

Methadone dosing for opioid use disorder in the setting of infective endocarditis and QT_c prolongation

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Background

- Injection drug use-associated infective endocarditis (IDU-IE) among patients with opioid use disorder (OUD) is associated with significant morbidity and mortality¹.
- Methadone is an effective treatment for OUD but carries a risk of QTc prolongation and torsades de pointes (TdP)².
- Limited data exists to guide methadone titration for concurrent OUD and QT_c prolongation in the setting of surgically managed IDU-IE.

QT Interval Correction

- The QT interval may be delayed in the setting of ventricular conduction delay or ventricular pacing, increasing the risk of TdP.
- Patients undergoing surgical tricuspid valve repair (TVR) are at risk for heart block due to proximity of the tricuspid annulus to the conduction system (Fig.1B).
- QT_c prolonging medications contribute to the risk of developing TdP.
- Accurate QT_c interpretation is essential for IDU-IE patients with acquired QT_c prolongation, ventricular pacing (VP), and/or use of QT_c prolonging medications (*i.e.*, methadone).
- The QT interval must be corrected (QT_c) for a widened QRS complex and heart rate³.
- A Bazett correction ($QT_{cB} = \frac{QT}{\sqrt{RR}}$) is commonly utilized but inaccurately estimates QT_c at heart rates higher or lower than 60 bpm.
- In this series, we use a Bogossian correction to determine QT_m followed by the Hodges formula for QT correction³.

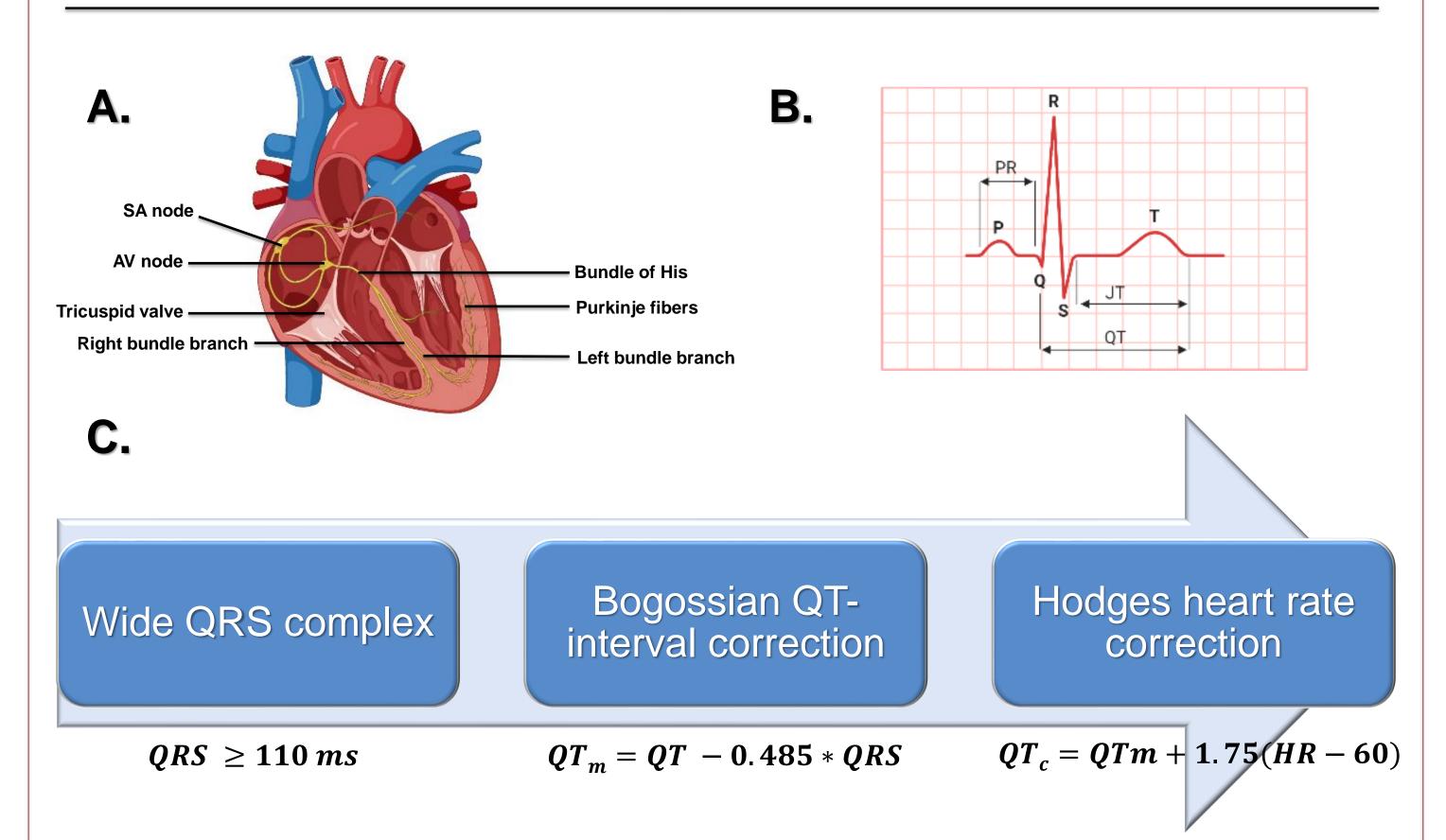
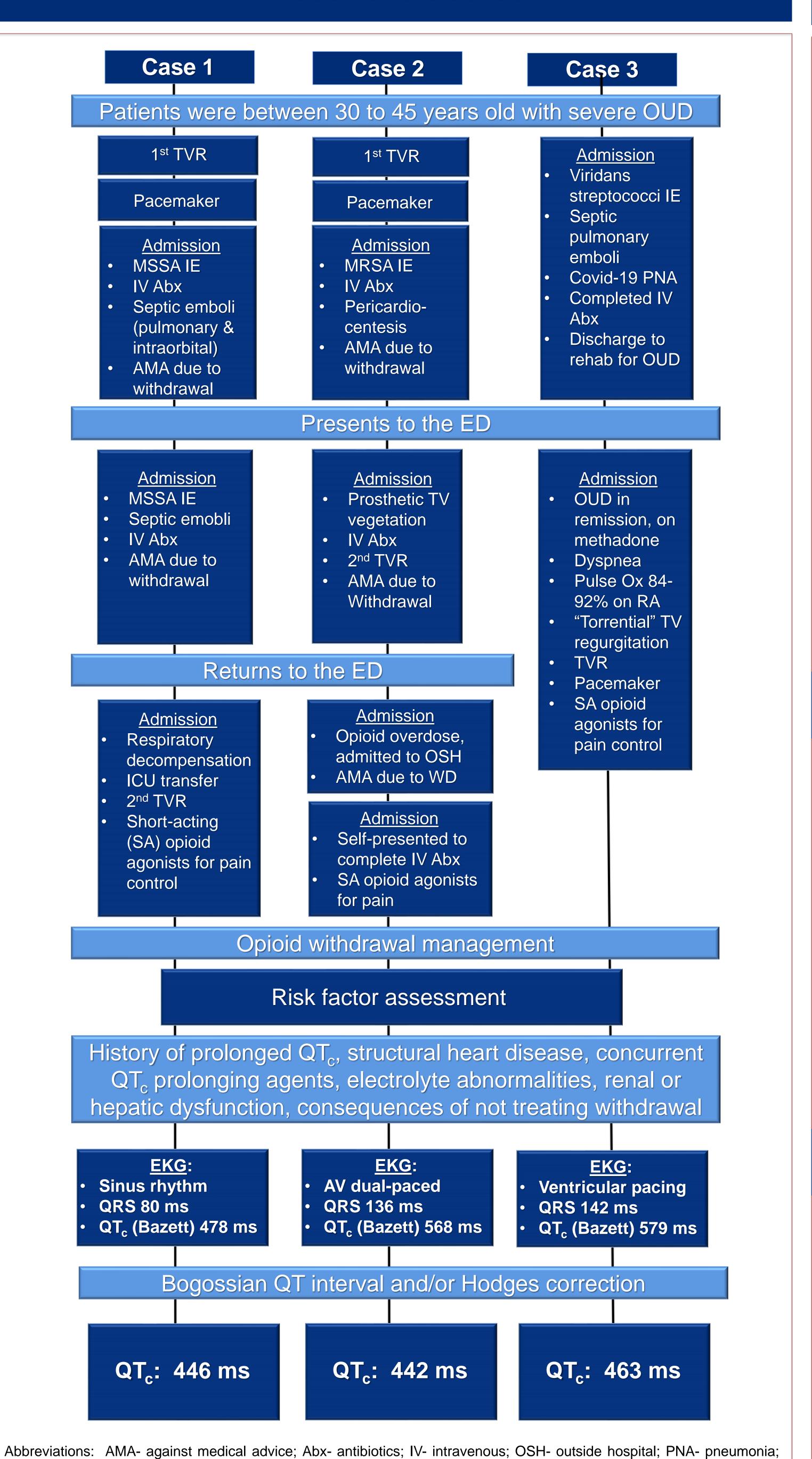


Figure 1. Cardiac conduction system and QT interval correction. Disruption of ventricular repolarization or QRS widening contribute to a prolonged QT interval. **Panel A-** Anatomical illustration of the cardiac conduction system (*yellow*). Ventricular depolarization starts at the atrioventricular node (AV) and travels through the Bundle of His to the left and right bundle branches. Disruptions along this path risk QT interval prolongation. **Panel B-** Electrocardiogram demonstrating a narrow QRS complex and normal QT interval. **Panel C-** Schematic outlining QT interval correction (QT_c) using a Bogossian formula for a widened QRS complex followed by the Hodges formula for heart rate correction.

Treatment Course



TV- tricuspid valve; WD- withdrawal

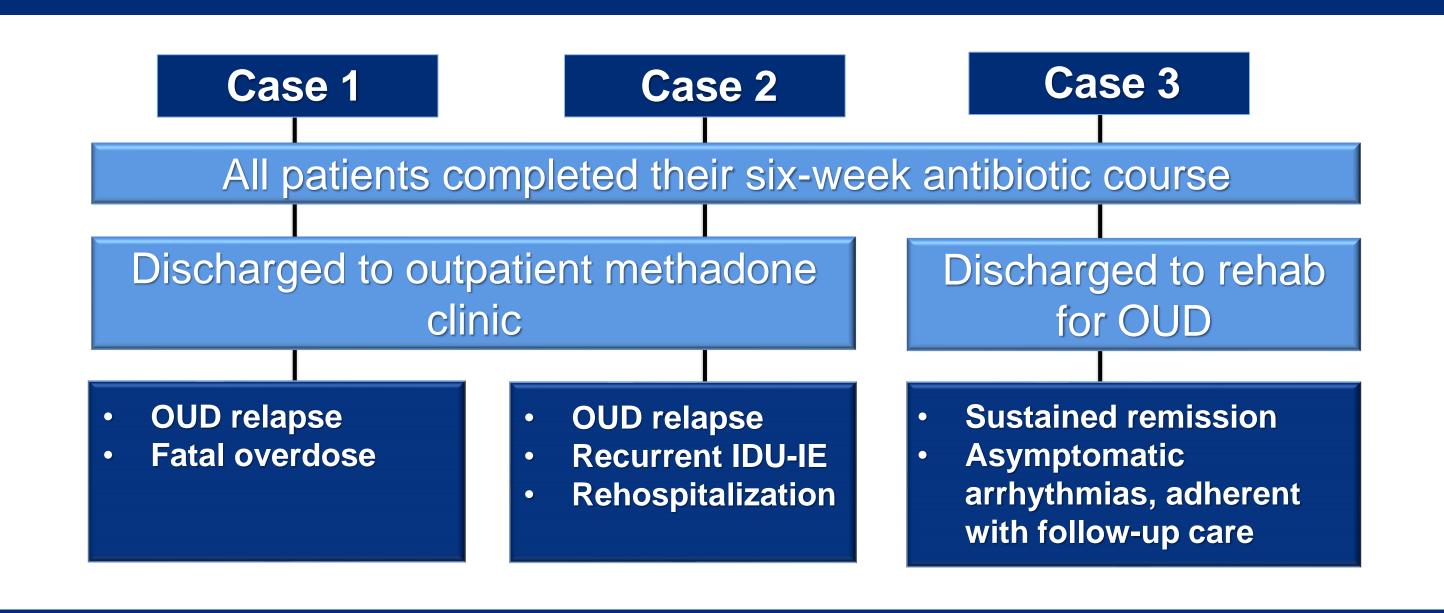
Methadone Dosing

Table 1. Methadone dosing for opioid withdrawal management

	Case 1	Case 2	Case 3
Initiation	30 mg daily	20 mg daily	140 mg daily**
Discharge	70 mg daily	100 mg daily	150 mg daily
Outpatient	_		180 mg daily

^{**}Verified outpatient dose prior to admission

Outcomes



Discussion

Guidelines for treatment of IDU-IE endorse surgery if medically indicated and incorporating addiction treatment⁴. Many patients strongly prefer to start or continue methadone postoperatively. This case series demonstrates that patients undergoing surgical management of IDU-IE may be at risk for QT_c prolongation. It is important to use accurate correction formulas to assess QT_c prolongation³, which may reveal QT_c ranges within normal limits. This case series also demonstrates that though all three patients suffered adverse events, the one death was associated with OUD and not a cardiac event. The patient who did experience arrhythmias was asymptomatic and remained in remission from her OUD, which allowed her to attend regular clinic visits and undergo successful hospitalization for further management.

Conclusion

This case series provides anecdotal observations to guide high-risk methadone titration in patients with IDU-IE while generating questions for future systematic evaluation.

References

- 1. Suzuki, J. et al. (2020) J Addict Med. 14(4): 282-286
- 2. Stringer, J. *et al.* (2009) Am J Health Syst Pharm. (9): 825-833
- Funk, M.C. *et al.* (2021) J Acad Consult Liaison Psychiatry. 62(5): 501-510
- 4. Pettersson, G.B. and Hussain, S.T. (2019) Ann Cardiothorac Surg. 8(6): 630-644