Generalised estimating equations for repeated postoperative pain scores in Stata: application to a randomised trial of intravenous methadone in cardiac surgery

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Background

- Pain after cardiac surgery remains substantial despite opioids.
- Methadone is long acting, but randomised comparisons with morphine are few.
- Repeated pain scores are correlated within patients and call for longitudinal analysis.

Objective

To compare intravenous methadone with morphine for analgesia after cardiac surgery, and to show how repeated pain scores were analysed with generalised estimating equations (GEE) in Stata.

Methods

- Single-centre, double-blind randomised controlled trial in Hong Kong.
- Adults having elective cardiac surgery with cardiopulmonary bypass: 86 randomised, 80 analysed per protocol (40 per group).
- Methadone or morphine 0.2 mg/kg intravenously at induction, then patient-controlled morphine in both groups.
- Pain scores (NRS 0–10) at rest and on coughing at 15min, 8h, 12h, 24h, 48h and 72h after tracheal extubation.
- Primary outcome: morphine consumption in the 24h after extubation.
- Secondary outcomes: pain scores, total morphine use, time to first morphine rescue, satisfaction and opioid-related adverse events.

Analysis in Stata

- Repeated pain scores were modelled in Stata 14 with generalised estimating equations (xtgee): Gaussian family, identity link, exchangeable correlation and robust standard errors.
- Models included group, time and their interaction; the interaction was tested jointly (testparm).
- Predicted means with 95% CI came from margins and were plotted with marginsplot.
- Other outcomes: t, Mann–Whitney U or chi-squared tests; $p < 0.05$ taken as significant.

Results

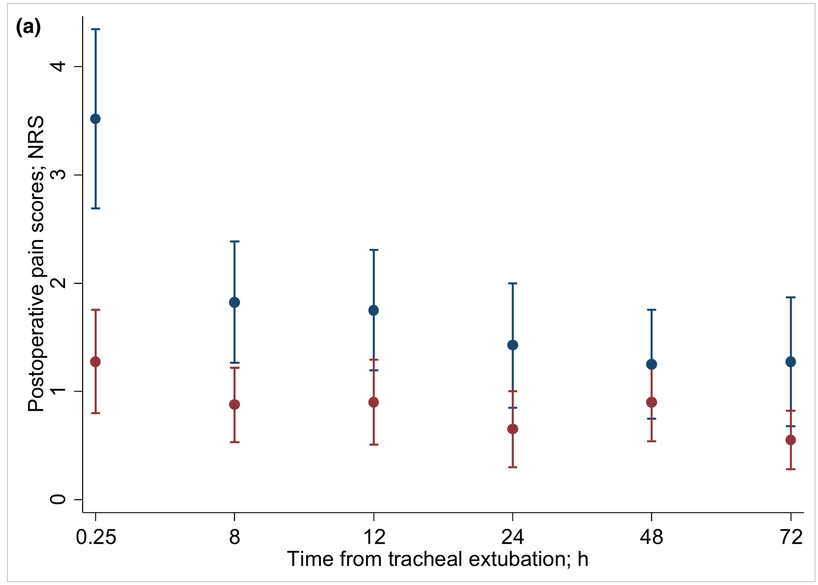


Figure. Generalised estimating equation analysis of postoperative pain scores at rest (a) and during coughing (b) in the methadone (red) and morphine (blue) groups, up to 72 h after tracheal extubation. Values are mean (95% CI). NRS, numerical rating scale (0–10).

Key results

Outcome	Methadone	Morphine	p
Morphine, first 24 h, mg (primary)	9 (5–16)	24 (17–43)	< 0.001
Morphine, total over 72 h, mg	11 (7–20)	35 (23–52)	< 0.001
Time to first morphine rescue, min	205 (103–397)	134 (82–214)	0.041

Median (IQR); n = 40 per group.

Pain score, GEE	Estimate	p
Methadone vs morphine, at rest	−2.24 (SE 0.49)	< 0.001
Methadone vs morphine, on coughing	−2.16 (SE 0.50)	< 0.001
Group × time interaction, at rest	$\chi^2(5) = 17.87$	0.003

GEE coefficients on the NRS scale. Predicted mean NRS at rest, 15 min to 72 h: methadone 1.28 to 0.55; morphine 3.52 to 1.27.

Conclusions

- A single 0.2 mg/kg dose of methadone at induction lowered pain scores at rest and on coughing for up to 72 h.
- Morphine use was 63% lower at 24 h and 69% lower over 72 h.
- Patient satisfaction was higher, and opioid-related adverse events did not differ between groups.
- In Stata, xtgee with margins and marginsplot gave a transparent, reproducible workflow for repeated outcomes.

Reference
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Registration and funding
ClinicalTrials.gov NCT05913284 and NCT06728371. Supported by the Health and Medical Research Fund, Health Bureau, Government of Hong Kong SAR.