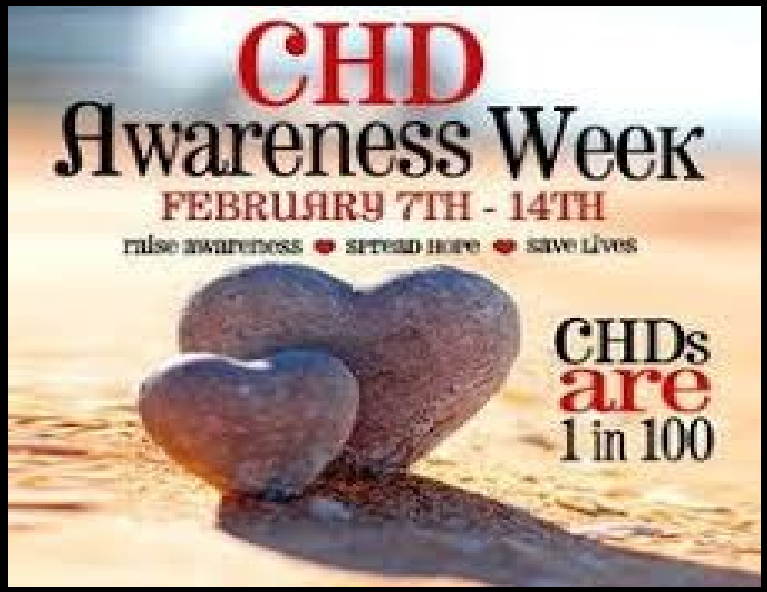
LEARNING OBJECTIVES

- Importance ACHD
- 2018 AHA/ACC Guidelines
- Anatomy and Physiology
- Repair/Palliation
- Sequelae of ACHD
- Fontan Patient



DID YOU KNOW?

- Most common birth defect
- 1 in ~ 110 newborns
- > 35 congenital heart defects
- Multiple surgeries
- 85-90% survival



Survival Prospects and Circumstances of Death in Contemporary Adult Congenital Heart Disease Patients Under Follow-Up at a Large Tertiary Centre

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Rafael Alonso-Gonzalez, MD, MSc; Lorna Swan, MD, FRCP; Anselm Uebing, MD, PhD;
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Stephen J. Wort, PhD; Konstantinos Dimopoulos, MD, MSc, PhD; Michael A. Gatzoulis, MD, PhD

Patient's age (years)

	20	25	30	35	40	45	50	55	60
ASD	25	26	32	38	42	47	52	57	61
Valvar disease	29	31	36	40	45	49	54	59	63
VSD	28	30	36	40	44	49	53	59	63
Aortic Coarctation	32	33	38	43	47	52	56	62	66
AVSD	33	34	39	44	48	52	57	62	66
Marfan syndrome	37	38	42	46	50	54	59	64	68
Tetralogy of Fallot	37	38	42	47	50	54	60	65	69
Ebstein anomaly	42	43	47	51	54	59	63	68	72
Systemic RV	46	48	51	55	59	63	67	72	76
Eisenmenger syndrome	57	58	62	65	69	73	77	81	84
Complex CHD	58	59	63	67	70	74	78	82	85
Fontan	64	65	68	72	75	78	82	86	91

Age difference:

- >40
- 30-40
- 20-30
- 10-20
- 5-10
- 2-5
- <2

- Leading causes of death
  1. Chronic Heart Failure
  2. Pneumonia
  3. Sudden Cardiac death

Circulation. 2015;132:2118-2125

Perioperative Outcomes of Major Noncardiac Surgery in Adults with Congenital Heart Disease

Anesthesiology 2013; 119:762-9

Bryan G. Maxwell, M.D., M.P.H.,* Jim K. Wong, M.D.,† Cindy Kin, M.D.,‡
Robert L. Lobato, M.D., M.S.§

Table 2. Outcomes

	ACHD Cohort	Comparison Cohort		
	n = 10,004	n = 37,581		
Outcome	n (%)	n (%)	*P* Value	OR (95% CI)
Death ★	407 (4.1)	1,355 (3.6)	0.031 ★	1.13 (1.01–1.27)
LOS (median [IQR])	4.8 (2.4–10.4)	2.9 (1.5–5.6)	<0.001	
Total charges (median [IQR])	$42,171 ($22,918–$93,847)	$26,982 ($15,814-$46,784)	<0.001	
ARF	620 (6.2)	1,826 (4.9)	<0.001	1.29 (1.18–1.42)
Pneumonia	942 (9.4)	2,998 (8.0)	<0.001	1.20 (1.11–1.29)
Respiratory failure	916 (9.2)	2,933 (7.8)	<0.001	1.19 (1.10–1.29)
DVT/PE	405 (4.1)	773 (2.1)	<0.001	2.01 (1.78–2.27)
Stroke	607 (6.1)	1,168 (3.1)	<0.001	2.01 (1.82–2.23)
MI/cardiac arrest	431 (4.3)	1,307 (3.5)	<0.001	1.25 (1.12–1.40)
Composite	2,145 (21.4)	6,003 (16.0)	<0.001	1.44 (1.36–1.52)

Values are reported as number (percentage) unless otherwise denoted as median (IQR). Composite = ARF, pneumonia, respiratory failure, DVT/PE, stroke, MI, and cardiac arrest.

ACHD = adult congenital heart disease; ARF = acute renal failure; DVT = deep venous thrombosis; IQR = interquartile range; LOS = length of stay; MI = myocardial infarction; OR = odds ratio; PE = pulmonary embolus.

Pregnancy in Women With a Fontan Circulation

A Systematic Review of the Literature

Circ Cardiovasc Qual Outcomes. 2018;11:e004575.

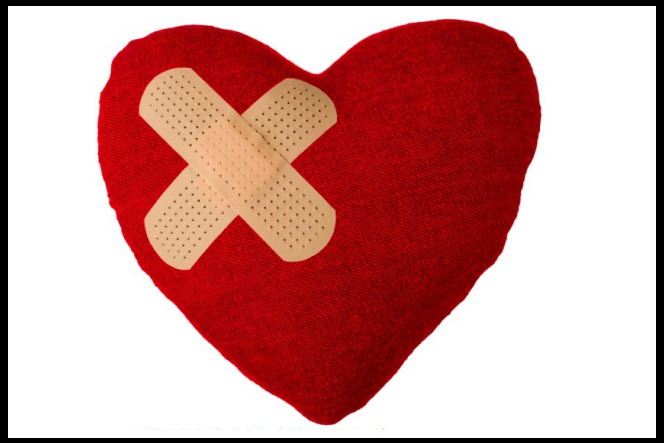
Maternal Morbidity (133 women)

- Antepartum hemorrhage
- Arrhythmia
- Heart Failure

Obstetric/Fetal M and M (255 pregnancies; 115 live births)

- Premature delivery
- Pregnancy losses ⟹ Spon miscarriage
- Postpartum hemorrhage
- Neonatal deaths
- 2 Deaths at birth

Tertiary Care Center or Local hospital



Emergency or Elective

Clinical Practice Guidelines

d in Collaboration With the American Association for Thoracic Surgery, American Socie
diography, Heart Rhythm Society, International Society for Adult Congenital Heart Dise
ty for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

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J Am Coll Cardiol 2018Aug 10. pii: S0735-1097(18)36846-3, Epub ahead of print

CHD AP Classification

omy + Physiological Stage = ACHD AP Classification)

dibular right ventricular outflow obstruction
m primum ASD
erate and large unrepaired secundum ASD
erate and large persistently patent ductus arteriosus
onary valve regurgitation (moderate or greater)
onary valve stenosis (moderate or greater)
heral pulmonary stenosis
of Valsalva fistula/aneurysm
venosus defect
alvar aortic stenosis (excluding HCM; HCM not addressed
ese guidelines)
avalvar aortic stenosis
dling atrioventricular valve
ired tetralogy of Fallot
with associated abnormality and/or moderate or greater
t

artery from the opposite

sinus

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- <u>All patients with ACHD Except Class I A</u>
  - Noncardiac surgery with/in consult with ACHD experts
  - Anesthetic provided by/in collaboration with anesthesiologist with expertise in ACHD
- Patients with moderate to great complexity CHD (Class II and III) and poor physiologic class (B-D)
  - Adult congenital heart disease program
- European Society of Cardiology 2020 similar

ANATOMY OF CHD

- AoDt Descending Aorta
- AsAo Ascending Aorta
- ASD Atrial Septal Defect
- AVVR Atrioventricular Valvular Regurgitation.
- CAVC Complete Atrioventricular Canal
- CoA Coarctation of Aorta
- CS Coronary Sinus
- DILV Double Inlet Right Ventricle
- DORV Double Outlet Right Ventricle
- HLHS Hypoplastic Left Heart Syndrome
- IVC Inferior Vena Cava
- IVS Intact Ventricular septum
- MCA Multiple congenital anomalies
- LVOTO Left Vent. Outflow Tract Obstruction
- PA Pulmonary Artery or Atresia
- PDA Patent Ductus Arteriosus
- PFC Persistent Fetal Circulation
- PFO Patent Foramen Ovale
- PS Pulmonic Stenosis
- SCA Subclavian artery
- SI Situs Inversus
- SV Single Ventricle
- SVC Superior Vena Cava
- TA Tricuspid atresia
- TAPVR Total anomalous pulm.venous return
- TGA Transposition of Great Arteries
- TOF Tetralogy of Fallot
- VSD Ventricular Septum defect

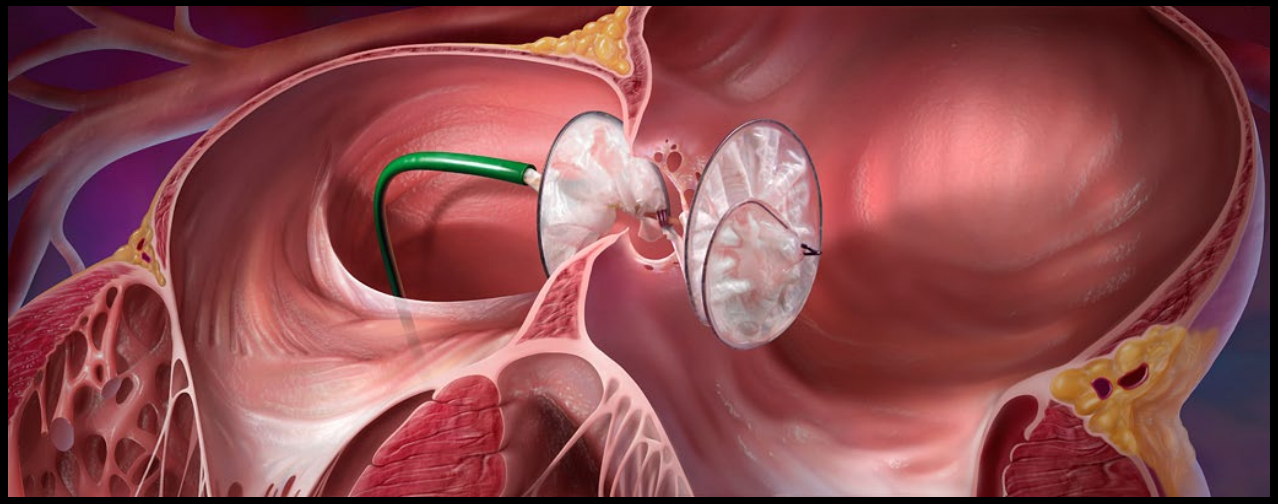
PHYSIOLOGY OF CHD

Physiologic Classification	Notes	Examples
Volume Overload Lesion	L to R shunt at atrial, ventricular or level of great vessels	ASD, VSD, PAPVR, CAVC
Obstruction to Systemic Blood Flow	Ductal dependent systemic blood flow, PGE_1	Critical AS, AoCo, IAA, HLHS
Obstruction to Pulmonary Blood Flow	Ductal dependent pulmonary blood flow, PGE_1	TOF, PS, PA with IVS
Parallel Circulation	Mixing of blood at atrial, ventricular or ductal level	D-TGA
Single Ventricle Lesions	Heterogeneous group, complete mixing of systemic and pulmonary venous blood	Unbalanced AVC, DILV, DORV, TA, Heterotaxy, HLHS
Intrinsic Myocardial Disorders	Primary or acquired	Cardiomyopathies

Modified from Gertler and Miller-Hance: "Essential of Cardiology", in Cote, Lerman, and Anderson:"A Practice of Anesthesia for Infants and Children", 5th ed, Elsevier, Ch 14 pp 291-326.

TYPES OF SURGICAL REPAIR

- DEFINITIVE
  - ANATOMIC VS FUNCTIONAL
- PALLIATIVE
- INTERVENTIONAL REPAIR



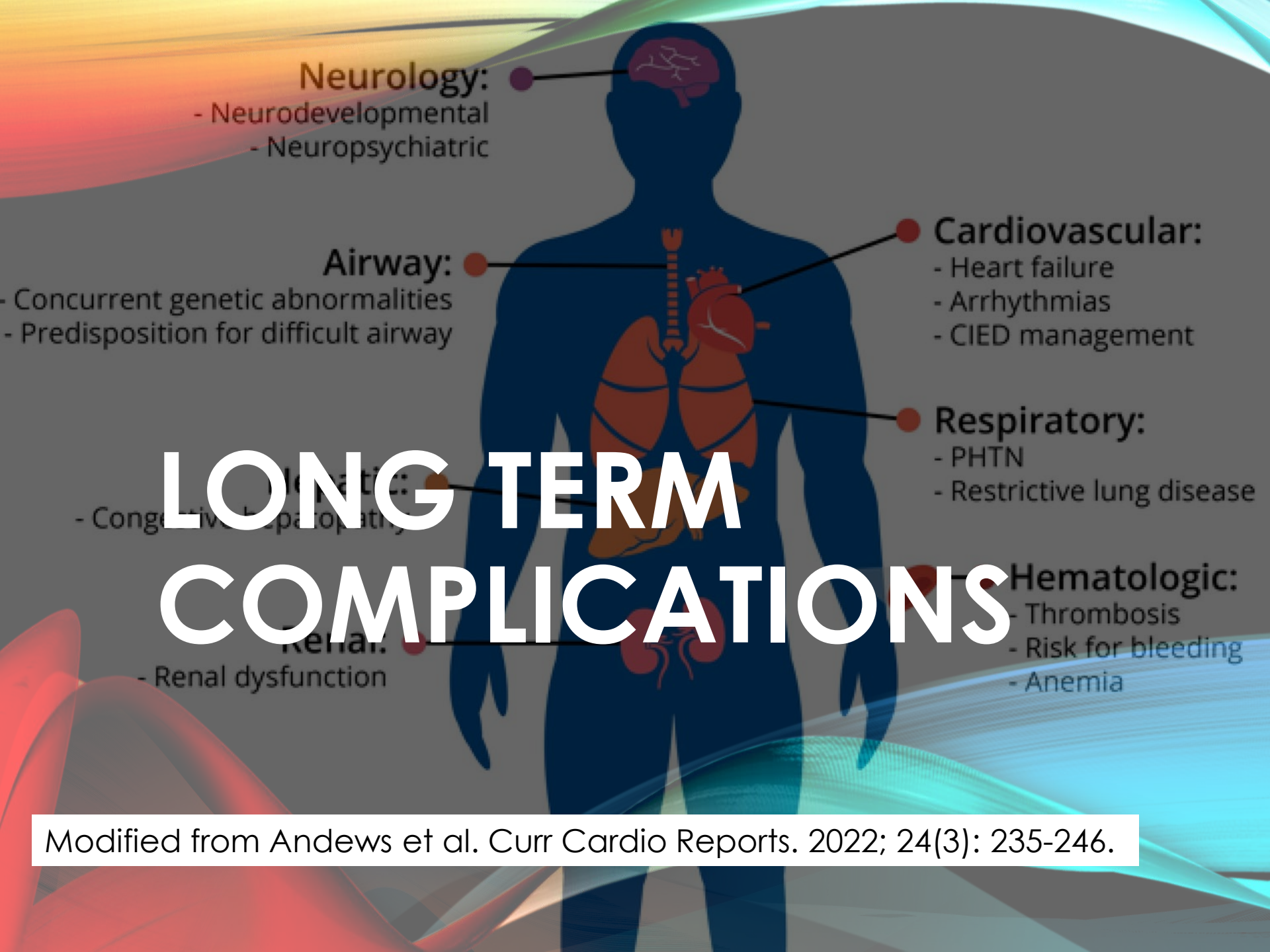
OUTCOME AFTER SURGERY

- RESIDUAL DEFECTS
  - Residual RVOT obstruction
  - Persistent valve regurgitation or stenosis
- COMPLICATIONS
  - AV Block
  - Coronary injury
  - Myocardial injury
- DIRECT SEQUELAE
  - Altered physiology
  - Systemic RV
- LONG TERM COMPLICATIONS

LONG TERM COMPLICATIONS

Congenital Heart Defect	Long Term Complications
ASD Primum, secundum Sinus venosus	Residual shunt, RV dilation, atrial arrhythmias, Pulmonary hypertension, mitral valve regurg/stenosis
CAVC Complete AV canal	Residual shunt, AV valve regurg/stenosis, Heart block, pulmonary hypertension,
Tetralogy of Fallot	Residual RVOTO or PS, residual VSD, hypoplastic PAs, PI with RV dilation, arrhythmias, sudden cardiac arrest
Coarctation of the Aorta	Residual coarctation, HTN
D-TGA Atrial switch (Mustard/Senning) Arterial switch (ASO)	Baffle leak, obstruction to systemic or pulmonary venous return, RV dilation and dysfunction, atrial arrhythmias Supravalvular stenosis (PV, AV), Coronary insufficiency, arrhythmias

Modified from Kratzert et al. Journal of Cardiothoracic and Vascular Anesthesia. 2018; 32: 1682-1700.



LONG TERM COMPLICATIONS

Modified from Andews et al. Curr Cardio Reports. 2022; 24(3): 235-246.

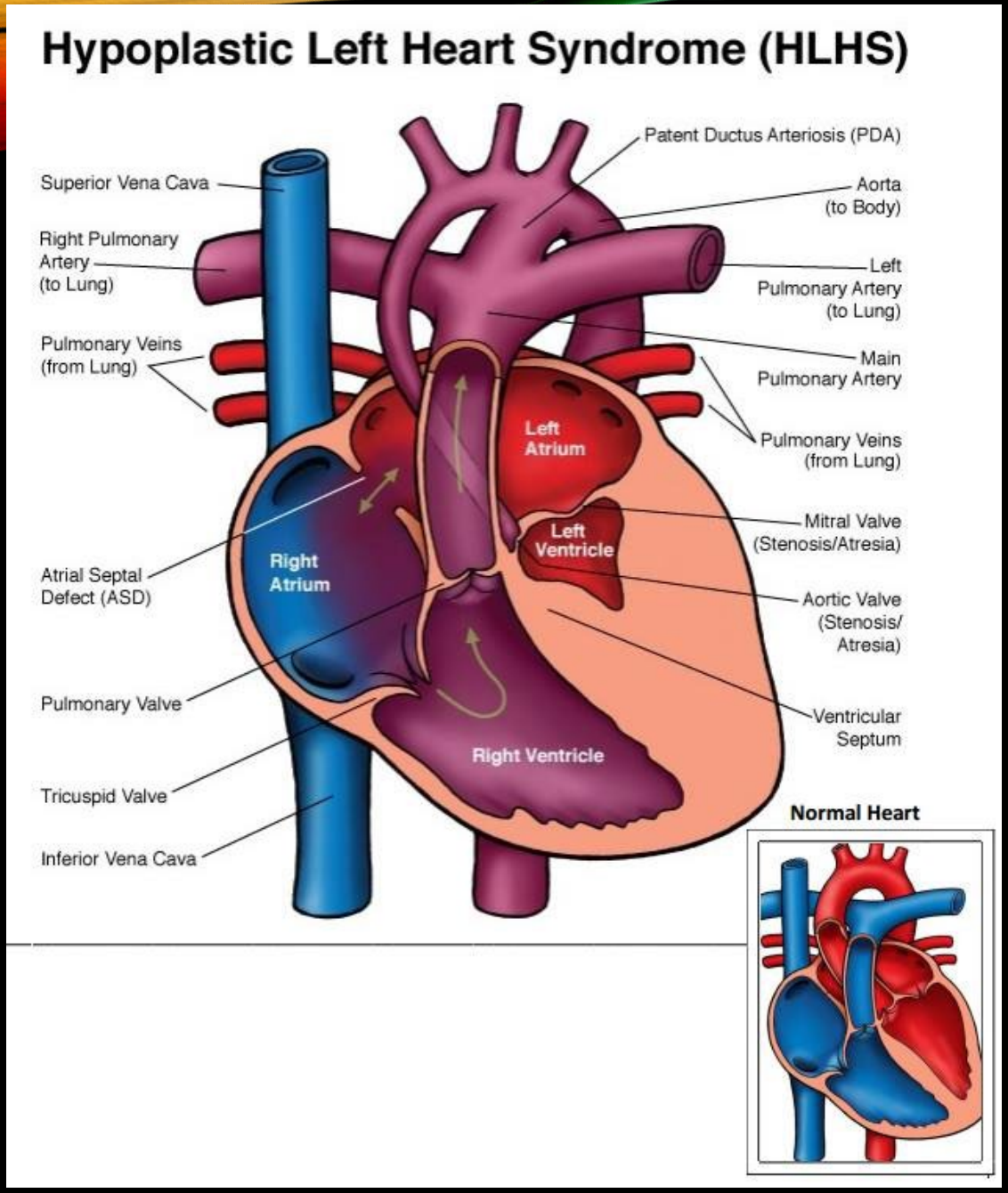
LONG TERM COMPLICATIONS

Congenital Heart Defect	Long term complications
Single ventricle: BT shunt/Sano	Shunt thrombosis, Coronary insufficiency
Glenn/Hemi Fontan	Cyanosis due to venovenous collateral circulation, hemoptysis AVM
Fontan	Increased central venous pressure, liver and renal dysfunction, protein losing enteropathy, ventricular dysfunction, SA node dysfunction, atrial arrhythmias, ascites, plastic bronchitis
Truncus Arteriosus	Truncal valve insufficiency, conduit stenosis

Modified from Kratzert et al. Journal of Cardiothoracic and Vascular Anesthesia. 2018; 32: 1682-1700.

OR SCHEDULE

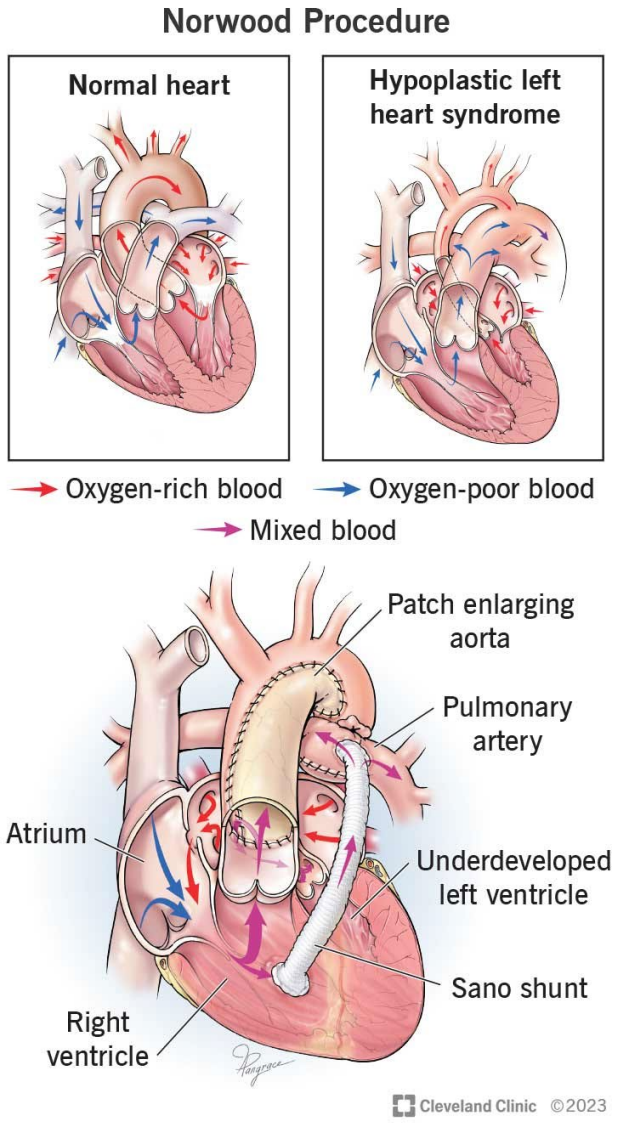
Orl/Dental	Ortho	Gen Surg	Ophthal	Ob/Gyn
23 yo, Trisomy 21 s/p CAVC repair, T & A	32 yo, dTGA s/p ASO, ORIF humerus fx	35 yo,HLHS with Fontan, lap appy	30 yo, Marfan's syndrome, detached retina	41 yo, Coarct Aorta, C section
19 yo, Heterotaxy with single ventricle/systemic RV, wisdom tooth extraction	27 yo, TOF, Hardware removal femur	45 yo, HLHS s/p OHT, ex lap bowel obstruction	6 yo, Williams syndrome, strabismus surgery	50 yo s/p Mustard, robotic hysterectomy



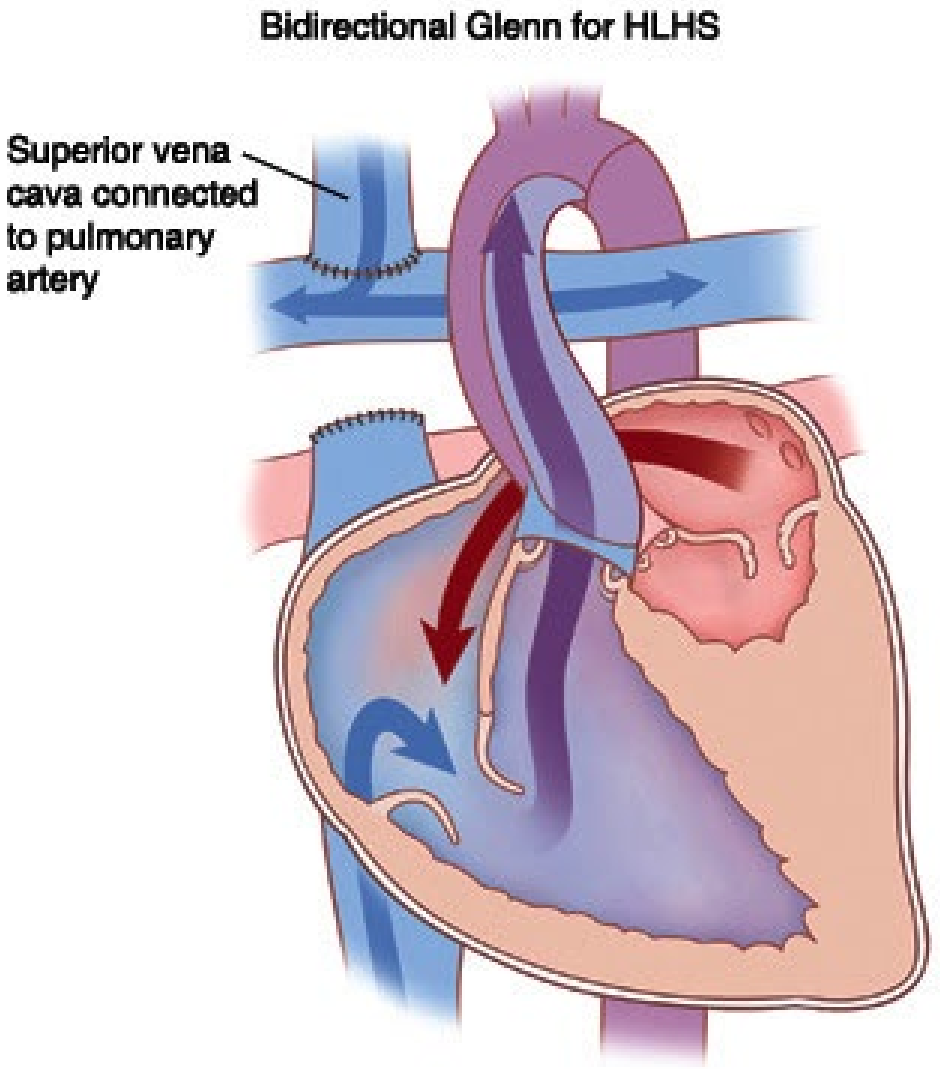
4 Subtypes:
MA/AA
MA/AS
MS/AA
MS/AS

STAGE I: NORWOOD/ SANO

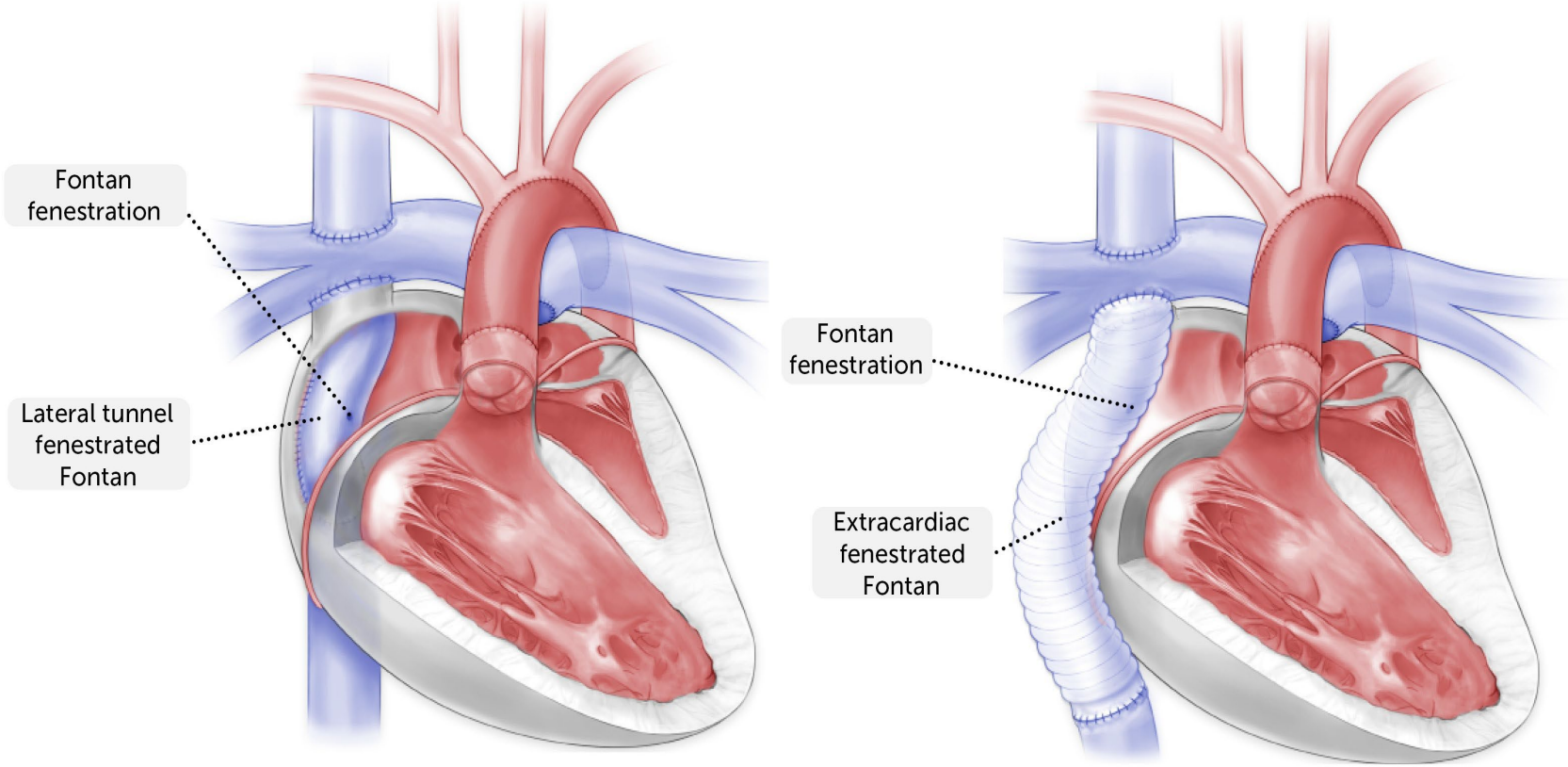
- Aortic root/Asc aorta to PA
- Arch patched
- Sano shunt
- Atrial septectomy



STAGE II: BIDIRECTIONAL GLENN

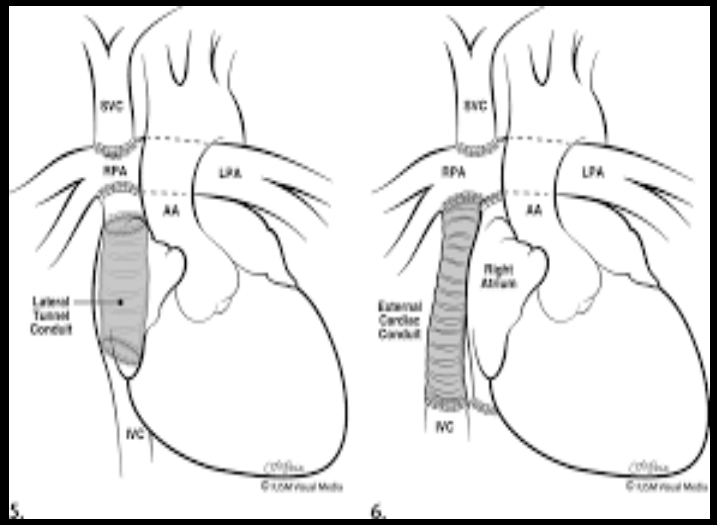


STAGE III: FONTAN/LATERAL CAVAL TUNNEL EXTRACARDIAC FONTAN



- **Biventricular circulation**
  - Series circulation: one ventricle/vascular resistance
  - CO: Preload (SV), HR, afterload, contractility
  - Preload reserve can increase 5x
- **Univentricular/Fontan circulation**
  - Series circulation with increased afterload
  - CO: Transpulmonary gradient

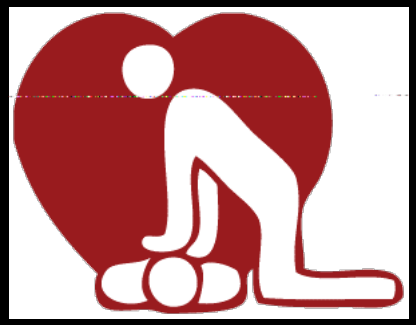
FONTAN PHYSIOLOGY



- Loss of preload reserve
- Impaired ventricular efficiency
- Blunted heart rate /chronotropic incompetence
- Limited increase in cardiac output with exercise
- Inverse relationship between mean airway pressure and cardiac output

Anesth Analg 2015; 121: 172-82

FONTAN AND CPR



- Limited efficacy
- Increased common atrial and central venous pressures limit coronary and cerebral perfusion
- Limited forward blood flow to
  - AV valve regurgitation
  - Lack of compressible chamber
  - Increased PVR
- Further increased CVP with worsening cerebral perfusion and neurologic outcome

Anesth Analg 2015; 121: 172-82

…..AND NOW ANESTHETIC MANAGEMENT

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Anesthetic Management of Patients with Fontan Physiology

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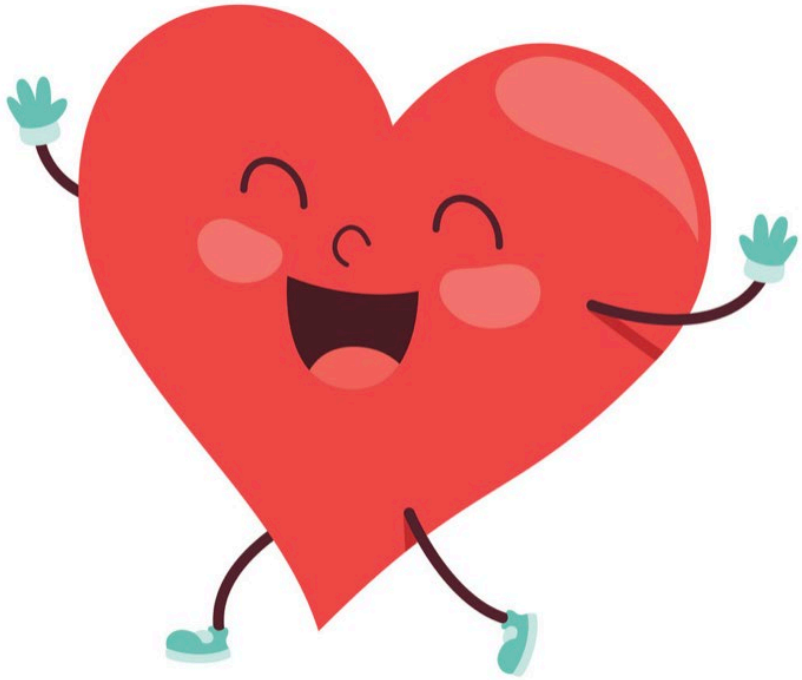
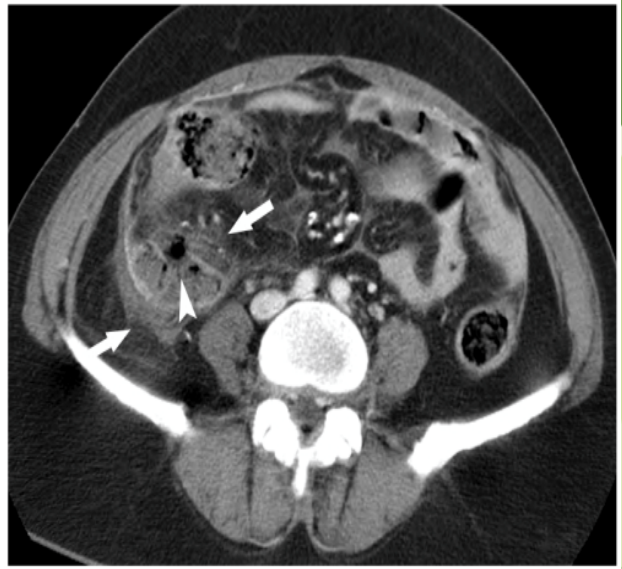
No conflicts of interest

No disclosures



23 yo Fontan Acute Appendicitis

- **3 days of periumbilical pain, nausea, vomiting**
- **Vital signs:** HR 100, BP 90/45, SpO_2 94% RA
- **Labs:** WBC 20, Hct 40 Plt 150, Na 148, Cr 1.4
- **Meds:** ASA, furosemide, enalapril, sotalol
- **PMH:**
  - Prenatal diagnosis of HLHS, Stage I on DOL 4, BDG at 5mo, Fontan at 3yo
  - Last cath at age 17y, last echo 3 months ago



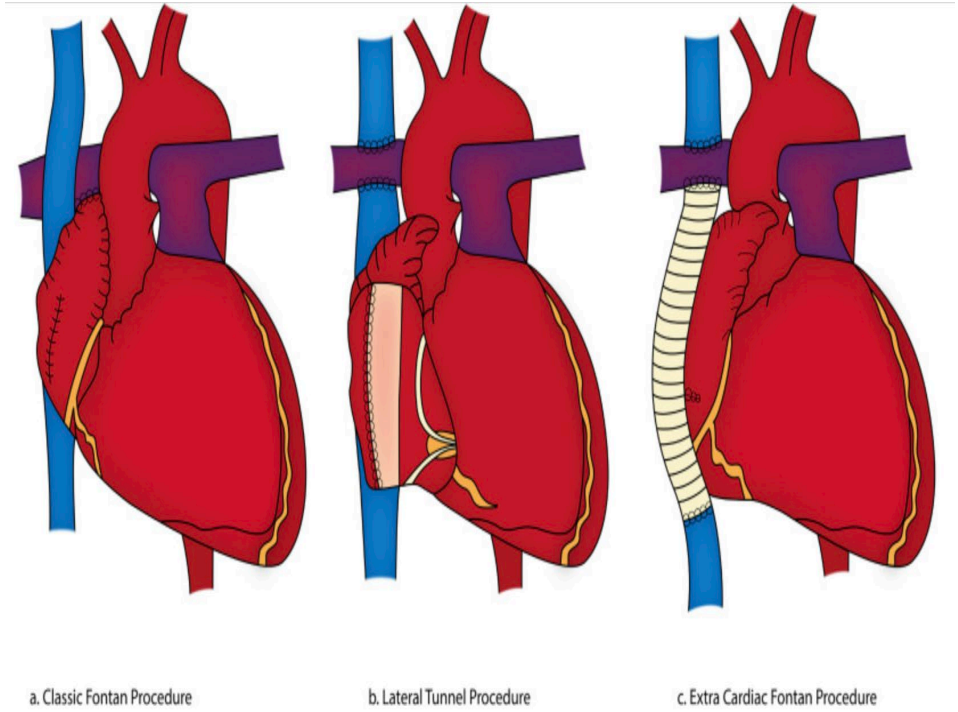
What To Do Next?

RUN!

Preoperative Evaluation

- Type of congenital heart disease - Fontan
  - Anatomy
  - Physiology
  - Types of interventions
  - Associated anomalies/ sequalae
- Past medical history
- Studies
  - Laboratory data
  - Cardiac studies (EKG, echo, cath report)
- Examination
  - Physical exam
  - Vital signs
  - Airway assessment
- Current Medications
- Type of surgery

Type of Congenital Heart Disease



- Type of CHD
- Type of Fontan
- Interventions

Associated Sequalae

- **Neurologic**
  - neurodevelopmental impairments
- **Cardiovascular**
  - Circulatory failure
  - Ventricular dysfunction
  - Arrythmias
  - Atrioventricular valve dysfunction
- **Pulmonary**
  - Plastic bronchitis
- **GI**
  - Protein losing enteropathy
- **Hematologic**
  - Elevated hemoglobin levels
  - Prothrombotic state
- **Orthopedic**
  - Bone structure and composition abnormalities
- **Hepatology**
  - Liver fibrosis
- **Genitourinary**
  - Renal dysfunction

Other Past Medical History

None

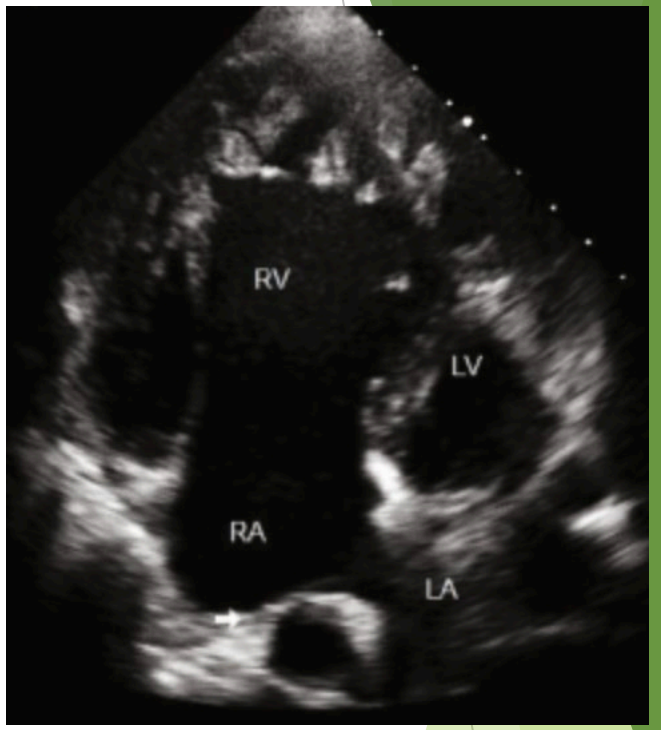
Laboratory Data

- CBC
- Electrolytes
- Renal studies - BUN/Cr
- Liver function tests
- Coagulation studies

Studies

Echo Report

- Patency of the Fontan pathway
- Presence of fenestrations
- Atrioventricular valve function
- Systolic and diastolic function of the single ventricle
- Aortic (or neoaortic) valve function and aortic patency



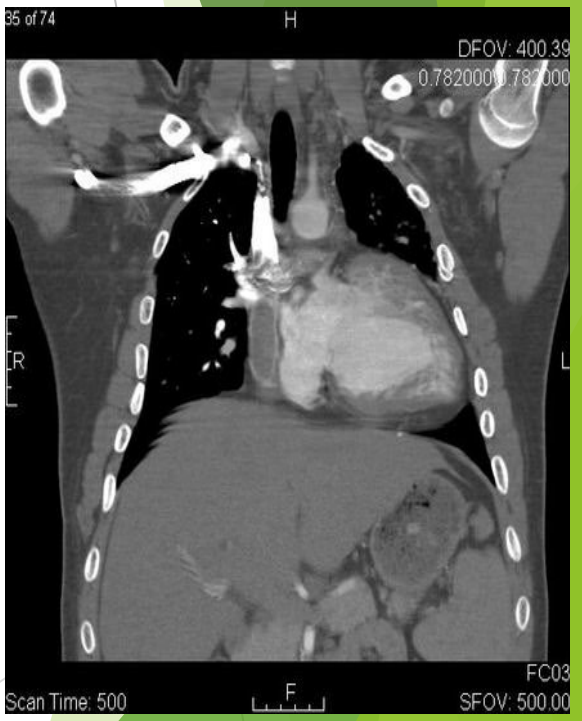
Studies

Cath Report

- fontan baffle pressure
- pulmonary artery and vein pressures
- common atrial pressure and transpulmonary gradient
- vascular occlusions

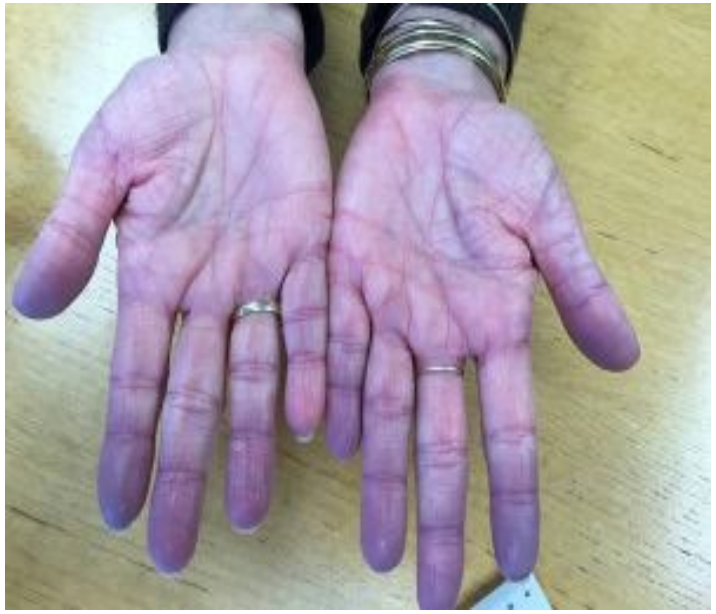
Cardiac MRI/ CT Imaging

- Thrombosis
- Intracardiac shunts
- Pulmonary vasculature assessment (presence of branch PA obstruction, pulmonary AVMs, collaterals)



Physical Exam

- **Vitals**
  - SpO2, BP, HR, RR, Temperature
- **Airway**
  - Hx of prolonged intubation?
  - Syndromic features
- **Cardiovascular**
  - Signs of volume overload
- **Pulmonary**
  - Signs of cyanosis
  - Work of breathing
  - Crackles or rales



Current Medications

- Afterload reducing agents
- Pulmonary vasodilators
- Diuretics
- Anticoagulation
- Antiarrhythmics

Type of Surgery

- IV access
- Monitoring
- Fluid shifts
- Risk stratification
- Urgency of surgery
- Position changes
- Laparoscopic vs open

Laparoscopic Vs Open

Laparoscopic

- **Advantages:**
  - Less post operative pain
  - Less pulmonary dysfunction
  - Possible shorter length of stay
- **Disadvantages:**
  - Impedance of venous return
  - Reduction in pulmonary compliance
  - Increased pCO_2 absorption from peritoneum

Open

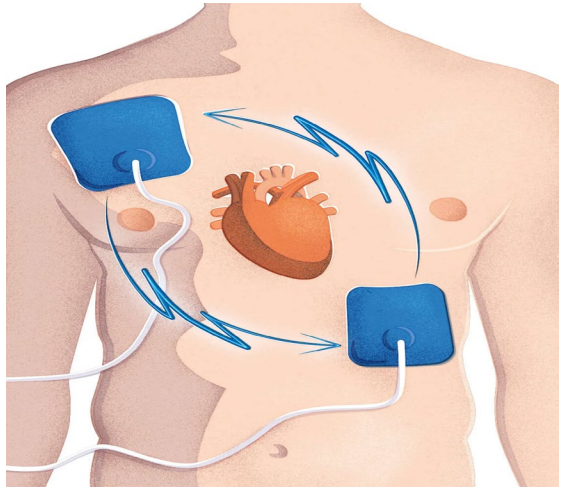
- **Advantages:**
  - Shorter procedure length
  - No insufflation
  - Less severe position changes
- **Disadvantages:**
  - Increased post operative pain which can affect respiratory mechanics

Special Considerations

- Setting – hospital, ambulatory surgery center, tertiary care center
- Experience in adult congenital heart disease?
- Specialists available
- Emergency vs elective
- Appropriate equipment available
- Monitoring available

Preoperative Care: Access and Monitoring

- **Monitoring**
  - Standard ASA monitors with 5 lead EKG
  - Arterial line?
  - Defibrillator
- **Access**
  - Central line?
  - Large bore IV access



AHA Guidelines for Infective Endocarditis Prophylaxis

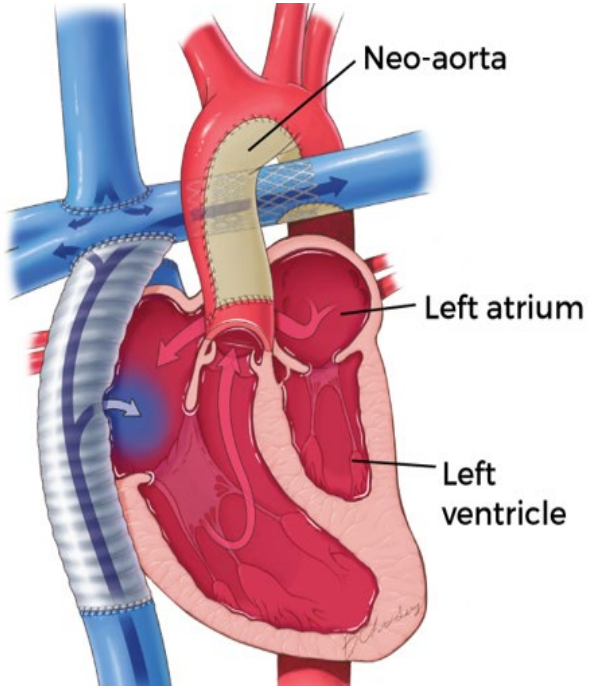
- Prosthetic cardiac valves
- Previous endocarditis
- Congenital heart disease
- Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
- Completely repaired congenital heart defects with prosthetic material or device whether placed by surgery or catheter intervention during the first 6 months after the procedure
- Repaired congenital heart disease with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device
- Cardiac transplantation recipients who develop cardiac valvulopathy

Thromboembolism Prophylaxis

- When to hold home anticoagulation?
- When to resume DVT prophylaxis?
- Sequential compression device
- Air filters

Intraoperative Management: Hemodynamic Goals

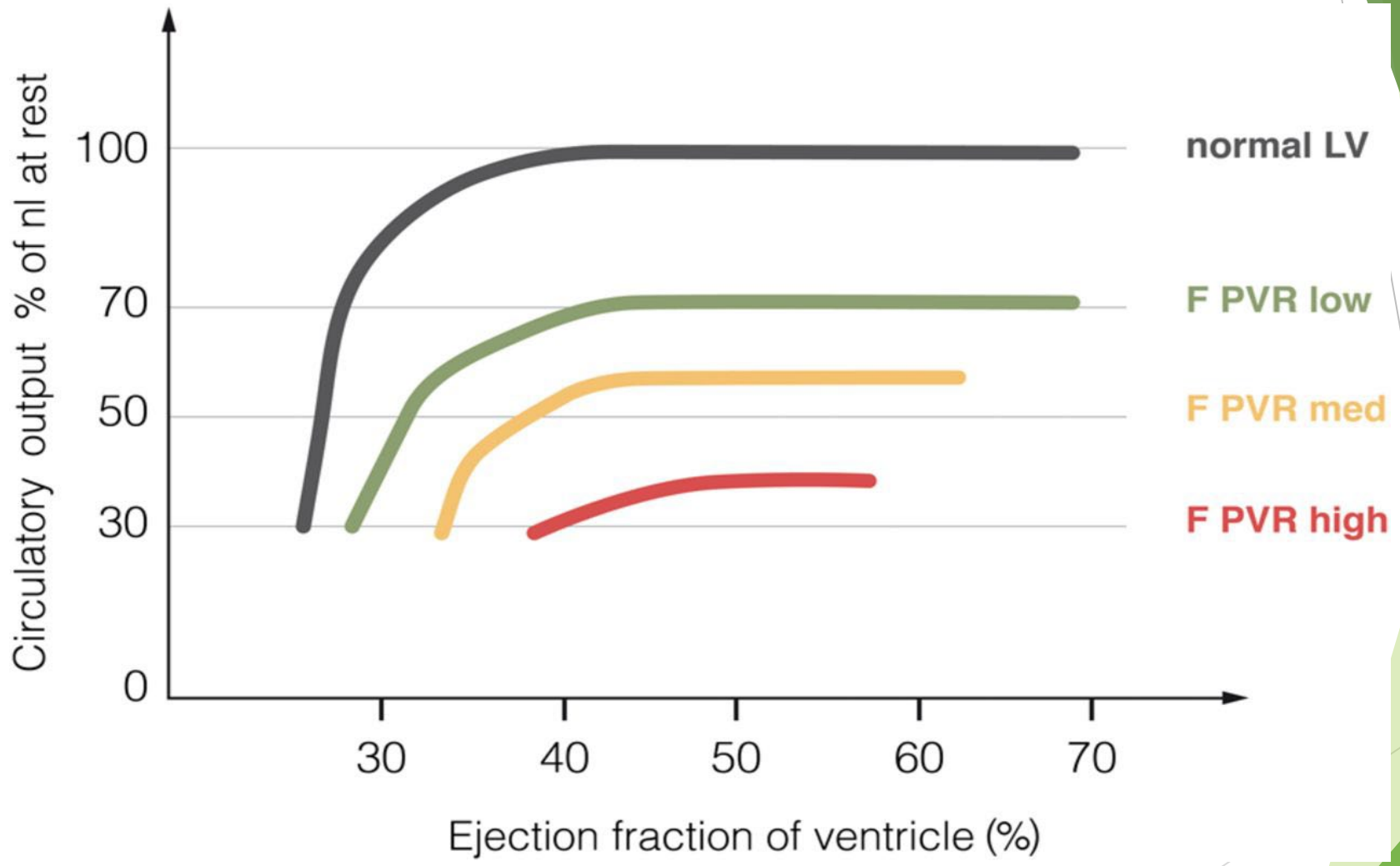
- Volume status
- Inotropes
- Vent strategies
- Arrhythmias
- Team discussion



Causes Of Reduced Cardiac Output In Fontan Circulation

Prepulmonary	Pulmonary	Postpulmonary
Hypovolemia Venodilation Increased intra-abdominal pressure Aortocaval compression Anastomotic obstruction	Pulmonary vasoconstriction • Hypercarbia • Hypoxia • Acidosis • Hypothermia PE PEEP Higher mean airway pressure	Increased LA pressure • Elevated common atrial pressure • Arrhythmia causing AV dyssynchrony • AV valve stenosis • AV valve regurgitation • Increased ventricular EDP • Systolic dysfunction • Diastolic dysfunction

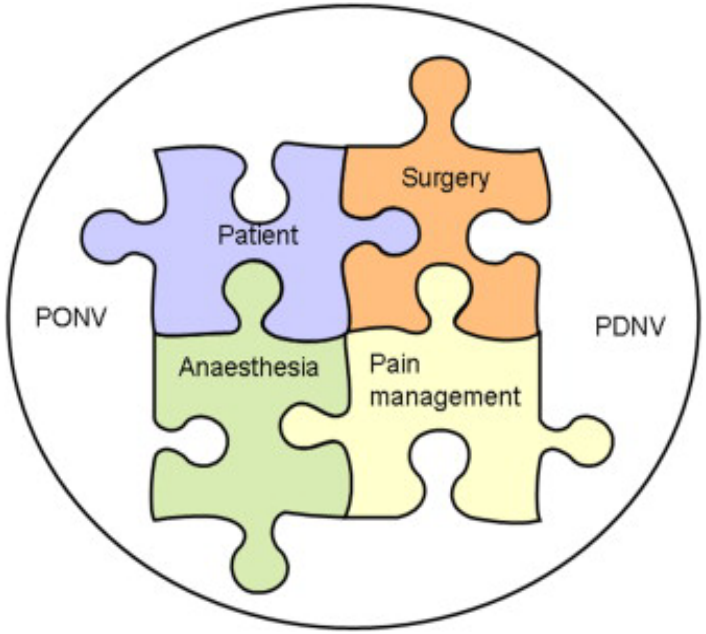
Output at rest modulated by pulmonary vascular resistance (PVR).



Marc Gewillig, and Stephen C Brown Heart 2016;102:1081-1086

Postoperative Care

- Pain control
- PONV prophylaxis and treatment
- Fluid status
- Recommencement of home medications
- Importance of early ambulation



Disposition

- ICU vs floor
- Telemetry monitoring
- Respiratory monitoring
- Involve patient's home cardiologist

Action Plan

- Conduct a thorough preoperative evaluation
- Consider access and monitoring
- Evaluate for endocarditis prophylaxis
- Remember thromboembolism prophylaxis
- Determine hemodynamic goals and fluid status
- Decide postoperative disposition
- Discuss plan and surgical considerations with surgeon

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Gewillig M, Brown SC. The Fontan circulation after 45 years: Update in physiology. *Heart*. 2016; 102: 1081-1086

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2018 AHA/ACC guideline for the management of adults with congenital heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019; 73: e81-192

Staudt GE, Hughes AK, Eagle SS. Anesthetic considerations for pediatric patients with Fontan physiology undergoing noncardiac surgery. *Int Anesthesiol Clin*. 2019; 57: 42-60

McNamara JR, McMahon A, Griffin M. Perioperative Management of the Fontan Patient for Cardiac and Noncardiac Surgery. J Cardiothorac Vasc Anesth. 2022 Jan;36(1):275-285

Rychik J, Atz AM, Celermajer DS, et al. Evaluation and management of the child and adult with Fontan circulation: A scientific statement from the American Heart Association. *Circulation.* 2019; 140: E234-E284

Use of Adjuvants in Peripheral Nerve Blocks

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Conflict of Interest

- None

Objectives

- To understand the need of using adjuvants in regional blocks
- To discuss various adjuvants that can be used in regional blocks
- To discuss in detail advantages and disadvantages of use of different adjuvants
- To go through evidence of use of adjuvants in regional block in scientific literature

Introduction

- Moderate-to-severe postoperative pain is common and remains an unresolved problem
- Compared with opioid-based analgesia alone, peripheral nerve blockade has been associated with better pain relief
- One drawback of single-shot peripheral nerve blockade is its limited duration of action
- Strategies have been explored to extend the benefits of peripheral nerve blockade beyond 8–14 h

TABLE 1. Benefits of regional anaesthetic techniques in trauma-orthopaedic surgery

Better pain management
Shorter hospital stays
Lower treatment costs
Reduced perioperative morbidity and mortality
Improved function of the affected joint
Reduced risk of surgical site infection
Reduced demands for homologues blood transfusions
Lower incidences of persistent postoperative pain
Improvement of patient's satisfaction

- Gola W, Zając M, Cugowski A. Adjuvants in peripheral nerve blocks - the current state of knowledge. Anaesthesiol Intensive Ther. 2020;52(4):323-329. doi: 10.5114/ait.2020.98213. PMID: 33165883; PMCID: PMC10183787.

These techniques include:

- continuous nerve/plexus block followed by an infusion of a local anesthetic
- liposomal forms of local anesthetics
- intravenous or perineural delivery of adjuvants

Continuous peripheral nerve blocks

- Associated with decreased rebound pain [1] and improved postoperative analgesia [2]
- Rate of secondary block failure has been reported to be as high as 20–50%, due to catheter migration, obstruction or shearing, fluid leakage and infusion pump malfunction
- Other complications include: inaccurate placement of the catheter tip; knotting; mechanical nerve irritation; inflammation at the insertion site; bacterial colonization; and local anesthetic systemic toxicity

1. Williams BA, Bottegal MT, Kentor ML, Irrgang JJ, Williams JP. Rebound pain scores as a function of femoral nerve block duration after anterior cruciate ligament reconstruction: retrospective analysis of a prospective, randomized clinical trial. Regional Anesthesia and Pain Medicine 2007; 32: 186–92.
2. Salviz EA, Xu D, Frulla A, et al. Continuous interscalene block in patients having outpatient rotator cuff repair surgery: a prospective randomized trial. Anesthesia and Analgesia 2013; 117: 1485–92.

TABLE 2. Problems associated with the use of continuous peripheral nerve blocks

Organizational and logistics problems
Possible catheter migration/spontaneous dislocation
Local anaesthetic leak along the catheter channel
Equipment problems – infusion pump dysfunctions
Catheter infections
Neurological complications
Higher daily dose of local anaesthetic
The risk of local anaesthetic systemic toxicity (LAST)

- Gola W, Zając M, Cugowski A. Adjuvants in peripheral nerve blocks - the current state of knowledge. Anaesthesiol Intensive Ther. 2020;52(4):323-329. doi: 10.5114/ait.2020.98213. PMID: 33165883; PMCID: PMC10183787.

Liposomal Bupivacaine

- Liposomal bupivacaine is a simpler alternative
- Meta-analyses, however, to date have not supported the additional benefit of these prolonged release formulations for operative site infiltration or single-shot peripheral nerve blockade [3] [4]

3 Kendall MK, Castro Alves LJ, De Oliveira G. Liposome bupivacaine compared to plain local anesthetics to reduce postsurgical pain: an updated meta-analysis of randomized controlled trials. Pain Research and Treatment 2018; 2018: 5710169.

4 Hamilton TW, Athanassoglou V, Trivella M, et al. Liposomal bupivacaine peripheral nerve block for the management of postoperative pain. Cochrane Database of Systematic Reviews 2016; 2016: CD011476.

Adjuvants

TABLE 3. Classification of adjuvants

Old	New
Adrenalin Sodium bicarbonate Clonidine Buprenorphine Tramadol Ketamine Midazolam	Dexamethasone Dexmedetomidine

- Gola W, Zając M, Cugowski A. Adjuvants in peripheral nerve blocks - the current state of knowledge. Anaesthesiol Intensive Ther. 2020;52(4):323-329. doi: 10.5114/ait.2020.98213. PMID: 33165883; PMCID: PMC10183787.

Epinephrine

- One of the oldest adjuvants
- Causes a decrease in the absorption of LA into blood vessels, prolonging the time of contact of LA with nerve
- Dose- 2.5–5 µg/mL of LA solution.
- Prolonged block after perineural adrenaline deposition ranges from 33 to 100 mins (average: 60 mins) [(5)]
- Limits the distribution of LA to the central compartment, thus reducing the risk of local anesthetic systemic toxicity

(5)Tschopp C, Tramer MR, Schneider A, Zaarour M, Elia N. Benefit and harm of adding epinephrine to a local anesthetic for neuraxial and locoregional anesthesia: a meta-analysis of randomized controlled trials with trial sequential analyses. Anesth Analg 2018; 127: 228-239.

- Concerns have been raised in regard to an increased susceptibility to neurotoxicity secondary to the decrease in blood flow to the peripheral nerve when perineural adrenaline is administered.
- In patients with acquired peripheral neuropathy, the American Society of Regional Anesthesia recommends that the anesthetic technique be modified with the elimination, or reduction in the concentration, of adrenaline (6)

(6)Neal JM, Barrington MJ, Brull R, et al. The Second ASRA Practice Advisory on neurologic complications associated with regional anesthesia and pain medicine: executive summary 2015. Regional Anesthesia and Pain Medicine 2015; 40: 401–30.

Sodium Bicarbonate

- Accelerates the block onset.
- MOA is to increase the pH of the solution and thus facilitate the dissociation of the LA to an alkaline form, which is fat-soluble and diffuses into the nerve fibre, where re-ionization and reversible blocking of sodium channels occur.
- Does not increase the duration of analgesia

- Most common problem is the precipitation of LA.
- To avoid this, the right dose of adjuvant in the solution should be used
- For lidocaine, 1 mL $NaHCO_3$ – per 10 mL LA,
- For bupivacaine, 0.1 mL $NaHCO_3$ – per 10 mL LA.
- No clinical effect for the bicarbonate-ropivacaine combination [7]

(7)Ramos G, Pereira E, Simonetti MP. Does alkalinization of 0.75% ropivacaine promote a lumbar epidural block of higher quality? Reg Anesth Pain Med 2001; 26: 357-62. doi.org/10.1053/rapm.2001. 24257

Alpha 2-Adrenoreceptor Agonists

- Clonidine
- Dexmedetomidine

- Clonidine selectivity for α-2 adrenergic receptors over α-1 adrenergic receptors is only 200 : 1
- Dexmedetomidine selectivity- 1600:1

Clonidine

- MOA after perineural administration is unlikely to be due to activity at a2-adrenoreceptors as they are not present on the axons of peripheral nerves.
- Instead, clonidine is thought to block the hyperpolarisation-activated nucleotide-gated channels that are responsible for the hyperpolarisation-activated cation currents.
- Able to maintain the Ad and C neurones in a hyperpolarised state, thereby inhibiting the generation of action potentials
- Also work by inducing localized vasoconstriction mediated through its less selective stimulation of a1-adrenoreceptors

- Meta-analysis of 20 RCTs, Popping et al. evaluated perineural clonidine at a dose range of 30–300 mcg in mainly brachial plexus blockade, but also ankle, cervical plexus, femoral, iliohypogastric, ilio-inguinal and sciatic nerve blocks [23].
- Demonstrated that its co-administration increased the mean duration of analgesia, sensory block and motor block by 123 min, 74 min and 141 min, respectively, irrespective of whether short-acting, intermediate-acting or long- acting LA

- Adverse effects- bradycardia, hypotension, fainting and sedation
- No clinically significant differences in the time to onset of sensory or motor block were found.

- Popping DM, Elia N, Marret E, Wenk M, Tramer MR. Clonidine as an adjuvant to local anesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology 2009; 111: 406–15.

Dexmedetomidine

- MOA likely to be similar to that of clonidine, although unlike clonidine it is not thought to mediate localized vasoconstriction through a1- adrenoreceptor stimulation.

- Meta-analysis of 34 RCTs, Vorobeichik et al. evaluated perineural dexmedetomidine in only brachial plexus blockade (8). demonstrating increased mean duration of analgesia, sensory block and motor block by 264 min, 228 min and 192 min, respectively.
- One of the trials indicated that dexmedetomidine can produce a differential sensorimotor effect, extending sensory block without prolonging motor block (9). This may reflect a possible greater inhibitory effect on Ad and C nerve fibers relative to motor neurons.
- Decreased time to onset of sensory block from 20 min to 11 min

- Reduced time to onset of motor block from 21 min to 13 min (8).
- Lowered the cumulative morphine consumption at 24 h
- Associated with improved patient satisfaction.
- Adverse effects- bradycardia, hypotension and sedation

(8)Vorobeichik L, Brull R, Abdallah FW. Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and meta-analysis of randomized controlled trials. British Journal of Anaesthesia 2017; 118: 167–81.

(9)Abdallah FW, Dwyer T, Chan VWS, et al. IV and perineural dexmedetomidine similarly prolong the duration of analgesia after interscalene brachial plexus block: a randomized, three arm, triple-masked, placebo-controlled trial. Anesthesiology 2016; 124: 683–95.

Opioids

- Inflammation induces the expression of opioid receptors in peripheral nerve fibers and on immune response cells
- Trauma and inflammation-induced ability to express opioid receptors and the production of endogenous opioids by the immune system is a time-delayed process and usually takes up to 96 hours after injury
- Injury to the nerve tissue in the dorsal root ganglion (DRG) results in an increased production of opioid receptors, followed by their axonal transport in microtubules towards the peripheral nerve endings, where they are incorporated into the nerve membrane.

- Extremely difficult to determine whether the analgesic effect of opioids is the result of their effect only on the peripheral opioid receptors, or is a central action occurring after redistribution

Buprenorphine

- Buprenorphine is a MOP partial opioid receptor agonist and KOP opioid receptor agonist.
- MOA is likely to be due to concentration-dependent blockade of voltage-gated sodium channels, inhibiting the generation of action potentials, and interaction with MOP opioid receptors on the axons of unmyelinated C fibers

- Meta-analysis of 11 RCTs, Schnabel et al. evaluated perineural buprenorphine in mainly brachial plexus blockade, but also femoral and sciatic nerve blocks
- They demonstrated that co-administration increased the mean duration of analgesia and motor block by 518 min and 13 min, respectively.
- No clinically significant differences in the time to onset of sensory or motor block
- Adverse effects- postoperative nausea, vomiting and pruritus

Schnabel A, Reichl SU, Zahn PK, Pogatzki-Zahn EM, Meyer- Frießem CH. Efficacy and safety of buprenorphine in peripheral nerve blocks: a meta-analysis of randomized controlled trials. European Journal of Anaesthesiology 2017; 34: 576–86.

Dexamethasone

- The mechanism responsible for prolonging block duration after the use of dexamethasone as an adjuvant to LA is multidirectional and extremely complex

TABLE 4. Mechanisms responsible for prolonging block duration after dexamethasone

Decrease in C-nociceptive activity (direct effect on glucocorticoid receptor)
Inhibition of potassium channels
Local vasoconstrictive effect
Systemic anti-inflammatory effect
Agonistic effects on central α-2-adrenergic receptors
Peripheral nerve fibre hyperpolarization support
Synaptic transmission block
Reduction of perineural inflammation

- Gola W, Zając M, Cugowski A. Adjuvants in peripheral nerve blocks - the current state of knowledge. Anaesthesiol Intensive Ther. 2020;52(4):323-329. doi: 10.5114/ait.2020.98213. PMID: 33165883; PMCID: PMC10183787.

- Meta-analysis of 29 trials, Albrecht et al. demonstrated increased mean duration of analgesia by 233 min and 488 min if injected with short, medium or long-acting LAs respectively
- Perineural dexamethasone prolonged the mean duration of motor block by 150 min and 286 min when injected with short or intermediate-acting and long-acting LAs, respectively.
- Dexamethasone can induce an increase in the postoperative blood glucose concentration subsequent to either perineural or i.v. administration.

- Albrecht E, Kern C, Kirkham KR. A systematic review and metaanalysis of perineural dexamethasone for peripheral nerve blocks. Anaesthesia 2015; 70: 71–83.

- In brachial plexus blockade, perineural dexamethasone has a ceiling effect on the mean duration of analgesia at a dose of 4 mg with short- or intermediate-acting and long-acting LAs

- Albrecht E, Reynvoet M, Fournier N, Desmet M. Dose–response relationship of perineural dexamethasone for interscalene brachial plexus block: a randomised, controlled, triple-blind trial. Anaesthesia 2019; 74: 1001–8.
- Kirkham KR, Jacot-Guillarmod A, Albrecht E. Optimal dose of perineural dexamethasone to prolong analgesia after brachial plexus blockade: a systematic review and meta-analysis. Anesthesia and Analgesia 2018; 126: 270–9.

Neuroprotection with Dexamethasone

- In-vitro study examining dexamethasone demonstrated that it attenuated the cytotoxic effect of bupivacaine on mouse neuroblastoma cells
- In another in-vitro study, dexamethasone at high concentration when coadministered with ropivacaine did not have an incremental neurotoxic effect relative to ropivacaine alone on dorsal root ganglia isolated from rats
- A follow up in-vivo study, sciatic nerve blocks performed with bupivacaine and dexamethasone in rats did not result in histopathological or neurobehavioural changes

- In human trials to date, perineural dexamethasone has not been associated with neurological complications and no neurological sequelae were reported in a series of over 2000 intrathecal injections of dexamethasone for posttraumatic visual disturbance

- Ma R, Wang X, Lu C, et al. Dexamethasone attenuated bupivacaine-induced neuron injury in vitro through a threonine-serine protein kinase B-dependent mechanism. Neuroscience 2010; 167: 329–42.
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- Williams BA, Butt MT, Zeller JR, Coffee S, Pippi MA. Multimodal perineural analgesia with combined bupivacaine-clonidinebuprenorphine- dexamethasone: safe in vivo and chemically compatible in solution. Pain Medicine 2015; 16: 186–98.

Cochrane Database Systemic Review

- included 35 trials of 2702 participants, 33 studies enrolled participants undergoing upper limb surgery and two undergoing lower limb surgery.
- Duration of sensory block was significantly longer in the perineural dexamethasone group compared with placebo
- Postoperative pain intensity at 12 and 24 hours was significantly lower in the perineural dexamethasone group compared with control

- Cumulative 24-hour postoperative opioid consumption was significantly lower in the perineural dexamethasone group compared with placebo

- Pehora C, Pearson AM, Kaushal A, Crawford MW, Johnston B. Dexamethasone as an adjuvant to peripheral nerve block. Cochrane Database Syst Rev. 2017 Nov 9;11(11):CD011770. doi: 10.1002/14651858.CD011770.pub2. PMID: 29121400; PMCID: PMC6486015

Recent Systemic Review

- 79 studies selected using our criteria showed a clear prevalence of dexamethasone (n = 24) and dexmedetomidine (n = 33) over other adjuvants.
- Results were reported according to the PRISMA guidelines
- Different meta-analyses comparing adjuvants suggest that dexamethasone administered perineurally achieves superior blockade with fewer side effects than dexmedetomidine.

- Moderate evidence to recommend the use of dexamethasone as an adjuvant to peripheral regional anesthesia in surgeries that can cause moderate to severe pain.

- Fernández Martin, M. T., Alvarez Lopez, S., & Aldecoa Alvarez-Santullano, C. (2023). Role of adjuvants in regional anesthesia: A systematic review. *Revista espanola de anestesiologia y reanimacion*, *70*(2), 97–107. https://doi.org/10.1016/j.redare.2021.06.006

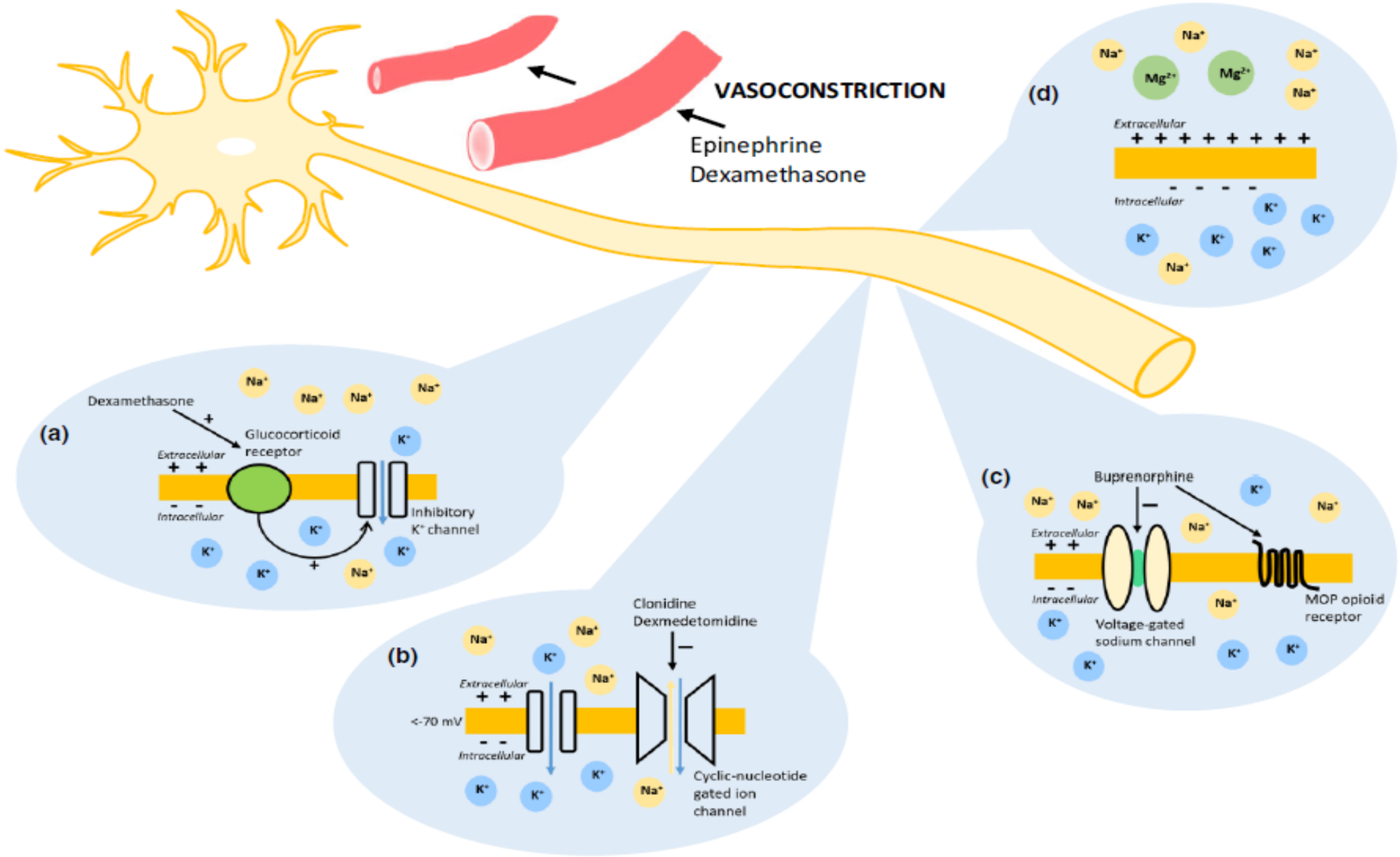

Figure 1 Mechanisms of action of local anaesthetic adjuncts on the cell membrane of neurones and the blood vessels. (a) Dexamethasone stimulates glucocorticoid receptors, increasing the expression of inhibitory potassium channels and decreasing the excitability of neurones. (b) Clonidine and dexmedetomidine inhibit the hyperpolarisation-activated nucleotide-gated channels, maintaining the neurone at a more negative potential and hence hyperpolarised state. (c) Buprenorphine inhibits voltage-gated sodium channels, preventing the generation of action potentials, and interacts with MOP (μ) receptors. (d) Magnesium results in the hyperpolarisation of the neurone secondary to the interaction between its positive divalent charge and the neuronal membrane.

TABLE 5. Summary of the most common adjuvants

Adjuvant	Perineural dose	Medium block extension (hours)	Side effects
Adrenaline	2.5–5 μg mL^{-1}	1	–
Clonidine	150 μg	2	Hypotension Bradycardia Sedation
Buprenorphine	0.1–0.3 mg	9	PONV
Dexmedetomidine	50–60 μg	5	Hypotension Bradycardia Sedation
Dexamethazone	4 mg	8	Slight increase in glycaemia

PONV – postoperative nausea and vomiting

- Gola W, Zając M, Cugowski A. Adjuvants in peripheral nerve blocks - the current state of knowledge. Anaesthesiol Intensive Ther. 2020;52(4):323-329. doi: 10.5114/ait.2020.98213. PMID: 33165883; PMCID: PMC10183787.

Table 2 Comparison of the effect of local anaesthetic adjuncts administered perineurally on indices of block characteristics and incidence of side-effects. All data have been extracted from meta-analyses and their included trials.

	Duration of analgesia; min	Onset of sensory block; min	Duration of sensory block; min	Onset of motor block; min	Duration of motor block; min	Block failure	Pain scores at less than or equal to 24 h	Cumulative postoperative opioid consumption at 24 h; morphine equivalents in mg	Side-effects
Historical local anaesthetic adjuncts									
Adrenaline [15]	+66	ND	Increased/ ND	ND	Increased/ ND	ND	Not studied	Not studied	Hypertension Tachycardia
Buprenorphine [20]	+518	ND	Increased/ ND	−0.3	+13	Not studied	Decreased	Not studied	PONV (RR 5) Pruritus (RR 6)
Clonidine [23]	+123	−2	+74	ND	+141	ND	Decreased/ ND	Not studied	Bradycardia (OR 3.1) Arterial hypotension (OR 3.6) Orthostatic hypotension (OR 2.3) Sedation (OR 5.1)
Magnesium [27]	+125	ND	+107	−1	+90	ND	Decreased	Decreased	ND
Novel local anaesthetic adjuncts									
Dexmedetomidine [34, 52]	+264	−9	+228 to 346	−8	+192	ND	Decreased	−10	Bradycardia (OR 7.4) Sedation (OR 11.8)
Dexamethasone [41]	+233 to 488	−1	+233 to 488	−1	+286	ND	Decreased	−19	Increase in mean blood glucose concentration by 0.2 mmol l^{-1}

ND, no difference; PONV, postoperative nausea and vomiting; RR, risk ratio; OR, odds ratio.

Table 3 Comparison of the characteristics of an ideal local anaesthetic adjunct with perineural dexmedetomidine and dexamethasone.

Characteristics of an ideal local anaesthetic adjunct	Dexmedetomidine	Dexamethasone
Available as a preservative-free preparation	+	+
Chemically compatible with local anaesthetics	+	+*
Plausible mechanism of action	+	+
Effective for all nerve blocks	+	+
No chrondrotoxic, myotoxic and neurotoxic effects	?	+
Evidence of dose-response relationship	–	+
Increase in the duration of analgesia	+	+
Increase in the duration of sensory block	+	+
No prolongation of motor block	–	–
No significant systemic side-effects	–	+

+, yes; ?, unclear; –, no.
*Dexamethasone is not compatible with ropivacaine in-vitro.

Table 1 Summary of evidence for local anaesthetic adjuncts that have demonstrated limited benefits and/or increased neurotoxicity and side-effects.

Adjunct	Evidence
Midazolam	Limited demonstrated perineural effectiveness Evidence of in-vitro and in-vivo neurotoxicity No increase in neurological symptoms after intrathecal injection in humans
Fentanyl	Conflicting findings for perineural effectiveness overall Possible efficacy if administered with bupivacaine Side-effects reported include hypercapnia, bradycardia and sedation
Morphine	Conflicting findings for perineural effectiveness No clear evidence of superiority over systemic administration
Tramadol	Conflicting findings for perineural effectiveness No clear evidence of superiority over systemic administration
Ketamine	Lack of demonstrated perineural effectiveness Evidence of in-vitro and in-vivo neurotoxicity Side-effects reported include drowsiness, hallucinations and nausea
Neostigmine	Lack of demonstrated perineural effectiveness Evidence of in-vitro and in-vivo neurotoxicity Significant side-effect profile, including nausea and vomiting

Adjuvant Use in IVRA

- Intravenous regional anaesthesia (IVRA) was first described in 1908 by the father of regional anesthesiology, August Bier
- Used for minor and short soft tissue procedures on the forearm and hand, much less frequently for the lower leg and foot procedures
- Also indicated for the management of the complex regional pain syndrome (CRPS)

- Over the years, many different substances have been used for this purpose, including opioids, α-2 adrenergic receptor agonists, muscle relaxants, neostigmine, alkalizing drugs (NaHCO3), non-steroidal anti-inflammatory drugs, and corticosteroids
- Most studies concern ketorolac: its addition to lidocaine in a dose of 20 mg significantly improves tourniquet tolerance and extends the time of postoperative analgesia without inducing any significant adverse effects

- Reuben SS, Steinberg RB, Kreitzer JM, Duprat KM. Intravenous regional anesthesia using lidocaine and ketorolac. Anesth Analg 1995; 81: 110-113. doi: 10.1097/00000539-199507000-00022.
- Seyfi S, Banihashem N, Bijani A, Hajian-Taliki K, Daghmehchi M, Caspian J. Analgesic effects of lidocaine-ketorolac compared to lidocaine alone for intravenous regional anesthesia. Intern Med 2018; 32-37. doi: 10.22088/cjim.9.1.32.

Conclusion

- Due to limitations and problems associated with continuous nerve and plexus blocking techniques, the use of adjuvants is a good and safe way to prolong postoperative analgesia
- None of the potential medications investigated to date fulfil all the criteria of the ideal local anesthetic adjunct, but dexmedetomidine and dexamethasone demonstrate the most supporting evidence.
- Dexmedetomidine is more limited by its adverse side-effect profile than dexamethasone

- In acknowledgement of the concerns regarding the neurotoxic effects of all potential local anesthetic adjuncts, use of dexamethasone is recommended
- An additional benefit of intravenous dexamethasone is the reduction in postoperative nausea and vomiting

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