

Population Pharmacokinetics of Lidocaine to Guide Drug Dosing of Erector Spinae Plane Catheters in Adult Cardiac Surgery

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Introduction

- Pharmacokinetics (PK) of local anesthetics administered via fascial plane catheters are inadequately described despite widespread adoption of fascial plane techniques.
- Primary aim:** to develop a PK model of lidocaine when administered via programmed intermittent autobolus into thoracic-level erector spinae plane (ESP) catheter/s

Methodology

Design: Single-center retrospective review

Population: Cardiac surgical patients receiving programmed intermittent bolus lidocaine via ESP catheters between May 2018 to June 2020.

Exclusions: lidocaine by any other route, non-lidocaine local anesthetic administered, incomplete record of lidocaine dosing or dose change.

Catheter technique: T4-5 ESP catheters placed in preop, parasagittal technique under in-plane ultrasound guidance, patients sitting or prone

Lidocaine dosing: Lidocaine 0.5% 0.75mg/kg q2h, alternating sides, using NIMBUS II PainPRO pumps (Infutronic LLC Natick, MA). Maximum dose per side 20mL. Initiated on arrival to ICU. Dose changes permitted at discretion of attending (ICU or pain service).

Lidocaine levels: in-house homogenous enzyme immunoassay, Cobas 8000 platform (Roche Diagnostics, Indianapolis, IN).

Pharmacokinetic analysis: non-linear mixed effects modeling (NONMEM) for one- and two compartment models, with and without an absorption compartment, using NONMEM, Version 6 (Icon PLC, Leopardstown, Dublin, Ireland). Likelihood profiles and bootstrap analysis calculated using “PLT Tools” (P Less Than, San Francisco, CA). Summary statistical and graphical analysis performed with R 4.3, “Already Tomorrow” (r-project.org).

Results

Final PK analysis : 43 patients (56 patients during study period, 13 excluded per protocol)
Demographics: age 64y (26-83), 81% male / 19% female
Procedures: CABG (n=15, 50%), valve repair or replacement (n=13, 30%), CABG combined with valve or aortic repair (n=6, 14%; CABG + valve, n= 3; CABG + aorta, n=2; CABG + Maze, n=1), aortic repair with (n=2, 5%) or without valve (n=3, 7%), or other (LVAD; Maze; ASD repair; tumor excision; n=4, 13%)

Figure 1. Goodness of fit models.
(A) Measured vs predicted values center around line of identity.
(B) measured/predicted values vs time.

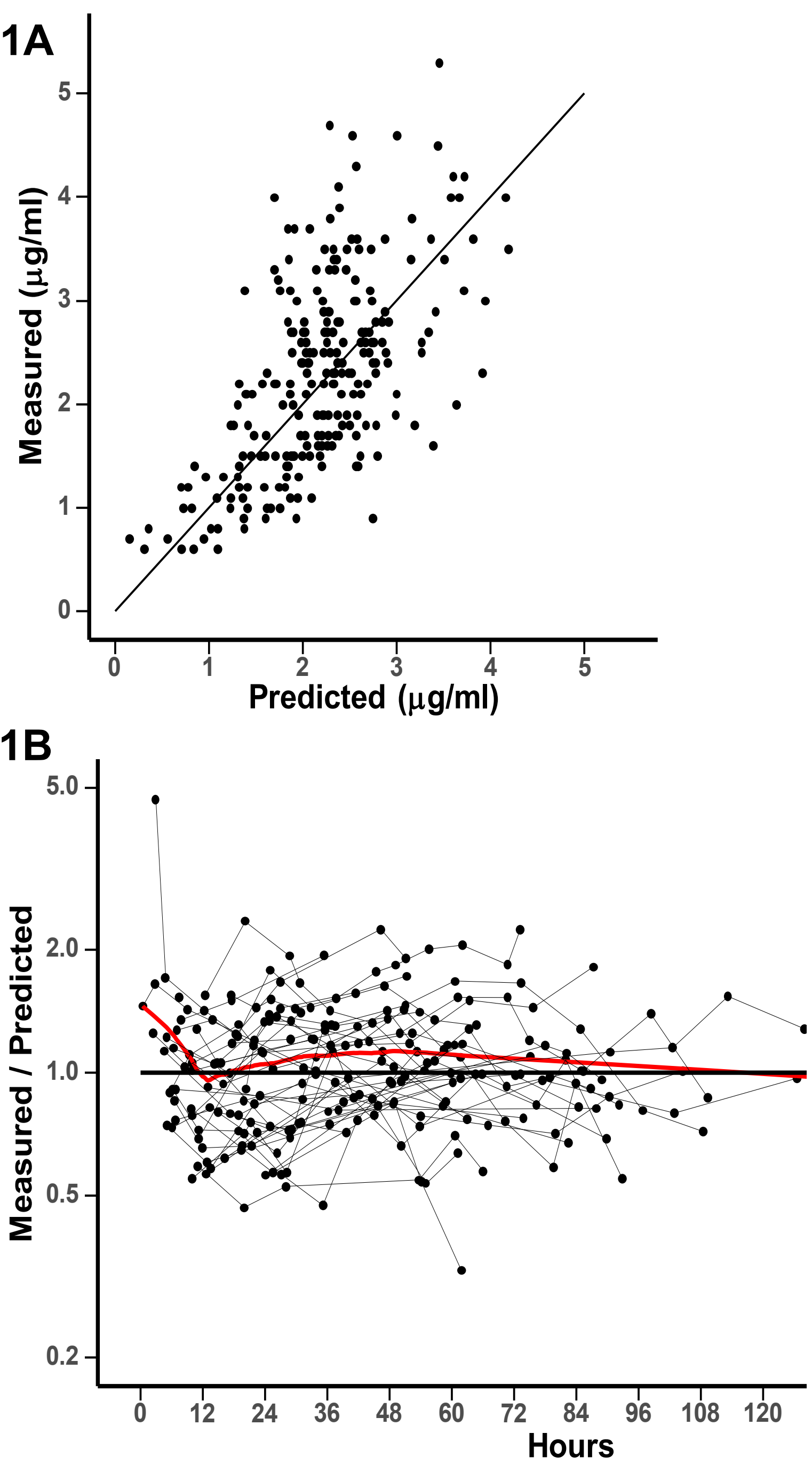
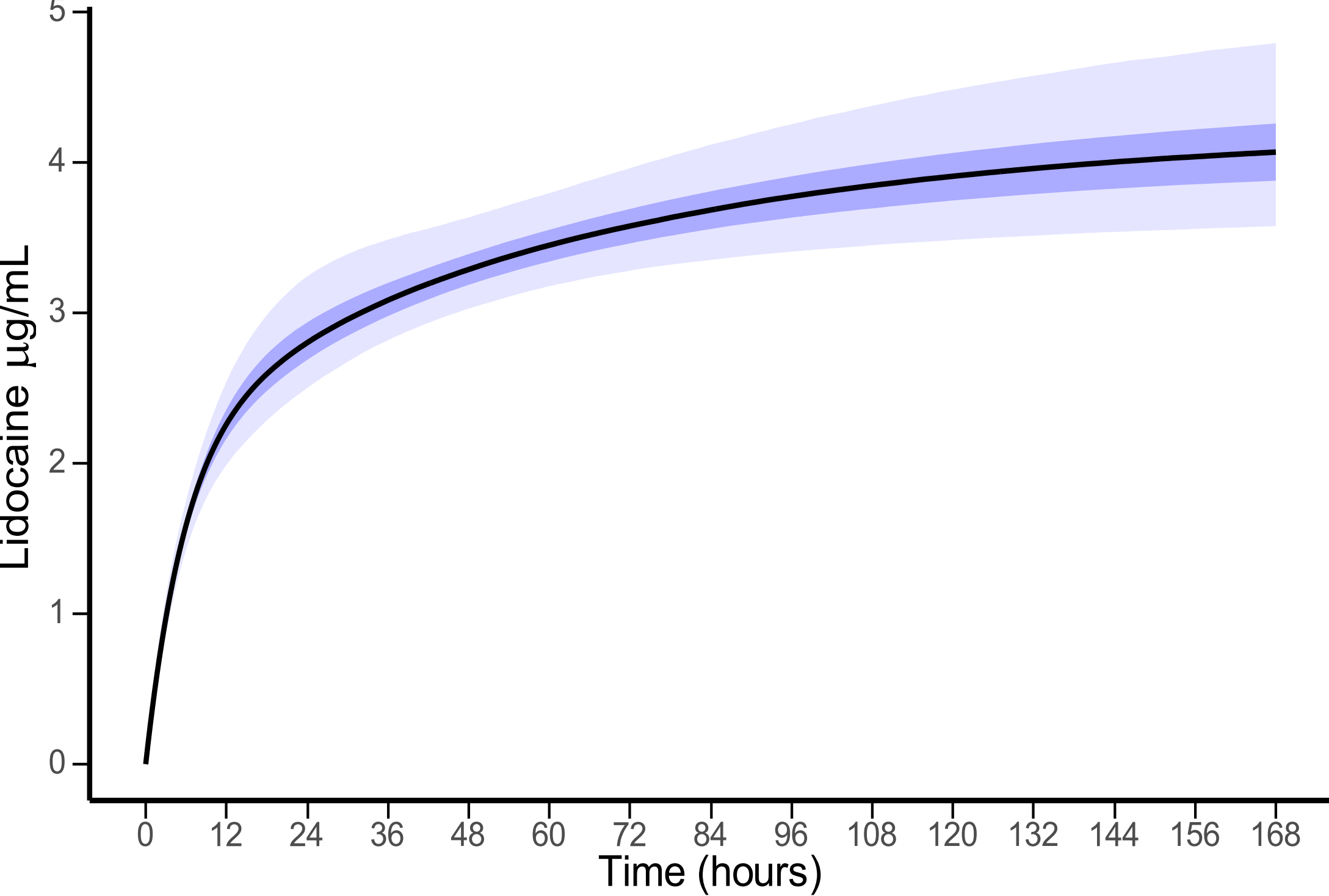


Table 1. NONMEM analysis

Parameters	Estimate	95% Confidence Interval	Approximate Coefficient of Variation
Clearances (liters/min)			
Systemic	0.327	0.266 - 0.381	36%
Peripheral	0.225	0.07 - 0.42	162%
Volumes (liters)			
Central	209	161 - 244	36%
Intercompartmental	484	290 - 830	fixed at 0
Half lives (hours)			
Rapid	4.1		
Slow	45		

Figure 2. PK prediction of lidocaine 1mg/kg/hr via ESP catheters



Discussion

- Our PK model of ESP lidocaine catheters predicts a 2-compartment model (i.e., central and intercompartmental) without significant contribution from absorption compartment
- PK modeling also predicts (Figure 2) attenuated peak serum level over time that does not exceed generally accepted LAST threshold (Figure 2)
- No evidence of bias as demonstrated by measured vs predicted data centered on line of identity (Figure 1A)
- No evidence of bias with time as demonstrated by trajectory of each patient over time (Figure 1B; limited by less data at >72hours)

Conclusion

- Our data provides a comprehensive analysis of serum lidocaine levels in cardiac surgical patients receiving autobolus lidocaine via ESP catheters.
- This robust 2-compartment PK model can guide safe administration of lidocaine via ESP catheters.
- Limitations
 - (1) 100% bioavailability assumed (drug retention in local tissues cannot be excluded)
 - (2) limited data immediately after bolus (may have informed an absorption compartment model)
 - (3) morphometric based analyses were limited to weight
 - (4) no adjustments were made for comorbidities, though model is designed to be utilized in the population it was created from (cardiac surgical patients)

References

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