

Intraoperative Methadone in Adult Cardiac Surgical Patients and Risks for Postoperative QTc Prolongation

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INTRODUCTION

- Methadone, a long-acting opioid agonist, is widely utilized in early recovery after surgery pathways. Its use has surged due to benefits including reduced postoperative pain scores, diminished opioid need, and fewer adverse effects like nausea and vomiting compared to other opioids.
- We hypothesized that a single perioperative dose of methadone in cardiac surgical patients was not inferior in causing postoperative QTc prolongation and arrhythmias compared to the non-methadone control group. The aim was to evaluate the effect of intraoperative intravenous methadone within a standardized enhanced recovery after cardiac surgery (ERACS) pathway on perioperative QTc..

OBJECTIVES

- To investigate whether a single perioperative methadone dose significantly prolonged QTc interval of adults undergoing cardiac surgery and whether it correlated with adverse post-operative arrhythmias.

METHODS

Design: A large retrospective study of 1040 patients undergoing cardiac surgery between July 2020 to July 2023 at UPMC hospitals utilizing validated electronic medical record data and Society of Thoracic Surgeons (STS) Adult Cardiac Surgery *Database* (ACSD) outcomes.

Participants

- 1040 adults undergoing major inpatient cardiac surgery

Exclusion Criteria

- Emergency surgeries, transplants, ventricular assist device (VAD) placements, and patients with history of recent opioid abuse.

Analgesia Protocol

Patients were administered intrathecal morphine ITM (0.25mg) or methadone (0.1mg/kg) if ITM was contraindicated, as part of an ERACS pathway utilizing current multimodal ERAS society guidelines

RESULTS

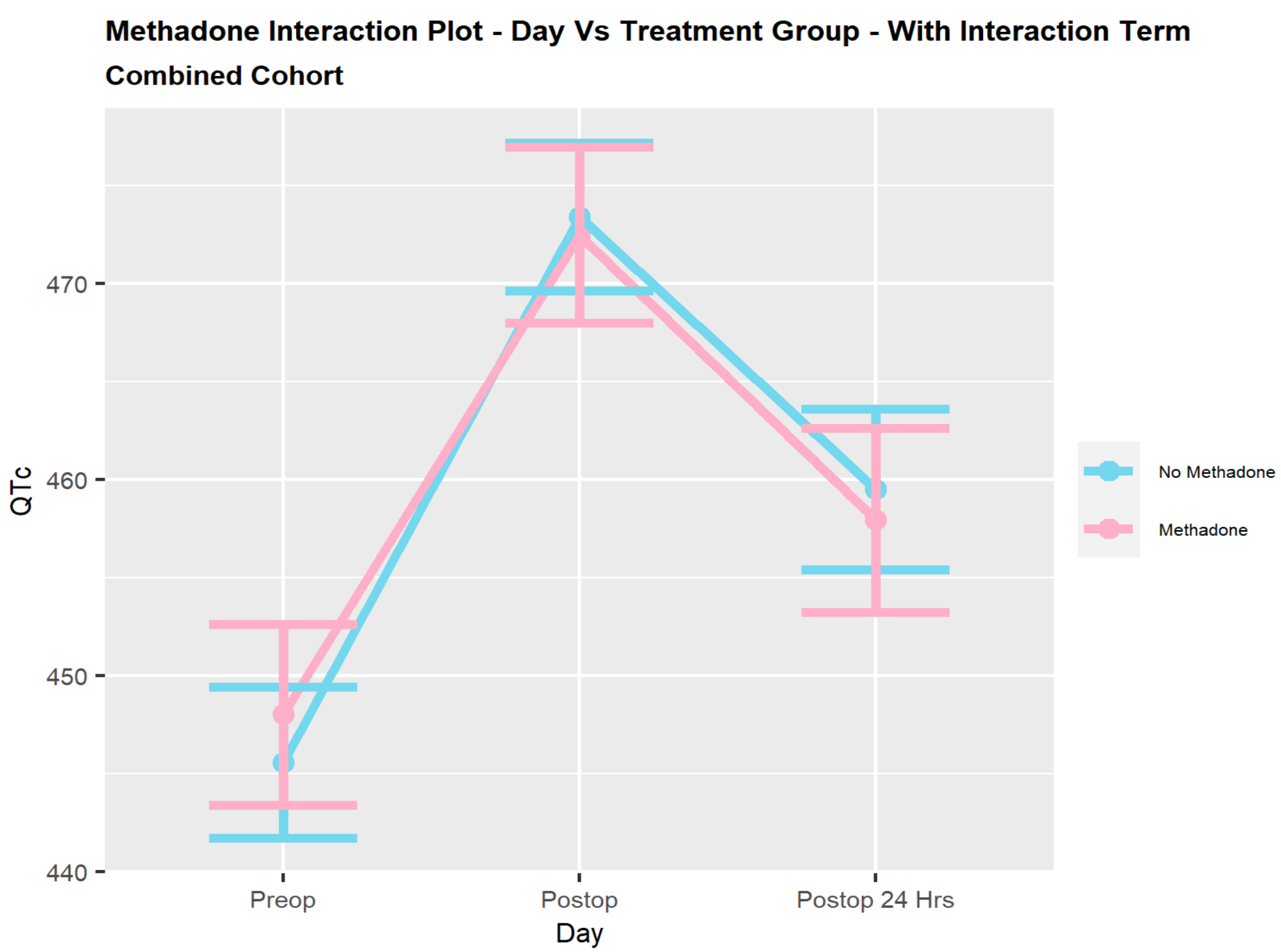


Fig 1. Pre-operative and Postoperative QTc with Intraoperative Methadone Use. Mixed models analyzing methadone QTc demonstrated that QTc prolongation immediately postoperatively normalized within 24 hours in both groups (Figure 1). The effects were similar for both male and female cohorts.

Table 1. QTc Outcomes: Methadone versus No methadone Groups, stratified by sex				
Outcomes - Whole Sample	Total	Control	Methadone	P-Value
Preop QTc Interval - Mean (sd)	446.63 (35.38)	445.4 (35.8)	448.4 (34.8)	0.21
Immediate Post Op QTc Interval	472.9 (56.53)	473.2 (56.1)	472.5 (57.2)	0.86
Delta QTc	26.7 (58.16)	28 (60.2)	24.9 (55.2)	0.43
% Change QTc	0.06 (0.13)	0.1 (0.1)	0.1 (0.1)	0.32
Days to Death	108.02 (140.65)	86.9 (133.1)	137.9 (149.6)	0.26
Post-op Ventricular Arrhythmias - n (%)	15 (1.5%)	11 (2%)	4 (1%)	0.30
Post-op Atrial Fibrillation	285 (27.9%)	167 (28%)	118 (28%)	0.96
30-day Mortality	19 (46.3%)	13 (54%)	6 (35%)	0.34
365-day Mortality	37 (90.2%)	22 (92%)	15 (88%)	1.00
QTc Elevated Post op (>440ms for men, >460ms for women)	731 (70.3%)	443 (72%)	288 (68%)	0.20
Outcomes – Men Alone	Total	Control	Methadone	P-Value
Preop QTc Interval - Mean (SD)	444.69 (36.38)	443.3 (37.3)	446.8 (34.9)	0.22
Immediate Post Op QTc Interval	470.95 (56.2)	471.2 (56)	470.5 (56.6)	0.87
Delta QTc	26.92 (58.44)	28.9 (61)	24.1 (54.6)	0.30
% Change QTc	0.06 (0.13)	0.1 (0.1)	0.1 (0.1)	0.21
Days to Death	106.81 (149.98)	94 (148.6)	129.8 (157.7)	0.56
Post-op Ventricular Arrhythmias - n (%)	10 (1.4%)	7 (2%)	3 (1%)	0.54
Post-op Atrial Fibrillation	211 (29.2%)	129 (30%)	82 (28%)	0.40
30-day Mortality	13 (46.4%)	10 (56%)	3 (30%)	0.25
365-day Mortality	25 (89.3%)	16 (89%)	9 (90%)	1.00
QTc Elevated Post op (>440ms for men)	545 (73.8%)	334 (76%)	211 (71%)	0.09
Outcomes – Women Alone	Total	Control	Methadone	P-Value
Preop QTc Interval - Mean (sd)	451.6 (32.3)	451.1 (31)	452.4 (34.2)	0.75
Immediate Post Op QTc Interval	477.82 (57.15)	478.1 (56.2)	477.4 (58.6)	0.91
Delta QTc	26.15 (57.52)	25.6 (58.2)	26.9 (56.8)	0.85
% Change QTc	0.06 (0.13)	0.1 (0.1)	0.1 (0.1)	0.89
Days to Death	110.62 (123.76)	65.3 (75.6)	149.4 (148.5)	0.24
Post-op Ventricular Arrhythmias - n (%)	5 (1.7%)	4 (2%)	1 (1%)	0.65
Post-op Atrial Fibrillation	74 (24.8%)	38 (22%)	36 (29%)	0.14
30-day Mortality	6 (46.2%)	3 (50%)	3 (43%)	1.00
365-day Mortality	12 (92.3%)	6 (100%)	6 (86%)	1.00
QTc Elevated Post op (>460ms for women)	186 (61.8%)	109 (62%)	77 (62%)	0.93

RESULTS

- Out of a total of 1,040 patients, 423 received intraoperative methadone and 617 did not.
- Preoperative corrected QT interval (QTc) did not significantly differ between no methadone mean (SD) 445.4 (35.8) vs methadone = 448.4 (34.8); p=0.205).
- Methadone QTc mixed models demonstrated that QTc is prolonged immediately postoperatively and normalized 24 hours post-surgery in both methadone and non-methadone groups (**Figure 1**).
- There were no significant differences in baseline QTc, immediate postoperative QTc, changes in QTc, or percent change in QTc between the methadone and non-methadone groups (**Table 1**).
- There were no significant differences in ventricular or atrial arrhythmias, 30-day, and 1 year mortality (**Table 1**).

DISCUSSION

- **A single intraoperative methadone administration did not significantly prolong postoperative QTc interval or increase the incidence of postoperative arrhythmias compared to the non-methadone control group in adult cardiac surgical patients.**
- Our study results support the safety and efficacy of methadone as an analgesic option in early recovery after cardiac surgery pathways.
- Future large prospective studies are needed to validate this finding and further improve perioperative methadone’s analgesia and safety.

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