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(Abstracts)

Contents

Analgesic Efficacy of Surgeon Placed Paravertebral Catheters Compared with Thoracic Epidural Analgesia After Ivor Lewis Esophagectomy: A Retrospective Non-Inferiority Study

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Background: The Ivor Lewis esophagectomy is an operation that involves a laparotomy and a right thoracotomy, both of which are associated with severe postoperative pain and subsequent impairment of respiratory function. [1] Currently, the accepted “gold standard” for postoperative analgesia for thoracotomies and upper abdominal incisions is the thoracic epidural. [2] A systematic review showed paravertebral catheters (PVC) were equivalent to epidural analgesia for post-thoracotomy pain control [3] and they have also been associated with less nausea and vomiting and hypotension. [3] To our knowledge, the use of the paravertebral catheter in open Ivor Lewis esophagectomy has not been formally studied.

Methods: We performed a retrospective chart review of the open Ivor Lewis Esophagectomy patients from 2012 to 2018 at our local institution. Local ethics board approval was obtained. A total of 96 patients underwent open Ivor Lewis esophagectomies: 44 patients had a surgeon placed paravertebral and 52 patients had a thoracic epidural.

Results: Our primary outcome was the area under the curve (AUC) pain scores in the first 48 hours after surgery using the trapezoid method as described by Aloia et al. [4]. Overall, the PVC group was non-inferior and statistically equivalent to the epidural group. A non-inferiority margin of 2 on the pain scale was used [5]. Although there was a significant difference between the two groups ($t(84.6)=2.61$, $p=0.011$), the mean difference of 35.2 was contained within the 90% CI equivalence bounds. With respect to our secondary outcomes, the highest pain score was non-inferior and equivalent between PVC and epidurals ($t(90)=1.53$, $p=0.13$). The total opioid consumption in the PVC group was significantly less compared to the epidural group. In addition to assessing pain through various outcomes, we also reviewed the patients' time to ambulation (TTA) and length of stay (LOS) in hospital as a surrogate of function: the PVC group had a mean TTA of 25.6 hours, versus 29.8 hours; the PVC group had a mean LOS of 14.02 days versus 13.86 days in the epidural group. One aspect of epidurals that clinicians often cite against them are the side effects. [3] This was also demonstrated in our study. Epidurals had a much higher incidence of pruritus than the PVC group (15 versus 4). The incidence of nausea/vomiting, somnolence and hypotension were similar.

Discussion: Our retrospective study continues to challenge the role of epidurals as the gold standard of pain control post thoracotomy and upper midline abdominal incision. A surgeon placed paravertebral under direct vision may be more safe than a thoracic epidural placement, and has less side effects postoperatively. Recently, a study is underway for minimally invasive esophagectomy comparing epidurals to PVC in the Netherlands. Further prospective studies, with a larger population are needed in order to better compare the two modalities.

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Association Between Handover of Anesthesiology Care and One-Year Mortality Among Patients Undergoing Cardiac Surgery

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Background: Recent studies have identified handover of care from one anesthesiologist to another during noncardiac surgery as a risk factor for increased morbidity and mortality(1,2). However, the impact of anesthesiologist handover (AH) has not been thoroughly investigated in the practice of cardiac anesthesiology, where the operative risk is higher and the probability of handover is greater due to longer operative duration. We hypothesized that complete AH during cardiac surgery is associated with higher rates of one-year mortality.

Methods: Ethics approval was waived by the local REB. We conducted a population-based, retrospective cohort study in Ontario, Canada, using clinical registry and administrative health care databases with information on all Ontario residents. Included were adult patients ≥ 18 years of age, who underwent coronary artery bypass grafting (CABG), and/or aortic, mitral, tricuspid valve surgery, or thoracic aorta procedures between October 1, 2008 and September 30, 2019. Excluded were patients who underwent cardiac transplantation and implantation of ventricular assist devices. The primary exposure was complete handover of anesthesiology care, as identified from physician billing codes on the day of or after surgery (in case of handover occurring after midnight). The primary outcome was all-cause mortality within one year after surgery. Mortality rates were calculated using the Kaplan-Meier method. The relative hazard of death was assessed using a multivariable Cox proportional hazard model.

Results: A total of 102,209 patients met the inclusion criteria, of whom 1,926 (1.9%) experienced a complete handover of anesthesiology care. Patients who experienced an anesthesiology handover were more likely to be male, be undergoing emergent and/or thoracic aorta surgery, and to have endocarditis and more advanced cardiac symptoms. In addition, anesthesiology handovers occurred more frequently at teaching hospitals, when the primary anesthesiologist was female, and when the surgeon was less experienced. Anesthesiology handover was associated with an increased rate of mortality at one-year (Figure), and was an independent predictor of this outcome (HR 1.41, 95% CI 1.12-1.76) after adjustment for patient, procedure, anesthesiologist, surgeon, and hospital characteristics.

Discussion: We found that the handover of anesthesiology care was associated with increase in one-year mortality after major cardiac surgery. Handover is a critical event that impacts patient safety. Further research is needed to qualitatively evaluate, and systematically improve the handover process.

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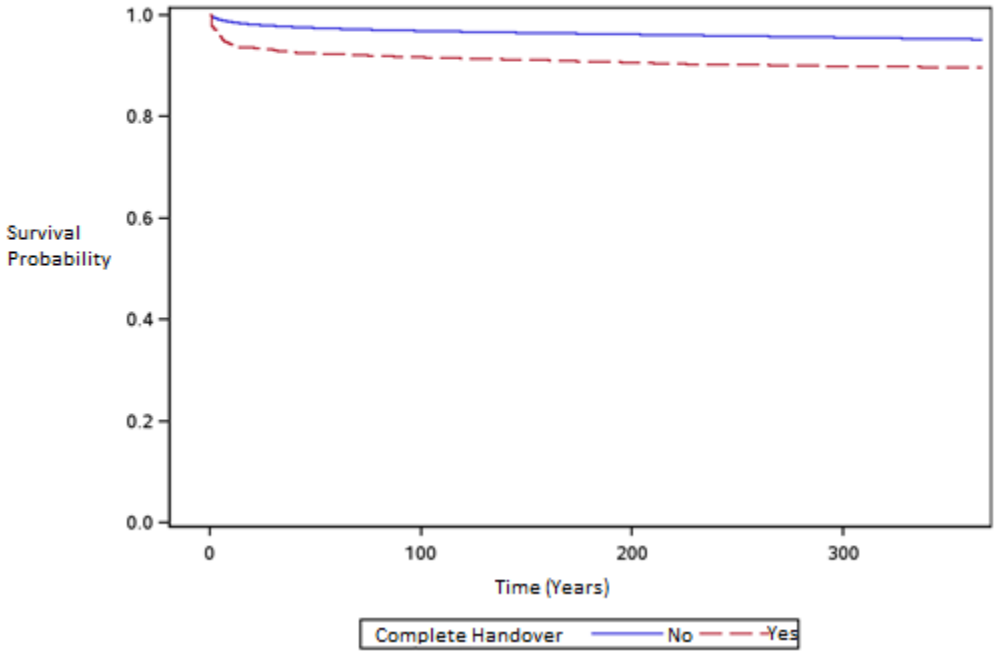
Estimated one-year survival after cardiac surgery in patients with and without anesthesiology provider handover.



IGFBP7 as a Pre-Operative Predictor of Congestive Acute Kidney Injury in Adults Undergoing Cardiac Surgery

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Introduction/Background: Right ventricular failure (RVF) and acute kidney injury (AKI) are known risk factors for morbidity and mortality following cardiac surgery[1-3]. Congestive acute kidney injury (c-AKI) refers to AKI in the presence of RVF and is deadlier than its individual components[1]. Early identification and prediction of these outcomes is critical for appropriate treatment, through clinical risk stratification that is complemented by biomarkers[1]. Prior work has shown N-terminal pro hormone B-type natriuretic peptide (NT-proBNP) and pulmonary artery pulsatility index (PAPi) to have good predictive power for post-operative AKI and RVF[1,4]. Insulin-like growth-factor binding protein 7 (IGFBP7) is a novel biomarker that has shown to be associated with diastolic dysfunction and heart failure[5]. This study will investigate the predictive ability of serum IGFBP7 in predicting c-AKI, AKI and RVF.

Methods: Ethics approval was obtained from the local REB. This prospective nested case-control study consisted of 350 adult patients undergoing major elective cardiac surgery at a tertiary center between 2015 and 2017. The primary outcome was c-AKI, while AKI and RVF were secondary outcomes. For each outcome, cases were matched 1:1 to controls based on age and sex. Conditional logistic regression was used to assess the predictive ability of IGFBP7 for c-AKI, AKI and RVF. NT-proBNP and PAPi were used as alternative predictors, for comparison. Univariable, as well as multivariable models were generated. Multivariable models included the biomarkers (IGFBP7 or NT-proBNP) and additional variables selected based on the strength of their known association with AKI and RVF in cardiac surgical patients. For each model, the area under the curve (AUC) was calculated as a measure of the model's ability to distinguish cases from controls.

Results: We identified 85 cases and 85 controls, of whom 18 developed c-AKI. For each of the outcomes, IGFBP7 outperformed NT-proBNP and PAPi as a univariate predictor (Figure 1). For prediction of c-AKI, the IGPBP7 model had an AUC of 0.81 (95% CI, 0.66-0.96), as compared to 0.51 (0.31-0.71) for NT-proBNP and 0.61 (0.36-0.87) for PAPi. IGFBP7 had less predictive power for AKI and RVF, while still outperforming NT-proBNP and PAPi. The optimal cutoff for predicting either AKI or c-AKI with IGFBP7 was 102 ng/mL. For each of the outcome variables, the multivariable NT-proBNP and IGFBP7 models had very similar AUCs. These multivariable models performed well for c-AKI, with AUCs of 0.90 (0.81-1.00) for IGFBP7 and 0.87 (0.76-0.99) for NT-proBNP.

Conclusion: In summary, IGFBP7 outperformed NT-proBNP and PAPi as a univariate predictor for all three outcomes. The AUCs for prediction of AKI and c-AKI with IGFBP7 are particularly promising, and these improve further with the addition of clinical variables. Thus, IGFBP7 is a promising biomarker for prediction of AKI and c-AKI and warrants further investigation in future studies.

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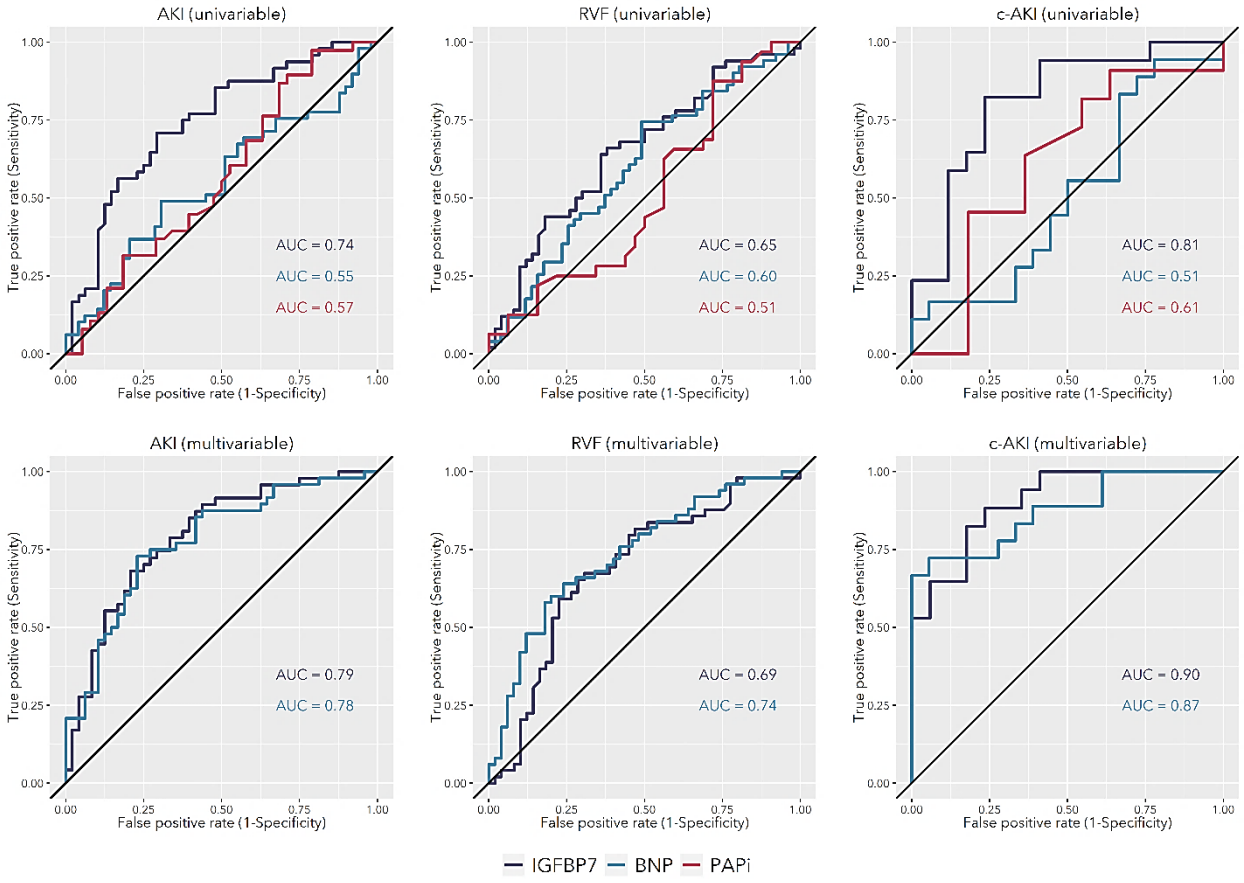
Figure 1


AKI (univariable)
AUC = 0.74
AUC = 0.55
AUC = 0.57
RVF (univariable)
AUC = 0.65
AUC = 0.60
AUC = 0.51
c-AKI (univariable)
AUC = 0.81
AUC = 0.51
AUC = 0.61
AKI (multivariable)
AUC = 0.79
AUC = 0.78
RVF (multivariable)
AUC = 0.69
AUC = 0.74
c-AKI (multivariable)
AUC = 0.90
AUC = 0.87
True positive rate (Sensitivity)
False positive rate (1-Specificity)
0.00
0.25
0.50
0.75
1.00
IGFBP7
BNP
PAPi

Introduction of the Serratus Anterior Plane Catheter with Programmed Intermittent Bolus for Minimally Invasive Cardiac Surgery: A Retrospective Study

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Introduction/Background: Minimally invasive heart surgery (MIHS) is rapidly progressing with proposed benefits over sternotomy including reduced recovery time, inflammatory response and transfusion requirements[1-3]. In addition to the surgical ports, MIHS requires a mini-thoracotomy in the 4-5th intercostal space resulting in significant postoperative pain for which regional anesthetic techniques may be used. One such technique is the serratus anterior plane (SAP) block, which has been described previously for thoracic surgery and MIHS[4-9]. The objective of this study was to compare postoperative analgesia efficacy and opioid consumption, as well as clinical outcomes between patients that did and did not receive SAP catheters.

Methods: REB approval was obtained from the local REB for this retrospective cohort study comparing analgesic control and patient outcomes from May 2017 until May 2020 in patients undergoing MIHS at a single cardiac surgery center. Clinical use of the SAP block and catheters was started in November 2018. Patients were excluded if they were less than 18 years of age, had incomplete documentation of anesthetic technique, conversion from MIHS to open or a surgical procedure within 72 hrs of the index surgery. Continuous data are expressed as means and standard deviations for variables with normal distribution and as medians and interquartile ranges (IQR) otherwise. Groups were compared using unadjusted t-tests and logistic regression models (adjusted for age, sex and BMI) or fisher's exact tests as appropriate. A value $p \leq 0.05$ was considered significant for differences between the two groups.

Results: There were 115 patients that met inclusion during the study period (41 in the SAP catheter group and 74 in the control group). Demographic data were balanced between the two groups. After adjusting for age, sex and body mass index, there was no difference in opioid consumption (OR: 0.995, 95% CI: 0.990 - 1.000) , pain score at extubation (OR: 0.93, 95% CI: 0.789 – 1.098) average pain score in the first 24 hours after surgery (OR: 0.869, 95% CI: 0.702 – 1.077), Intensive Care Unit length of stay (OR: 0.990, 95% CI: 0.773 0 1.268) or hospital length of stay (OR: 0.998, 95% CI 0.904 – 1.101) between groups. There was a significant decrease in opioid related side effects in the SAP group (OR: 2.702, 95% CI: 0.773- 1.268). As well, the duration of post-operative intubation was 218 minutes shorter in the SAP group compared to the usual care group (OR: 0.998, 95% CI: 0.904 – 0.999).

Discussion: We have shown that patients undergoing MIHS who have a SAP catheter placed for post-operative analgesia do not have a decrease in opioid consumption, pain at extubation or pain scores. They do experience less time intubated and have less opioid related adverse effects.

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Is Negative Aortic Wall Strain Possible?

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Introduction: Non-invasive measures of aortic biomechanical properties, obtained using speckle-tracking echocardiography (STE), have demonstrated potential for studying the pathogenesis and risk-stratifying aortic disease.[1] Previous STE-based studies of aortic biomechanics have focused on global strain.[2] Given the known regional heterogeneity of aortic tissue microstructure and function in the diseased state, a global approach risks missing data on local material properties.[3] We report preliminary findings of segmental STE-derived strain in patients with ascending aortic aneurysms.

Methods: Ethics approval was obtained from the local REB. Adult patients undergoing elective resection of ascending aortic aneurysms were included. Intra-operative trans-esophageal echocardiography was performed (Philips iE33, Koninklijke Philips N.V.,Netherlands) and a short-axis image of the aneurysm acquired prior to resection. Post-acquisition STE analysis was performed (EchoInsight, Epsilon Imaging, USA) to obtain circumferential aortic strain values through the cardiac cycle on 4 subdivided aortic regions (anterior, lateral, medial, and posterior) [Figure 1A]. Tracking quality was assessed using 4 parameters: the software's Data Quality Index (both minimum and average values), wall drop-out, and subjective grading of adequate wall tracking. Segments failing in ≥ 3 parameters were excluded.

Results: Ten patients were included in this preliminary analysis. Most segments (27/40) had excellent wall-tracking with ≤ 1 sub-optimal quality parameter, while 7 were excluded. The posterior (3/7) and lateral (3/7) segments had the highest proportion of excluded segments, often due to wall dropout. Eight patients, and 10 of 33 segments (8 with excellent tracking indices) demonstrated a significant degree of negative strain during systole, with the lateral (5/10) and posterior (3/10) segments accounting for the majority [Figure 1B]. Global strain (average of all included segments) was positive for all patients.

Discussion: Intuitively, negative strain of the ascending aortic wall during systole seems implausible. However, it has been previously observed with STE and could reflect an intrinsic error in software algorithms, or external error from out-of-plane motion or torsion.[2] Its regular appearance in our study, on tissue tracking optimally, and localizing to the posterior/lateral wall segments suggests this may be an actual phenomenon warranting additional study. One potential explanation could be external compression by mediastinal structures, a hypothesis supported by a previous study demonstrating reduced posterior wall aortic expansion using m-mode ultrasound.[4] Another could be tissue heterogeneity causing an "accordion-effect" from a rapidly expanding adjacent segment. If this is the cause, then regional aortic strain should be included in imaging-based biomechanical studies so that local material properties, and the underlying microstructural pathology they represent, are not missed.[5] Our study, which is currently ongoing, includes a 4-segment analysis of pre-operative MRI strain, as well as

biomechanical and histologic testing of excised aortic tissue. With this additional information, we should be better able to elucidate the cause of our observed negative aortic strain.

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Figure 1 (A & B)

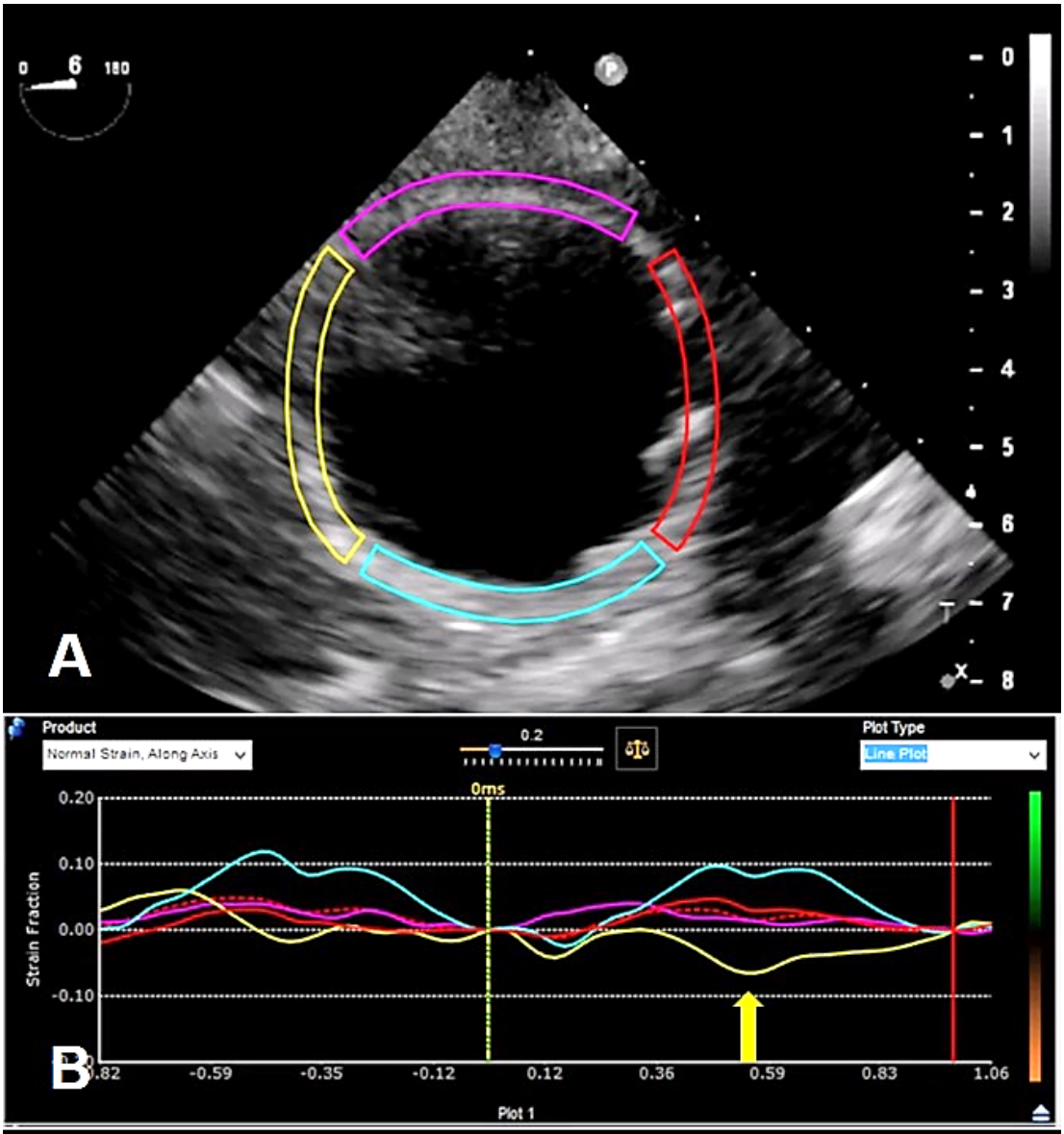

Figure 1. Selected example of circumferential ascending aortic strain analysis from our study using EchoInsight speckle-tracking echocardiography software (Epsilon Imaging, USA). (**A**) The short axis image of the ascending aortic aneurysm obtained from intra-operative TEE is divided into 4-regions: anterior (**cyan**), lateral (**yellow**), posterior (**purple**), and medial (**red**). (**B**) Strain analysis during systolic pulse-wave transmission shows the lateral wall with negative strain (yellow arrow) while the other walls have positive strain. *Note: Color of solid plot lines in (**B**) correspond to regions identified on (**A**), while the red-hashed line demarks global strain.*

Pilot Study Measuring the 7-Day Stability of Epinephrine, Norepinephrine and Phenylephrine in Syringes for Intravenous Infusions Using Liquid Chromatography-Tandem Mass Spectrometry

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Introduction/Background: Syringe infusion pumps are increasingly used in critical care to allow accurate small volume administration of medications. Medication safety guidelines recommend the use of pre-prepared medications by pharmacy or industry.[1] Health Canada has published concerns about decreased potency of pre-prepared medications in syringes.[2] There is conflicting information regarding sympathomimetic drug stability related to methodology and experimental conditions.[3] The objective of this pilot study was to develop a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method to determine the stability of epinephrine (EPI), norepinephrine (NE), and phenylephrine (PE), stored in Becton Dickinson© (BD) syringes. A secondary objective was to derive a power analysis for a larger study.

Methods: Ethics approval was not applicable because the study did not involve human or animal research. Research grade (purity >99.9%) EPI, NE and PE were used as standards for the calibration curves spanning the target concentrations. The calibration standards and test samples were each spiked with the corresponding isotope labeled internal standard. The area under the curve (AUC) of each drug was obtained by LC-MS/MS using a custom-developed Selected Reaction Monitoring (SRM) method.[4,5] Each drug was normalized by the AUC of the appropriate internal standard. Medical vials of EPI 4 mg, NE 4 mg, and PE 5 mg were diluted with normal saline solution to 50 mL in BD© syringes. Syringes were prepared aseptically, protected from UV radiation with plastic amber bags, and stored in a medical fridge (5-8 °C) for fresh (<4h), 3 days, and 7 days until testing. Preparations were analyzed in triplicate using LC-MS/MS with the investigator blinded to the preparation date. Linear regression analysis for the calibration standard and power analysis for a future study using three syringe brands and 6-time periods up to 14 days were performed.

Results: Total AUC ratio calibration standard linear regressions of the drugs were robust (EPI R^2; 0.96, NE R^2: 0.97, PE R^2: 0.98, ($p< 0.001$ for all)). Estimated fresh syringe concentrations were higher than expected. Compared to fresh, the percentage decrease in concentration at 3 and 7 days for EPI and NEPI was less than 10%. Compared to fresh, PE percentage decrease in concentration was 20% at 3 days with no significant further decrease at 7 days (Table 1). The power analysis estimated a sample size of 4 syringes per time period for six time periods using 3 syringe brands.

Discussion: The sample preparation and LC-MS/MS methods demonstrated high through-put (acquisition times <2min per sample), good reproducibility and a strong positive correlation between drug concentration and MS signal. Medical preparation concentrations were likely

higher than expected due to measurement error. A future study is planned with a larger sample size and three syringe brands to determine sympathomimetic drug stability stored up to 14 days.

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Table 1. Medication concentrations at fresh (< 4 hours), 3 days, and 7 days.

	Concentration in Micrograms/mL [95 % Confidence Interval]		
Storage time	**EPI**	**NE**	**PE**
Fresh (< 4 hours)	105 [92 – 120]	80 [73.5 – 88.5]	120 [108 – 130]
3 Days	96 [85 – 110]	80 [73.5 – 88.5]	95 [85 – 106]
7 Days	105 [92 – 120]	80 [73.5 – 88.5]	95 [85 – 106]