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JOINT ANNUAL MEETING 2023

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ORAL PRESENTATIONS I

OP 1

Trajectories of pain and opioid use up to 12 months after surgeryHofer D¹, Harnik M¹, Lehmann T², Stüber F^{1,3}, Stamer UM^{1,3}¹Department of Anaesthesiology and Pain Medicine, Bern University Hospital, University of Bern, Switzerland; ²Institute of Medical Statistics, Computer and Data Sciences, University Hospital of Jena, Jena, Germany; ³Department of BioMedical Research, University of Bern, Switzerland

Background: Chronic postsurgical pain (CPSP) and associated long-term postoperative opioid prescriptions are considered as major healthcare problem in some countries. Data from Europe are heterogeneous, e.g., in previous trials rates for postoperative persistent opioid prescriptions varied between 2-41%.

Aim of the study: To evaluate trajectories of pain and opioid use from the preoperative phase up to 12 months after surgery in a mixed surgical cohort.

Methods: Ethics approval for analysis of registry data derived from the European PAIN OUT project. Endpoints: Pre- and postoperative morphine equivalents, long-term use of opioids at 6 and 12 months (M6/M12). Subgroups without or with pre-existing chronic pain (pre-CP), with/without opioids before surgery, and with postoperative CP Unrelated (CP not within the surgical area), CP Related (CP at surgical site not meeting the ICD-11 definition) and CPSP (ICD-11 definition) at M6/M12 were compared. Statistics: χ^2 test, ANOVA, binary logistic regression; level of significance $p < 0.05$.

Results: Of 2233 patients, 42% reported pre-CP at the site of surgery, elsewhere or both. Opioids were taken by 5.6% of the patients due to the following reasons: back or joint pain, cancer pain, a chronic pain syndrome, or opioid use disorder ($n = 9$). Postoperative opioid doses were higher in patients with pre-CP compared to patients without pre-CP (mean (95% CI): 21 (19-23) vs. 13 (12-14) mg/24 h; $p < 0.001$). At M12, 34.0% of the patients reported CP, with 7.7% having moderate to severe pain (CP Unrelated 2.2%, CP Related 3.2%, CPSP 2.1%). Opioids were taken by 4.6% and 3.7% at M6/M12 (M12 without pre-CP 1.0%; with pre-CP 6.7%; $p < 0.001$). Cessation of opioids was observed in 56% of the preoperative opioid users. Of previously opioid-naïve patients, 1.2% were new opioid users (CP Unrelated, CP Related, CPSP: 7.1%, 2.3% and 0.7%; $p < 0.001$). Variables associated with M12 opioids were preoperative opioid use (estimated OR (95% CI): 28.3 (14.1-56.7); $p < 0.001$) and pain during the first 24 h after surgery (pain composite score: OR 1.2 (1.0-1.4); $p = 0.012$).

Conclusions: The rate of patients on postoperative long-term opioids was lower, the strong association of pre-existing CP comparable to US data. A more detailed assessment of preoperative CP and a differentiation of CP Unrelated, CP Related and CPSP with the reason for opioid use could improve perioperative care. Not all CP after surgery is CPSP, not all long-term opioid use is due to CPSP.

OP 2

Sevoflurane postconditioning protects from an early neurological deficit after subarachnoid hemorrhage. Results of a randomized laboratory study in rats.Morax Laurent^{1,2}, Beck-Schimmer Beatrice^{1,2}, Neff Jonah¹, Flury-Frei Renata³, Roth Z'graggen Birgit¹, Schläpfer Martin^{1,2}¹Institute of Physiology, University of Zurich, Zurich, Switzerland; ²Institute of Anesthesiology, University Hospital Zurich, Zurich, Switzerland; ³Institute of Pathology, Cantonal Hospital Winterthur, Winterthur, Switzerland

Background: Neurocognitive impairment is linked to Subarachnoid hemorrhage (SAH). Studies show that sevoflurane can reduce edema formation shortly after SAH in rats, but its effectiveness in the long-term repair phase is unknown. This research aimed to investigate whether sevoflurane postconditioning could enhance long-term neurological function by promoting the growth of new blood vessels near the hemorrhage site.

Methods: In this study, 53 animals underwent either SAH or sham surgery with 2 hours of postconditioning using either sevoflurane or propofol. Survival and the animals' neurological function (measured by the Garcia score) were evaluated. Garcia score was assessed 2 hours after recovery, on day 1, 2, 7, and 14. On day 14, blood samples and brain tissue were collected to measure vessel density (number of CD31-positive vessels) and activated glial cells (GFAP-positive astrocytes).

Results: The survival rate for sham animals was 100%, 69% in the SAH-propofol, and 92% in the SAH-sevoflurane group. Survival curves were different ($p = 0.021$). The short-term neurologic deficit was higher in SAH-propofol vs. SAH-sevoflurane animals 2h after recovery and on postoperative day 1 (propofol vs. sevoflurane: 14.6 ± 3.4 vs. 15.9 ± 2.7 points, $p = 0.034$, and 16.2 ± 3.5 vs. 17.8 ± 0.9 points, $p = 0.015$). Complete recovery from neurologic deficit was observed in all animals after day 7. Vascular density and activated glial cells, a surrogate for neuroinflammation, were more pronounced in SAH-propofol compared to SAH-sevoflurane animals (+14%, $p < 0.001$ and +50%, $p < 0.001$, respectively).

Conclusion: Sevoflurane postconditioning improves survival by 23%. The sevoflurane intervention could attenuate the early neurologic deficit, while the long-term outcome was similar across the groups. A higher vascular density close to the SAH area in the propofol group was not associated with improved outcomes.

OP 3

The postoperative analgesic efficacy of liposomal bupivacaine versus long-acting local anaesthetics for peripheral nerve and field blocks: a systematic review and meta-analysis, with trial sequential analysis.

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Background: Liposomal bupivacaine is claimed by the industry to provide analgesia for up to 72h postoperatively.

Objectives: To compare the postoperative analgesic efficacy of liposomal bupivacaine versus long-acting local anaesthetics for peripheral nerve or field blocks.

Design: Systematic review and meta-analysis with trial sequential analysis.

Data sources: MEDLINE, Embase, and Web of Science, among others, up to June 2022.

Eligibility criteria: We retrieved randomised controlled trials comparing liposomal bupivacaine versus bupivacaine, levobupivacaine or ropivacaine for peripheral nerve and field blocks after all types of surgery. Our primary endpoint was rest pain score (analogue scale 0–10) at 24h. Secondary endpoints included rest pain score at 48h and 72h, and interval morphine consumption at 24h, 48h and 72h.

Results: Twenty-seven trials including 2122 patients were identified. Rest pain score at 24h was significantly reduced by liposomal bupivacaine with a mean difference (95%CI) of -0.9(-1.4 to -0.4), $I_2 = 87\%$, $P < 0.001$. This reduction persisted at 48h and 72h with mean differences (95%CI) of -0.7(-1.1 to -0.3), $I_2 = 82\%$, $P = 0.001$ and -0.7(-1.1 to -0.3), $I_2 = 80\%$, $P < 0.001$, respectively. There were no differences in interval morphine consumption at 24h ($P = 0.15$), 48h ($P = 0.15$) and 72h ($P = 0.07$). The quality of evidence was moderate.

Conclusions: There is moderate level evidence that liposomal bupivacaine statistically reduces pain scores after peripheral nerve or field blocks for up to 72h postoperatively when compared with long-acting local anaesthetics. The mean difference in rest pain scores of less than one unit without impacting morphine consumption questions the medical relevance of liposomal bupivacaine, especially in the light of the high cost. These results should be interpreted with caution due to the elevated heterogeneity coefficient.

OP 4

Copeptin for the Prediction of all-cause Mortality Following Cardiac Surgery

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Background: Traditional markers of preoperative stress and inflammation such as C-reactive protein (CRP) or cortisol have been associated with worse clinical outcome in cardiac and non-cardiac surgery. The stress marker copeptin has recently been introduced as a biomarker in cardiovascular disease. However, the potential of copeptin to predict clinical outcomes in patients undergoing cardiac surgery remains elusive, especially in adults. We aimed to investigate the association of perioperative copeptin levels with adverse outcomes in adult patients undergoing cardiac surgery, in comparison to CRP and cortisol.

Methods: We analyzed blood samples of the Bern perioperative Biobank, a prospective cohort of adults who underwent cardiac surgery with the use of cardiopulmonary bypass at the Bern University Hospital between January and December 2019. Levels of copeptin, cortisol and CRP were analyzed in blood samples collected before induction of general anesthesia (preoperative) and 24 hours after surgery (postoperative). One year mortality and length of hospital stay were the primary outcome measures.

Results: A total of 192 patients (75.5% male, median age 67.0 [IQR 60.0–73.0]) underwent heart surgery and were included in this analysis. A higher copeptin level at baseline was associated with a higher body mass index (BMI; beta coefficient 0.49; 95%-CI (0.08, 0.89); $p = 0.019$), preoperative renal disease (beta coefficient 9.5; 95%-CI (4.7, 14.0); $p < 0.001$), a lower ejection fraction (beta coefficient -0.29; 95%-CI (-0.48, -0.11); $p = 0.002$) and a higher EuroSCORE II (beta coefficient 0.86; 95%-CI (0.32, 1.40); $p = 0.002$). Levels of all three biomarkers increased perioperatively ($p < 0.001$). Preoperative copeptin levels, but not a perioperative increase, were associated with 1-year all-cause mortality (odds ratio 9.32; 95%-CI (1.39, 65.4); $p = 0.020$) and length of hospital stay (beta coefficient 3.6; 95%-CI (1.1, 6.1); $p = 0.005$) before and after adjustment for age, BMI and gender. For the traditional stress markers cortisol and CRP, no association of preoperative levels or perioperative increase with all-cause mortality or length of hospital stay could be found.

Conclusions: Preoperative copeptin levels independently associate with 1-year all-cause mortality and length of hospital stay following cardiac surgery. No such relation was observed for CRP and cortisol, suggesting copeptin an attractive candidate for risk prediction.

OP 5

Preoperative Gastric Ultrasound in Patients at Risk for Aspiration - Toward a new Standard of Care to Improve Perioperative Patient Safety: A Prospective Observational Study in 2003 Patients

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Background: Perioperative pulmonary aspiration is accountable for a significant proportion of anesthesia-related morbidity and mortality. Although point-of care gastric sonography offers a fundamentally new and objective approach to assess individual aspiration risk prior to anesthesia, its practical implications remain largely unclear. Therefore, we aimed to evaluate the possible impact of routine preoperative gastric ultrasound on the perioperative management of elective and emergency adult patients at risk of pulmonary aspiration.

Methods: Patients with one or several aspiration risk factors according to a predefined catalogue, scheduled for elective or emergency surgery at a mid-sized Swiss teaching hospital in

2021 were included. Gastric ultrasound was performed by a trained physician immediately before anesthesia. Patients were categorized into low risk (empty, fluids ≤ 1.5 ml/kg body weight) or high-risk (solid, mixed or fluids >1.5 ml/kg body weight). After sonography, examiners were asked to state hypothetical changes in aspiration risk management (none, upgrading, downgrading) to their predefined anesthesiologic plan and adapt in case patient safety was at risk.

Results: Two thousand and three patients (mean age 60.5 (standard deviation 17.8), 50% female) were included, whereof 1246 underwent elective and 757 emergency surgery. In elective patients, 86% presented with a low and 15% with a high-risk stomach, with 79% versus 21% in emergency patients, respectively. In elective patients, preoperative gastric sonography would have led to a 14% downgrading and 4% upgrading, while in contrast 18% of emergency patients would have been downgraded and 3% upgraded.

Conclusions: We show that preoperative gastric ultrasound reliably identifies high- and low risk situations in patients at risk for aspiration and adds critical information to perioperative management. We recommend routine preoperative gastric ultrasound at least in patients at risk to aid decision making, with the aim of improving patient safety, and tailoring perioperative care to the individual patient.

ORAL PRESENTATIONS II

OP 6

Inspired Oxygen Fraction of 80% Aggravates Segmental Left Ventricular Diastolic Dysfunction in Anaesthetised Patients with Coronary Artery Disease

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Background: Use of high inspired fractions of oxygen (FIO₂) is common during general anaesthesia (GA), despite its vasoconstrictive properties on the coronary vascular bed. This may pose problems for coronary artery disease (CAD) patients who are at an increased risk for perioperative ischaemia. One of the first features of ischaemia is diastolic dysfunction. Perioperative evaluation of diastolic function usually involves Doppler assessment of transmitral inflow and mitral annular tissue doppler (TDI) velocities by echocardiography. However, these provide only a global information and cannot assess regional dysfunction. This however can be overcome using strain rate analysis. In this study, the impact of hyperoxia on regional myocardial diastolic function was quantified by strain rate analysis in CAD patients undergoing GA.

Methods: CAD patients (n = 106, 66 ± 8y, 87% male) scheduled for elective coronary surgery were prospectively recruited for this randomized, controlled crossover trial. Normoxaemic (FIO₂ = 0.3, SpO₂ 95-98%) and hyperoxic (FIO₂ = 0.8) states were titrated and three left ventricular short axis transoesophageal echocardiography cine loops were acquired, along with early transmitral inflow (E) and early septal and lateral TDI (e') velocities at each FIO₂ level. Subendocardial circumferential strain rate was analysed by a blinded reader and peak early diastolic strain rate was determined (edSR) for each myocardial segment and a ratio to mitral valve inflow was derived (E/edSR). Segments were classified as post-stenotic or remote based on coronary-angiography.

Results: The standard global results showed already presence of diastolic dysfunction (septal and lateral TDI e': 7.0 ± 1.5 and 8.7 ± 2.0 cm/s) at FIO₂ = 0.3, which worsened further when FIO₂ was titrated to 0.8 (mitral inflow to averaged tissue Doppler mitral velocity ratio (E/e'): 8.2 ± 2.4 to 8.6 ± 2.6, p = 0.01). Regional analysis by strain rate showed that E/edSR only worsened in post-stenotic myocardial segments (42.5 ± 17.8 to 44.7 ± 19.2, p = 0.04), while for remote myocardium there was no difference (51.8 ± 25.5 to 53.5 ± 28.5, p = 0.47).

Conclusions: Targeting hyperoxia perioperatively appears to attenuate diastolic function in CAD patients under GA. Moreover, regional strain rate analysis suggests that this change is especially pronounced in myocardium downstream of coronary lesions. During GA, CAD patients may benefit from conservatively titrated FIO₂ levels to avoid aggravation of diastolic dysfunction.

OP 7

Characterization of oscillatory pressure signal loss across the tracheobronchial tree: a pediatric experimental model

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Background: High-frequency oscillatory ventilation (HFOV) is characterized by small tidal volumes and rapid sinusoidal pressure changes with supraphysiological frequencies. HFOV is considered as a rescue therapy in neonates and children with severe respiratory failure since it improves gas exchange. The effectiveness of the transmission of the oscillatory signals from the airway opening to the gas exchange zone has not been characterized. Thus, we aimed at quantifying the transmission of the pressure oscillations to the alveolar compartment in a pediatric experimental model of HFOV.

Methods: Six piglets were anesthetized and mechanically ventilated, then an intercostal window to the lungs was surgically opened allowing placement of alveolar capsules (n = 16) on the visceral pleura. Pressures were measured at the airway opening (Pao), at the tip of the endotracheal tube (Ptr) and in the alveoli (Palv) through the alveolar capsule. Oscillatory signals of 5 and 10 Hz were introduced into the airway opening by a loudspeaker during 8-second-long apnoeic periods and the pressures transfer functions such as Ptr/Pao, Palv/Ptr and Palv/Pao were determined.

Results: Marked diminishments were observed in the transmission of the 5 and 10 Hz pressure signals inside the endotracheal tube with Ptr/Pao values of 37.5 ± 2.5% and 19.0 ± 2.4% respectively. A further significant reduction by 36.2 ± 1.7% for 5 Hz and 42.7.0 ± 2.2% for 10 Hz in the pressure oscillations was evidenced intrapulmonary (Palv/Ptr). These pressure drops resulted in a net transmission from airway opening to the alveoli (Palv/Pao) of 13.5 ± 0.6% for 5 Hz and 8.7 ± 4.1% for 10 Hz.

Conclusion: Results obtained in this pediatric experimental model revealed a massive oscillatory signal loss from the airway opening to the alveoli reaching as much as 85% for 5 Hz and may exceed 90% for 10 Hz. The majority (about 60%) of this pressure dissipation can be attributed to the impedance of the endotracheal tube. These findings may have importance in better understanding the lung behaviour under HFOV.

OP 8

Perioperative predictors of postoperative delirium after non-cardiac surgery: an individual patient data meta-analysis

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Background and Objectives: Delirium is a common and serious complication after surgery, associated with adverse patient and healthcare system outcomes. We performed an individual patient data (IPD) meta-analysis to identify perioperative prognostic factors associated with postoperative delirium (POD) and assessed their relative predictive value among adults undergoing non-cardiac surgery.

Methods: We searched MEDLINE, EMBASE, and CINAHL from inception to May 2020 and included studies that: (1) enrolled adult patients undergoing non-cardiac surgery, (2) assessed perioperative risk factors for POD, and (3) measured the incidence of delirium using a validated delirium assessment tool. Among 14,973 unique studies, 714 were assessed in full text, and 192 met our eligibility criteria, from which we successfully acquired individual patient data from 21 studies. We pooled IPD from 21 studies and performed one-stage meta-analysis using multilevel mixed-effects logistic regression after a multivariable imputation via chained equations model to impute missing data. Our end point of interest was POD diagnosed up to 10 days post procedure.

Findings: The probability of developing POD was 17.7% among 8,382 patients in our analysis. In the final adjusted model, male sex, older age, being underweight, less educated, currently smoking, having a past history of delirium, being institutionalized, having a greater number of co-morbidities, prescribed >5 medications, having a higher Charlson comorbidity index, higher preoperative serum C-reactive protein level, ASA status III or IV, and longer duration of surgery/anesthesia were independent prognostic factors for POD.

Interpretation: Prognostic factors found to be important in this study can be used in clinical practice to inform patients and care givers about the expected risk of developing delirium after surgery and to explain which features should prompt clinicians to consider perioperative preventive strategies to optimise patient outcomes.

OP 9

Side-effects after intrathecal morphine administration: a systematic review and meta-analysis with meta-regression

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Intrathecal morphine provides good analgesia after a wide range of operations. However, widespread implementation into clinical practice is hampered by concerns of its potential side effects. We undertook a systematic review, meta-analysis and meta-regression with the primary objective of determining whether a threshold dose for each of the side effects could be defined. We systematically searched the literature for any trials comparing intrathecal morphine vs control in patients undergoing any type of surgery under general or spinal anaesthesia, or for labour. Primary outcomes were rates of PONV, pruritus, urinary retention, sedation, respiratory depression and hypoxaemia within the first 24 postoperative hours. Subgroup analyses according to doses (0-100µg; 101-200µg; 201-500µg; >500µg) were performed for each outcome. Trials were excluded if doses were not specified. We captured 163 trials including 9545 patients. Rates of PONV, pruritus, urinary retention within 24 postoperative hours and respiratory depression were significantly increased in the intrathecal morphine group with a risk ratio (95%CI) of 1.3 (1.3-1.4), I² = 35%, p < 0.0001; 4.2 (3.5-5.2), I² = 60%, p < 0.0001; 1.2 (1.1-1.4), I² = 48%, p = 0.0005; and 1.9 (1.4-2.6), I² = 14%, p < 0.0001, respectively. No correlation between doses and rates could be established. There was no difference between groups in rates of sedation (risk ratio [95%CI] = 1.1 (1.0, 1.3), I² = 18%, p = 0.09) and hypoxaemia (risk ratio [95%CI] = 1.2 (1.0-1.5), I² = 0%, p = 0.10). In conclusion, intrathecal morphine significantly increased PONV, pruritus, urinary retention and respiratory depression after surgery or labour, without impact on sedation or hypoxaemia. A threshold dose for the first four outcomes could not be identified.

OP 10

Early sevoflurane sedation in severe COVID-19-related lung injury patients. A pilot randomized controlled trial

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Background: This study aims at assessing the potential organ protective effects of early sevoflurane sedation in patients suffering from COVID-19-related lung injury requiring invasive mechanical ventilation and sedation.

Methods: From April 2020 to May 2021, a pilot multicenter randomized controlled trial took place at four hospitals in Switzerland. Patients who required mechanical ventilation due to severe COVID-19-related lung injury were randomly assigned to either 48-hour sedation with sevoflurane or continuous intravenous sedation (control) within 24 hours after intubation. The primary combined outcome was mortality or persistent organ dysfunction (POD), defined as the need for mechanical ventilation, vasopressors, or kidney replacement therapy at day 28. Secondary outcomes included complications, length of stay in

the intensive care unit (ICU) and hospital, as well as plasma inflammatory mediators.

Results: The study involved 60 patients, with 28 randomly assigned to sevoflurane and 32 to control (intravenous) sedation. The primary endpoint was reached in a similar fraction of patients in the sevoflurane (11 patients = 30%) and the control arm (13 patients = 41%; $p = 0.916$). There was a noticeable difference in vasopressor dependence on day 28 with 1 (4%) patient in the sevoflurane and 7 (26%) in the control arm ($p = 0.028$). No other differences for the individual components of the composite were found. Length of ICU and hospital stay, as well as registered complications within 28 days were comparable, except for acute kidney injury (AKI), occurring in 11 (39%) sevoflurane versus 2 (6%) control patients ($p = 0.001$). Over the first 8 days, plasma levels of inflammation (i.e. C-reactive protein) and endothelial activation (i.e. angiotensin-2, soluble urokinase-type plasminogen activator receptor (suPAR)) were higher in the sevoflurane vs. the control group ($p = 0.018$, $p < 0.001$, and $p = 0.009$). No difference was detected for procalcitonin, interleukin-6, and angiotensin-1. In contrast to early COVID-19 research reports, inflammatory markers were just moderately increased.

Conclusion: There were no outcome differences upon 48h sevoflurane sedation compared to control. The extent of inflammation was lower than expected. Given the proposed pleiotropic anti-inflammatory mechanism, it could very well be that sevoflurane only provides protection if, indeed, a certain level of inflammation is present. It is important to keep a close watch on AKI in future studies.

POSTERS

P 1

Single-bolus injection of local anaesthetics, with or without continuous infusion, for interscalene brachial plexus block in the setting of multimodal analgesia: a randomised controlled trial

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Background and aims: Previous trials favoured a continuous interscalene brachial plexus block over a single injection for major shoulder surgery. However, these trials did not administer a multimodal analgesic regimen. The null hypothesis of this randomised, controlled trial is that a continuous infusion of local anaesthetic after a single injection for an interscalene brachial plexus block does not provide additional analgesia after major shoulder surgery in the setting of multimodal analgesia, inclusive of intravenous dexamethasone, magnesium, acetaminophen and ketorolac.

Methods: Sixty patients undergoing shoulder arthroplasty or arthroscopic rotator cuff repair were randomised to receive a bolus of ropivacaine 0.5%, 20mL, with or without a continuous infusion of ropivacaine 0.5% 4–8 mL.h⁻¹, for an interscalene brachial plexus block. Patients were provided with intravenous morphine patient-controlled analgesia. The primary outcome was cumulative intravenous morphine consumption at 24h postoperatively. Secondary outcomes included pain scores at rest and on movement, and functional outcomes, measured over 48h after surgery.

Results: Median (interquartile range) cumulative intravenous morphine consumption at 24h postoperatively was 10mg (4–24) in the continuous infusion group and 14mg (8–26) in the single injection group ($p = 0.74$). No significant between-group differences were found for any of the secondary outcomes.

Conclusions: A continuous infusion of local anaesthetics after a single injection for an interscalene brachial plexus block does not provide additional analgesia after major shoulder surgery in the setting of multimodal analgesia, inclusive of intravenous dexamethasone, magnesium, acetaminophen and ketorolac. The findings of this study are limited by performance and detection biases.

P 2

PROSPECT Guideline for Haemorrhoid Surgery: A Systematic Review and Procedure-specific Postoperative Pain Management Recommendations

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Background and aims: Haemorrhoidectomy is associated with moderate-to-severe postoperative pain. The aim of this systematic review was to assess the available literature and update previous PROSPECT (PROcedure SPECific Postoperative Pain Management) recommendations for optimal pain management after haemorrhoidectomy.

Methods: A systematic review utilizing PROSPECT methodology was undertaken. Randomized controlled trials published in the English language from January 1, 2016 to February 2, 2022 assessing postoperative pain using analgesic, anaesthetic, and surgical interventions were identified from MEDLINE, EMBASE and Cochrane Database.

Results: Of the 371 RCTs identified, 84 RCTs and 19 systematic reviews, meta-analyses met our inclusion criteria (total: 103 publications). Interventions that improved postoperative pain relief included: paracetamol and non-steroidal anti-inflammatory drugs or cyclooxygenase-2 selective inhibitors, systemic steroids, pudendal nerve block, topical metronidazole, topical diltiazem, topical sucralfate or topical glyceryl trinitrate, and intramuscular injection of botulinum toxin.

Conclusions: This review has updated the previous recommendations written by our group. Important changes reside in abandoning oral metronidazole and recommending topical metronidazole, topical diltiazem, topical sucralfate, topical glyceryl trinitrate. Botulinum toxin can also be administered. Contemporary publications confirm the analgesic effect of bilateral pudendal nerve block but invalidate recommendations on perianal infiltration. The choice of the surgery is mostly left to the discretion of the surgeon based on his experience, expertise, type of haemorrhoids, and risk of relapse. That said, excisional surgery is more painful than other procedures.

P 3

Visualizing diastolic function with 4D Flow cardiovascular magnetic resonance imaging after elective electrical cardioversion in patients with atrial fibrillation

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Introduction: Anaesthetists often perform electrical cardioversions (ECV) to terminate atrial fibrillation but success rates are mixed. Most attention is paid to recovery of systolic function and not diastolic function; despite the fact this is when active atrial contribution occurs. 4D-Flow cardiovascular magnetic resonance (CMR) non-invasively quantifies blood flow in any plane throughout systole and diastole. It also measures kinetic energy (KE) of the blood, a novel parameter for intraventricular haemodynamics as turbulent flow will reduce KE. This study assessed the acute and long-term effects of ECV on diastolic function using 4D-Flow CMR.

Methods: Ten patients with atrial fibrillation scheduled for elective ECV were prospectively recruited to undergo three CMR exams: a baseline CMR (#1) prior to ECV, an acute CMR (#2) performed 2-5h after ECV, and a long-term CMR (#3) performed 6-12 weeks later. 4D-flow images were obtained of the thoracic cavity and cardiac output from the outflow tract, peak blood flow through the mitral valve, along with left intraventricular KE were quantified.

Results: Patients required 1-3 shocks ranging from 120-600J cumulative biphasic energy. Total cardiac output did not change between visits (CMR-1: 3.8 ± 1.3 L/min, CMR-2: 4.4 ± 1.3 L/min CMR-3: 4.2 ± 1.0 L/min, all $p > 0.05$). Early diastolic flow through the mitral valve was initially 352 ± 71 ml/s with no acute change at CMR-2 (400 ± 151 ml/s $p = 0.21$) but decreased to 273 ± 74 ml/s by CMR-3 ($p = 0.03$). Prior to ECV, no patients had a visible late diastolic transmitral flow peak (A-wave). Shortly after ECV this A-wave returned in 7/10 patients (84 ± 49 ml/s) and late diastolic flow was 210 ± 74 ml/s by CMR-3 ($p = 0.06$). This return in transmitral late diastolic flow corresponded to a redistribution in intraventricular KE. While at CMR-1 all diastolic KE occurred in early diastole (3.4 ± 3.0 KJ) by CMR-2 early diastolic KE had non-significantly increased to 3.9 ± 3.6 KJ ($p = 0.09$) before dropping to 1.6 ± 0.8 KJ ($p = 0.02$). Late diastolic KE was present at both CMR-2 (1.2 ± 0.9) and CMR-3 (2.6 ± 2.0 KJ).

Conclusion: Multi-parametric 4D-Flow CMR quantifies the acute return of late diastolic activity associated with returning atrial contraction after ECV in patients with atrial fibrillation. It demonstrates that the relationship between early and late diastole continues to evolve weeks after ECV. Advanced imaging techniques may have the potential to investigate how cardiac function adapts over time in response to ECV.

P 4

Kir2.1 modulation in macrophages sensitises dorsal root ganglion neurons through TNF secretion after nerve injury

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The spared nerve injury (SNI) is a model of neuropathic pain. Ligating the tibial and peroneal branches of the sciatic nerve, results the development of painful hypersensitivity in the lateral part of the paw that is innervated by the intact sural branch. We hypothesize that macrophages in the dorsal root ganglion (DRG) contribute to the sensitization of DRG neurons. We aim to characterize the activation state of macrophages after SNI, and their ability to sensitize DRG neurons.

The CX3CR1+ macrophages proliferate in the L3 and L4 DRG, where injured and uninjured neurons are present, but not in the L5 DRG which consists mainly of uninjured neurons. The proteomic profile of macrophages ipsilateral to SNI is significantly different from contralateral macrophages, indicating their activated state. Culture medium conditioned by macrophages from SNI mice was transferred onto a culture of DRG neurons from naïve mice and induced their hyperexcitability. Sensitized neurons fired more action potentials spontaneously and in response to current stimulation. They also had larger voltage-gated sodium channel (Nav) Nav1.7 and Nav1.8 current densities. Blocking the microtubule transport of Nav channels with Nocodazole prevented the sensitization of DRG neurons with the conditioned medium.

Whole-cell voltage clamp recordings revealed an upregulation of Kir2.1 inward currents in macrophages from ipsilateral DRG after SNI. Inhibiting Kir2.1 currents in macrophages from SNI mice prevents them from sensitizing DRG neurons. We demonstrate that blocking TNF in the medium conditioned by macrophages is sufficient to prevent the sensitization of naïve DRG neurons. Furthermore, blocking p38, downstream of TNF signaling, in the DRG neurons also prevented their sensitization by the macrophage conditioned medium.

This study demonstrates that SNI-primed DRG macrophages are able to sensitize DRG neurons from naïve mice through the TNF-p38 pathway by increasing their Nav1.7 and Nav1.8 currents. Modulating the electrophysiological state of macrophages may be a promising tool to switch their pro-inflammatory state and prevent their sensitizing effects.

P 5

Investigating the Response in Cardiovascular Function to Haemodynamic Stress Using an Isometric Handgrip Exercise

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Background: Perioperative hypertension commonly occurs during surgery and can instigate a haemodynamic stress on the heart. Under such a stress, cardiovascular dysfunction can be unmasked or attenuated further. Thus, it is important to investigate how a haemodynamic stimulus impacts the cardiovascular system. While current diagnostic exams utilize injected pharmacological agents or exercise tests (i.e. ergometer or treadmill) a handgrip squeeze is a potential simple alternative as it is an isometric exercise known to increase blood pressure. Ideally this is combined with non-invasive imaging to comprehensively assess cardiovascular function, measuring not only the left ventricle but incorporating atrial and aortic function as well. In healthy controls, we investigated if the handgrip exercise influences cardiovascular function detected by cardiovascular magnetic resonance (CMR).

Methods: Healthy volunteers (n = 15, age: 21-43 years) underwent a 3-Tesla CMR exam. Functional images were taken of the 4-chamber views of the heart and of the ascending aorta at both rest and after 2.5 minutes into the handgrip exercise. For this exercise, participants gripped a pressure ball at 30% of their maximal handgrip strength for the entire exercise duration. Non-invasive blood pressure was obtained before and during exercise.

Results: From rest to handgrip the haemodynamic measurements were: heart rate: 68 ± 9bpm to 71 ± 8bpm, p = 0.05; systolic blood pressure: 118 ± 24mmHg to 122 ± 9mmHg, p = 0.47; and diastolic blood pressure: 62 ± 11mmHg to 76 ± 11mmHg, p < 0.01. Left atrial strain (36.9 ± 5.9% to 40.6 ± 8.5% p = 0.02) and left ventricular strain (-17.4 ± 2.3% vs -18.5 ± 2.3%, p = 0.01) improved with the handgrip. There was also an increase in maximum aortic diameter (30.4 ± 3.2mm to 31.1 ± 3.5mm, p = 0.02) and maximum aortic pressure gradient (5.2mmHg ± 1.5mmHg to 4.4mmHg ± 1.5mmHg, p < 0.01). This decreased the aortic strain from 27.3 ± 6.1% to 24.2 ± 7.2% (p < 0.01).

Conclusion: The handgrip test had a significant impact on ventricular, atrial and aortic function in awake, healthy controls. Its suitability as a haemodynamic stress test can now be investigated in patient cohorts to assess its role in unmasking cardiovascular dysfunction and to potentially determine who may be increased risk for cardiac complications during perioperative hypertension.

P 6

Use of the portable vaporizer SEDACONDA-ACD® for anesthesia induction in children dentistry: a prospective observational quality study.

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Background: Most pediatric dental treatment occurs in the dental office without the need for interventions to address the child's fear and anxiety¹. However, because of compliance issues, certain population of children or patients requiring multi-site procedures often need general anesthesia. Usually, induction of anesthesia is made by inhalation through a face mask using Sevoflurane, the IV infusion is inserted after the loss of consciousness. Sevoflurane is delivered by a specific vaporizer². This device is routinely used in hospitals; however, it is attached to a heavy and non-transportable classical anesthesia workstation. We describe here an alternative method, using a portable vaporizer: the SedaConDa-ACD®³. We conducted a prospective, observational, quality study.

Methods: The SedaConDa-ACD® is a simple and easy to transport device. It allows the delivery of Sevoflurane through a porous rod, by a draw-over rebreathing technique, using a special syringe attached to an electrical pump. This set-up avoids the need for a bulky vaporizer. After written consent of parents, we prospectively observed each induction and collected quality data.

Results: 50 children were included. Age 6,84 years (median of 6; 4-18) and weight 23,65 kg (median of 20; 13-60). ASA score 1-2.

Primary outcome: Induction time⁴ = Loss Of Eyelid Reflex (LOER) 1,33 minutes (median of 1; 0,5-4)

Secondary outcomes: quality of induction 2,74 (scale 0-3: median 3; 2-3), quantity of Sevoflurane used 5,3 ml (median 5; 2-12), end-tidal Sevoflurane 3,97% (median 4; 1,6-7,1). Complications: 1 (laryngospasm), no failed induction (no score of 0).

Discussion: Due to demographic pressure and widespread waiting lists in hospitals, the demand for advanced pediatric dental care in the office-based setting has increased. For patients that need general anesthesia, inhalational induction is favored over IV by most pediatric patients, especially young ones or those with special needs. The use of this device enables a standard and smooth mask induction without the need for a heavy anesthesia workstation.

Conclusion: This clinical quality study shows that the SedaConDa-ACD® enables mask induction in children in the office-based setting. Induction times (LOER) and mask acceptance are similar to general literature⁴ without failures or major complications.

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P 7

Efficacy and safety of sugammadex in patients with neuromuscular disease: a systematic review and an original quality assessment of the literatureSchneider A¹, Tramèr M¹, Keli-Barcelos G¹, Elia N¹¹Department of Anaesthesiology, Clinical Pharmacology, Intensive Care and Emergency Medicine, Geneva University Hospitals, Geneva, Switzerland**Objectives:** To summarize the evidence on the efficacy and safety of using sugammadex for the reversal of neuro-muscular blocking agents (NMBA) in patients with neuromuscular diseases, and to evaluate the quality of published reports.**Eligibility criteria:** Articles (any study design) reporting on the usage of sugammadex for the reversal of an NMBA in patients (any age) with any neuromuscular disease.**Information sources:** MEDLINE, EMBASE, Cochrane, SciELO to 31.12.2021.**Risk of bias:** We used a modified CARE checklist (maximum score, 23) to assess the quality of data reporting and a specific content checklist for NMBA reports (maximum score, 41) that was developed, using a two rounds Delphi survey, with eight experts in the field.**Results:** We retrieved 105 reports (283 patients): 72 case reports (81), 28 correspondences (29), 4 case series (163) and one prospective cohort study (10). Neuromuscular diseases were myasthenia gravis (202 patients) or diseases of the muscles (38), central nervous system (21), motor neurons (19) or peripheral nerves (3). NMBAs were rocuronium (273 patients), vecuronium (9) or unknown (1). Sugammadex regimens ranged from 1 to 17 mg·kg⁻¹. Return to a TOF ratio ≥ 0.9 , reported in 258 patients, was successful in 252 (97.6%). Adverse outcomes were reported in 8 patients (3%): 5 had respiratory insufficiencies (of whom 2 required reintubation), and one each had anaphylaxis, myasthenic crisis or recurarization. In the 72 case-reports, the median score of the CARE checklist was 13 (IQR, 11 to 16). In all 105 reports, the median score of the specific NMBA checklist was 24 (IQR, 21 to 27). There was a significant positive correlation between the scores.**Discussion:** These data suffer from major limitations. Firstly, most reports were uncontrolled observations and therefore did not allow to assess the efficacy and safety of pharmacological reversal of NMBAs in patients with neuromuscular diseases. Secondly, most patients received rocuronium and suffered from myasthenia gravis. Thus, extrapolation of these data to other NMBAs or neuromuscular diseases remains speculative. And finally, the quality of data reporting was low to moderate. To add significant information to the existing database, any further case-report should follow recommended reporting guidelines, include specific information deemed critical for the interpretation of reports in this field, and describe what this new case-report adds to the current knowledge.

P 8

Predicting myocardial hypoperfusion under hyperaemic conditions with ventricular strain analysis at restSchmid B¹, Weiner J², Heinisch C², Kujawski T², Szucs-Farkas Z^{3,4}, Zbinden R², Guensch DP¹, Fischer K¹¹Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; ²Cardiology, Hospital Centre of Biel, Biel, Switzerland; ³Radiology, Hospital Centre of Biel, Biel, Switzerland; ⁴Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland**Background:** Perioperative myocardial ischaemic injury is known to occur in more than 25% of non-cardiac surgeries but can be difficult to predict. Especially in the presence of underlying coronary artery disease (CAD), regional hypoperfusion and subsequent myocardial ischaemia can be triggered by vasoactive stimuli, which are abundant during general anaesthesia. Thus, it is important to investigate if diagnostic measures performed preoperatively under rest conditions can predict which patients are prone to inducible myocardial blood flow (MBF) deficits during stress. While anaesthetists try to avoid myocardial ischaemia, in a cardiovascular magnetic resonance (CMR) exam, vasodilators and stress agents are intentionally administered to quantify how MBF responds to stimuli in a diagnostic environment. We investigated if left ventricular systolic function assessed by strain at rest predicts poor MBF during a hyperaemic stimulus in awake patients with suspected CAD.**Methods:** Fifty patients with suspected CAD were prospectively recruited to undergo a CMR exam to test for inducible ischaemia. Functional images at rest were acquired for three long-axis views and in a full short-axis stack. Circumferential and longitudinal peak strain was calculated per myocardial segment. Strain was then compared to MBF quantified under a hyperaemic stress induced by intravenous regadenoson (400µg).**Results:** Median segmental MBF was 1.6 [1.1-2.4]ml/g/min with 357/784 (46%) segments affected by hypoperfusion under stress (<1.5ml/g/min). Strain at rest discriminated which myocardial segments would yield a poor MBF under stress conditions, with circumferential strain performing better than longitudinal. The optimal cut-off of -18% for segmental circumferential strain had a sensitivity of 79% (specificity = 48%) for detecting stress-induced hypoperfusion. A cut-off of -9.8% improved specificity to 90% (sensitivity = 16%). For longitudinal strain, cut-offs of -15.0% (specificity = 49%, sensitivity = 64%) and -8.8% (specificity = 90%, sensitivity = 18%) were calculated.**Conclusion:** Segmental ventricular strain analysis predicts myocardium that is prone to hypoperfusion under a pharmacological hyperaemic stimulus. Preoperative strain analysis in routine imaging could help enhance risk assessment by identifying patients potentially at risk for perioperative ischaemia. Further investigation is needed to assess if these findings in awake patients translate to a general anaesthesia setting.

P 9

Supplemental oxygen negatively influences right ventricular pulmonary artery coupling in awake healthy controls quantified by non-invasive kinetic energy analysis

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Background: Independent of pre-existing right heart failure, right heart dysfunction can arise perioperatively and is associated with difficult anaesthetic management and poor outcome. Consequently, it is important to investigate if common agents used in an anaesthetic environment can have a negative influence on right heart function. A key component of right heart dysfunction is coupling between the right ventricle (RV) and pulmonary artery (PA). RV-PA uncoupling occurs when RV contractility can't increase to match the afterload, leading to deterioration of right heart function. The RV and PA often have to be evaluated in separate measurements but using non-invasive 4D-flow cardiovascular magnetic resonance (CMR), the RV and PA can be quantified simultaneously. Kinetic energy (KE) can be quantified in both, the ventricles and great vessel, as flow is driven by pressure gradients. Unlike volume analysis or movement of the tissue, KE can account for both laminar flow and vortices. We investigated the impact of supplemental oxygen on RV-PA-coupling, using KE derived by 4D-flow CMR.

Methods: Healthy volunteers (<45y, n = 11) were recruited to undergo a 3-Tesla CMR. A set of 4D-flow images was acquired of the thoracic cavity first in resting conditions while participants breathed in room air, and then after 10 minutes of oxygen inhalation (100%, 10L/min) administered through a rebreathing facemask. KE was assessed for the RV, indexed for end-diastolic volume, and for the main trunk of the PA.

Results: After oxygen administration, the KE in the RV decreased from $9.0 \pm 2.6 \mu\text{J}\cdot\text{ml}^{-1}$ to $7.3 \pm 3.0 \mu\text{J}\cdot\text{ml}^{-1}$ ($p = 0.03$) while the maximal KE in the PA did not change after oxygen administration ($11634 \pm 5521 \mu\text{J}$ vs $10446 \pm 5494 \mu\text{J}$, $p = 0.18$). Consequently, the RV/PA KE ratio decreased after oxygen administration from $0.88 \pm 0.31 \text{ nJ}\cdot\text{ml}^{-1}/\mu\text{J}$ to $0.72 \pm 0.20 \text{ nJ}\cdot\text{ml}^{-1}/\mu\text{J}$ ($p = 0.03$).

Conclusion: Using non-invasive quantification of intraventricular and intravascular KE by 4D-flow CMR imaging, we observed ten minutes of supplemental oxygen attenuates haemodynamics in the RV of awake healthy participants, leading to a worsening of RV/PA coupling. As oxygen is frequently used in anaesthetic and intensive care management, the impact of excessive oxygen titration should be considered when managing right heart function.

P 10

Depression of four-chamber cardiac function during the induction of general anaesthesia in patients without cardiovascular co-morbidities

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Background: Induction of general anaesthesia (GA) is a complex sequence of events including breathing pattern changes, intubation, positive pressure ventilation, anaesthetics and medication with cardiovascular effects. Yet, it is relatively unknown how GA induction impacts cardiac function, especially when looking beyond the left ventricle at the right heart and atria. Developments in cardiovascular magnetic resonance (CMR) can acquire a four-chamber cine while free-breathing, allowing for continuous imaging. Applying CMR, we investigated changes in bi-atrial and bi-ventricular function throughout GA induction.

Methods: Three patients (ASA-PS \leq II, <45years) scheduled for elective orthopedic surgery underwent GA induction inside the MRI. Four-chamber long-axis images were acquired approximately every 45s from the awake state through induction, and for 10 minutes of the maintenance phase. Long-axis-shortening of the chambers was calculated for the left and right atrium (LA, RA) and left ventricle (LV). Right ventricular function was calculated using tricuspid annular planar systolic excursion (TAPSE).

Results: In comparison to the awake baseline state (LV: $-15.5 \pm 0.3\%$, TAPSE: $20.6 \pm 3.2\text{mm}$, LA: $30.7 \pm 4.2\%$, RA: $37.9 \pm 5.3\%$), the deep-paced breathing at 14bpm during preoxygenation increased function in all chambers (LV: $-17.3 \pm 0.8\%$, TAPSE: $24.0 \pm 2.5\text{mm}$; LA: $41.7 \pm 6.8\%$, RA: $41.1 \pm 6.0\%$). With the administration of sufentanil ($0.5\mu\text{g}/\text{kg}$), propofol ($2\text{mg}/\text{kg}$) and then rocuronium ($1\text{mg}/\text{kg}$), breathing slowed and function subsequently worsened back to or below baseline (LV: $-15.6 \pm 1.3\%$, TAPSE: $17.3 \pm 3.2\text{mm}$, LA: $23.9 \pm 2.8\%$, RA: $31.4 \pm 3.5\%$). Prior to intubation, manual bag ventilation again increased function (LV: $-17.6 \pm 0.2\%$, TAPSE: $18.0 \pm 4.7\text{mm}$, LA: $28.5 \pm 4.7\%$, RA: $34.0 \pm 4.5\%$). Upon the start of positive pressure mechanical ventilation (tidal volumes $6\text{ml}/\text{kg}$) and maintenance with sevoflurane, four-chamber function gradually dropped. By 10min after intubation, a reduction was observed in ventricular function (LV: $-13.7 \pm 0.6\%$, TAPSE: $15.3 \pm 2.5\text{mm}$), with the largest depression observed in the atria (LA: $16.6 \pm 4.0\%$, RA: $22.8 \pm 2.0\%$) corresponding to more than a 40% decline.

Conclusion: In the first study to use continuous CMR imaging during GA induction, we can quantify that in patients with no history of cardiovascular disease, GA induction has a dynamic effect on cardiac function, with atrial depression observed during the maintenance phase. This will be further investigated in cardiovascular patients.

P 11

Fluctuations in blood gases induced by breathing maneuvers induce myocardial deoxygenation to the same extent as pharmacological vasodilators in patients with suspected ischemic heart disease

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Introduction: Inducible oxygen supply-demand mismatch is one of the most common causes of perioperative myocardial ischemia. Patients with coronary artery disease (CAD) are especially vulnerable to factors that trigger vasodilation, as blood flow is redistributed away from compromised tissue leading to deoxygenation. While attention is paid to anesthetics for triggering perioperative ischemia, blood gases can also have an important role because of their vasoactive properties. Patients experience blood gas changes routinely during general anesthesia, commonly from alterations in breathing patterns and ventilation settings. However, it is unknown if blood gases impact oxygen supply-demand balance to the same extent as pharmacological stimuli. This can now be quantified non-invasively with oxygenation-sensitive cardiovascular magnetic resonance (OS-CMR). Thus, we compared the myocardial oxygenation response to blood gas changes induced by breathing maneuvers to a pharmacological vasodilator using OS-CMR.

Methods: Patients (n = 33, 66 ± 11 years, 33% female) with suspected CAD referred for a diagnostic CMR exam were prospectively recruited. For the blood-gas stimulus, patients breathed deeply and rapidly at a respiration rate of 30bpm for 60s to induce hypocapnia, followed by 30s of apnea to induce hypercapnia. The established pharmacological stress protocol was performed with regadenoson (400µg). OS-CMR images were acquired during both techniques and the change in myocardial oxygenation for each stimulus was calculated.

Results: During the short breathing maneuver, 79% of patients had an attenuated myocardial oxygenation response (<+8%) across the myocardium, and 33% yielded a deoxygenation (<0%). The myocardial oxygenation response was similar between the breathing maneuvers (3.2 ± 6.7%) and regadenoson (5.0 ± 6.9%, p = 0.20). Patients with pharmacologically induced poor oxygenation response also showed a poor oxygenation response when the breathing maneuver was performed (r = 0.39, p = 0.04)

Conclusion: Patients with suspected CAD are at risk for myocardial deoxygenation during blood gas changes triggered by voluntary breathing maneuvers. These breathing maneuvers had an equal impact on the oxygen supply-demand balance as a pharmacological vasodilator. Blood gas fluctuations during general anesthesia, whether intended or unintended may increase cardiac vulnerability in patients with CAD. Further studies will evaluate the presence of deoxygenation events in a perioperative setting

P 12

Analysis of myocardial function during induction like breathing maneuvers in awake healthy controls

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Introduction: The induction of general anesthesia bears many different triggers for inducing myocardial dysfunction. One of these triggers is blood CO₂ which has vasoactive properties and can be altered through fluctuations in breathing rate and depth. Alterations in breathing patterns frequently occur during induction from voluntary paced breathing during preoxygenation, to hypoventilation and apnea occurring during anesthetic administration and intubation. Yet, it is unknown how these alterations in breathing patterns affect biventricular function. We investigated if breathing maneuvers simulating the induction of anesthesia impacted left and right ventricular function in awake healthy controls, measured by myocardial strain analysis.

Methods: Thirty-two healthy awake controls (age: 29 ± 6 years, 69% male) were prospectively recruited. In an MRI, participants performed a breathing protocol simulating the induction of general anesthesia consisted of paced breathing at 14bpm for 150 seconds followed by five deep breaths and then apnea, the latter representative of successful intubation. The heart was imaged with a short-axis cine (frame rate: 25images/s) and global peak circumferential strain (GCS) was analyzed for the left (LV) and the right (RV) ventricle as a marker of systolic function.

Results: The paced breathing followed by five deep breaths significantly improved both LV (GCS: -16.3 ± 2.3% to -17.9 ± 2.0%, p<0.01) and RV systolic function (GCS: -11.3 ± 3.4% to -13.3 ± 3.8%, p <0.01) from baseline. This coincided with a heart rate increase from 57 ± 8 to 71 ± 13bpm (p <0.01). With the subsequent apnea, heart rate normalized to baseline (60 ± 8bpm, p = 0.17), but LV strain worsened beyond baseline values for both the 30s apnea timepoint (-15.7 ± 2.0%, p = 0.04) and the end of apnea: (-15.1 ± 2.0%, p <0.01, 38s). RV strain normalized back to baseline (30s apnea: -11.4 ± 3.8%, p = 0.76, end apnea: -11.2 ± 3.8%, p = 0.99) but did not worsen further.

Conclusion: In healthy awake participants, changes in myocardial systolic function are triggered through breathing maneuvers simulating the induction of general anesthesia, with LV dysfunction observed during short periods of apnea. It is warranted to further investigate strain in a perioperative setting to assess if this systolic dysfunction is observed in patients with cardiovascular disease following the changes in breathing occurring during the induction of general anesthesia.

P 13

Effects of cytokines on nociceptin and the nociceptin receptor expressionZhang L^{1,2}, Stüber F^{1,2}, Huang Y-Y M^{1,2}, Stamer UM^{1,2}¹Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland; ²Department for BioMedical Research, University of Bern, Bern, Switzerland

Introduction: The nociceptin system has been described as a therapeutic target in the treatment of pain and inflammatory diseases.1-2 Nociceptin and the nociceptin receptor (NOP) are constitutively expressed in human peripheral blood leukocytes. These cells can secrete nociceptin under inflammatory conditions.3-4 In this study, the influence of cytokines on nociceptin and its receptor expression was investigated.

Methods: Human monocytic cells (THP-1) were cultured with or without different concentrations of phorbol myristate acetate (PMA) for 24h. Prepronociceptin (ppNOC) and NOP mRNA were quantified by RT-qPCR. Intracellular nociceptin and cell membrane NOP proteins were measured using flow cytometry. To investigate effects of cytokines on the regulation of nociceptin and NOP, cells were cultured with or without PMA 5 ng/ml, tumor necrosis factor- α (TNF α) 10 ng/ml, interleukin (IL)-1 β 10 ng/ml, interferon- γ (IFN γ) 10 ng/ml, IL-6 10 ng/ml, IL-10 10 ng/ml, or the combination of PMA+cytokines for 24h. mRNA expression statistics: Kruskal-Wallis with post hoc test, Wilcoxon test with correction for multiple testing; level of significance $p < 0.05$.

Results: Basal mRNA level of ppNOC was below the detection limit, whereas intracellular nociceptin protein could be detected in THP-1 cells. NOP was constitutively expressed at mRNA and protein levels. PMA 5 ng/ml significantly upregulated ppNOC mRNA after 24h compared to untreated controls ($p < 0.05$). TNF α , IL-1 β and IFN γ partially prevented the upregulating effect of PMA on ppNOC (all $p < 0.05$). No effects on ppNOC mRNA was observed in the cells treated with cytokines only. As for NOP, PMA had no impact on NOP mRNA expression after 24h compared to the untreated control. IFN γ as well as IL-6 suppressed NOP mRNA (both $p < 0.05$). A decrease of NOP mRNA was detected in the PMA+IFN γ samples, compared to PMA-treated groups ($p < 0.05$). However, no changes were observed in the samples co-stimulated with PMA+IFN γ , compared to the IFN γ group. No effect of IL-10 was observed on NOP mRNA expression.

Conclusions: Inflammatory cytokines impact nociceptin and the nociceptin receptor mRNA levels in human THP-1 cells under inflammatory conditions. Mechanisms contributing to the regulation of nociceptin and its receptor by cytokines need to be further investigated.

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Feasibility of quality indicators on prehospital advanced airway management in a physician staffed emergency medical service: a provider point of viewKottmann Alexandre^{1,2,3,4,7}, Pasquier Mathieu¹, Carron Pierre-Nicolas¹, Maudet Ludovic^{1,5}, Suppan Laurent⁶, Rouvé Jean-Daniel⁵, Riva Thomas⁴, Albrecht Roland³, Sollid Stephen⁷¹Emergency department, Lausanne University Hospital, Lausanne, Switzerland; ²Research and Development department, Norwegian Air Ambulance Foundation, Oslo, Norway; ³Department Medicine, Rega – Swiss Air Ambulance, Zurich Airport, Switzerland; ⁴Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; ⁵Division of Anesthesiology, Department of Interdisciplinary Centres, Lausanne University Hospital and Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland; ⁶Division of Emergency Medicine, Department of Anesthesiology, Clinical Pharmacology, Intensive Care and Emergency Medicine, University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland; ⁷Faculty of Health Sciences, University of Stavanger, Stavanger, Norway

Introduction: Prehospital Advanced Airway Management (PAAM) requires specific and complex skills to be delivered at a high standard. In 2018 international experts developed 17 quality indicators (QI) covering all steps of PAAM. The main objective of this study was to determine the feasibility of these QI from the provider point of view by means of a survey.

Methods: In 2019, the systematic collection of the data required to calculate these 17 QI through a dedicated electronic case report form (CRF) was introduced in two physician staffed emergency medical services (PEMS). For the study, an online questionnaire was developed and sent to all emergency physicians who documented at least one CRF between January 1, 2019 and December 31, 2021. The feasibility assessment was based on three criteria: reliability of data collection, relevance and acceptance.

Results: Among the 45 physicians who received the questionnaire, 42(95%) responded. The median number of CRF completed per physician during the study period was 11 (interquartile range 4-17; range 1-48). The median time to complete the CRF was seven minutes (interquartile range 3-6; range 1-25) and was considered reasonable by 95% of physicians. The reliability of data collection was rated as good or excellent for each of the 17 QIs, with the lowest rated for the following three QIs: duration of preoxygenation, duration of laryngoscopy, and occurrence of desaturation during laryngoscopy. Overall, 75% of physicians assessed the set of QI to be relevant and thus meaningfully measure the quality of PAAM and 74% accepted the set of QI to assess the quality of PAAM.

Discussion: Feasibility assessment by field testing allows to improve a set of QI by removing or modifying less relevant QI, or optimize data collection method if necessary. Technological solutions facilitating automatic collection of vital parameters and timings during the procedure itself could improve the reliability of data collection necessary for certain QI. For monitoring of larger QI sets, efforts towards automated data collection and/or directly in the electronic medical record should enhance feasibility.

Conclusion: The collection of a set of 17 QI on PAAM through a dedicated CRF is feasible from a provider point of view. The QI obtained a high acceptance and relevance. The collection of the data is reliable and the effort to complete was considered reasonable. Studies in other EMS are needed to determine the external validity of our results.

P 15

Haemolysis contributes to insulin loss during cardiopulmonary bypass: an in-vitro study

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Background: In patients undergoing cardiac surgery, hyperglycaemia is commonly found during cardiopulmonary bypass and it is associated with poor postoperative outcomes. Experience shows that more insulin is required while on cardiopulmonary bypass than in other surgeries to correct blood glucose. We suspect that insulin may be lost on the surfaces of the extracorporeal circulation circuit (ECC) or is being degraded by haemolysis products. Thus, using an in-vitro model we investigated changes in blood-insulin levels in an isolated running ECC.

Methods: In an in-vitro experiment (n = 18), red packed blood cells were introduced into different ECC systems. For the first two groups, red packed blood cells were first passed through a cell salvage system (CSS) to remove haemolyzed red blood cells and allocated to either a standard (ECCSS+, n = 6), or into a mini-ECC (MiECCSS+, n = 6). For another six, MiECC unwashed red blood cells were used (MiECCSS-). Along with one unit of plasma, human insulin was added to target a plasma insulin concentration of 400 mU/l. The circuits then ran at an output set to 3.5L/min for 4h. Plasma insulin levels and haemolysis index (HI) were measured after 4h.

Results: Insulin dropped in all groups after 4h (MiECCSS+: 316 ± 72mU/l to 144 ± 72 mU/l p <0.01, MiECCSS-: 336 ± 63 mU/l to 92 ± 19 mU/l p <0.01, ECCSS+: 289 ± 15 mU/l to 25 ± 6 mU/l, p <0.01). There was no significant difference in insulin loss if CSS was used or not in the MiECC (MiECCSS+: -63 ± 11%, MiECCSS-: -68 ± 10%, p = 0.62), but insulin decrease was larger when the ECCSS+ was used (-92 ± 2%, p <0.05 versus both MiECC groups). HI increased in all three groups (MiECCSS+: 68 ± 16 to 76 ± 16, p = 0.02, MiECCSS-: 68 ± 9 to 85 ± 14, p = 0.02, ECCSS+: 81 ± 4 to 121 ± 5, p <0.01). After 4h, the HI increase also did not differ between the MiECC groups (MiECCSS+: 8 ± 3, MiECCSS-: 18 ± 7, p = 0.21). HI increase was most pronounced in the ECCSS+ system (p <0.01). The loss in insulin was highly correlated to a higher HI (r = -0.84, p <0.01).

Conclusions: Plasma insulin levels decrease over time in a cardiopulmonary bypass system. Since there is a strong correlation between the degree of haemolysis and insulin loss, data suggests, that degradation from haemolyzed erythrocytes may play a large role in the loss of insulin. Both, insulin loss and HI were greater in the standard ECC. These findings could have implications for the management of perioperative hyperglycaemia.

P 16

Does adopting the Safe Brain Initiative perioperative care bundle potentially decrease postoperative delirium in a Swiss hospital?

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Introduction: We introduced the Safe Brain Initiative project at the Salemspital Bern to systematically address the feedback gap in perioperative care by collecting and analysing real-world health outcome data. From the patient's perspective, the initiative focuses on monitoring and preventing postoperative delirium (POD) and neurocognitive dysfunction, providing effective anaesthesia care, and assessing patient satisfaction. We aimed to introduce and evaluate the impact of the Safe Brain Initiative (SBI) in perioperative care, to enhance patient-centred precision anaesthesia and prevent postoperative delirium and neurocognitive disorders.

Methods: We started the SBI care bundle, comprising 18 core recommendations, in January 2023. Data was collected before induction (T0), after emergence (T1) and at the end of the PACU stay (T2). We collected data on demographics, orientation, communication, pre-procedural pain assessment, stress, fluid fasting and dehydration, delirium monitoring, anxiety, pain, postoperative nausea and vomiting, and satisfaction with treatment. Our primary outcome was to estimate POD by screening for delirium systems during patients' PACU stay. Data were descriptively and comparatively analysed with SPSS v7. Categorical variables were described as absolute (n), relative frequencies (%), and continuous variables with mean ± SD. We used the Mann-Whitney or Kruskal-Wallis for continuous variables and the Chi-square or Fisher's exact test for categorical variables for the inferential analysis. P significant when <0.05.

Results: We screened 721 patients (51,6% female, age: 57,66 ± 17.3 years) in the first 5 months. The average fluid fasting time was 6.27 ± 3.64h. There was no significant increase in PONV (p = 0.9), pain (p = 0.1) or thirst (p = 0.06) after surgery. Patient satisfaction with the pre-anaesthetic consultation was 89%, with induction of anaesthesia 68%, and with the PACU stay 88%. Preliminary results from the SBI project showed a significant reduction in postoperative delirium (p = 0.04) in the first 5 months of implementation.

Discussion: The Safe Brain Initiative presents an innovative, cost-effective, and patient-centred approach to perioperative care. By integrating PROMs and systematic feedback mechanisms, the SBI aims to expedite the advancement of efficient, patient-centered precision perioperative care, improve patient outcomes, and elevate the overall quality of care. The initiative has shown promising results at a local level.

P 17

Regulatory effects of microRNAs on monocytic HLA-DR surface expression

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Background: Decreased monocytic HLA-DR surface expression is the most studied biomarker of sepsis-induced immunosuppression. Until now, the underlying regulatory mechanisms remain largely unknown. One probable HLA-DR dysregulation is through miRNAs. The aim of this study was to investigate the effects of specific miRNAs on HLA-DR expression in human monocytic THP-1 cells.

Methods: THP-1 cells were transfected with eight candidate miRNAs followed by qPCR and flow cytometric analyses of HLA-DR expression. The miRNA co-regulatory effects of either anti-inflammatory glucocorticoid medication or pro-inflammatory cytokines were investigated. Plasma miRNA analysis was conducted in patients before and after undergoing surgery with cardiopulmonary bypass. In silico approaches were applied for functional miRNA-mRNA interaction prediction.

Results: Four up- and four down-HLA-DR-regulating miRNAs were identified in THP-1 cells, with hsa-miR-let-7f-2-3p showing the most significant upregulation and hsa-miR-567 and hsa-miR-3972 downregulation. qPCR analysis confirmed similar gene-regulating trends. Dexamethasone-decreased HLA-DR was significantly restored by hsa-miR-let-7f-2-3p and hsa-miR-5693; contrarily, IFN- γ and TNF- α -increased HLA-DR was significantly reversed by hsa-miR-567. Paired plasma samples from patients before and one day after cardiac surgery revealed up-regulated expression of hsa-miR-5693, hsa-miR-567, and hsa-miR-3972, following the major surgical trauma.

Conclusions: Novel monocytic HLA-DR miRNA modulators were identified and validated in vitro. Both the interaction between the miRNAs and anti- and pro-inflammatory molecules and the up-regulated miRNAs identified in cardiac surgery highlight the potential clinical relevance of our findings. Our results promote the study of miRNA-mediated HLA-DR regulation under both physiological and pathological conditions, and may pave the way for future clinical applications.

P 18

Non-nociceptive neuronal activity is necessary to induce spinal microglial reactivity and chronic pain

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Globally, postoperative chronic pain affects 10-50% of individuals. This neuropathic pain (NP) is a complex pathology with a strong neuroimmune interplay in which microglia has been shown to be a key player. In the spinal cord, these macrophages of the central nervous system react strongly to nerve injury with morphological changes, proliferation, and release of pro-inflammatory factors. This microglial reactivity has been linked to abnormal peripheral activity coming from primary sensory neurons (PSN). Indeed, previous studies in rats demonstrated that a preventive block of electrical activity from nociceptive and non-nociceptive PSN after nerve injury is sufficient to prevent microglial reactivity and pain and that electrical stimulation of PSN per se induces spinal microglial activation. In particular, it was shown that electrical activity from nociceptive C fibers is necessary to trigger spinal microglial reactivity. However, it is still unclear whether spinal microglial activation depends on nociceptive C fibers inputs alone or if a combined activity from nociceptive and non-nociceptive PSN is required.

Thus, our goal is to further investigate the contribution of nociceptive and non-nociceptive inputs to spinal microglial reactivity in the context of chronic pain.

To address this question, we first replicated electrical stimulation on the sciatic nerve in CX3CR1-eGFP mice and could observe increased microglial reactivity in the spinal cord 2 days after stimulation and a prolonged sensitization. We then used optogenetics to selectively activate nociceptors alone using the SNS-Cre/ChR2-TdTomato line and all sensory neurons (i.e. nociceptive and non-nociceptive) using the Advillin-Cre/ChR2-TdTomato line. Microglial proliferation in the dorsal horn of the spinal cord was observed 2 days after both optogenetic stimulation. However, an increase in number of microglial cells at two days was only observed after activation of all sensory neurons using the Advillin-Cre/ChR2-TdTomato line but not after activation of nociceptors alone. Finally, thermal and mechanical hypersensitivities was observed after optogenetic activation of all sensory neurons but not after activation of nociceptive neurons alone. Thus, our data suggest that non-nociceptive neuronal activity is necessary to induce spinal microglial reactivity and chronic pain.

P 19

Impaired classical and non-classical monocytes are associated with aggravated disease progression in critically ill Sars-Cov-2 patients.

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Despite the tremendous impact of the Sars-CoV-2 pandemic and excessive scientific efforts, many aspects of the disease's inflammatory pathophysiology, especially concerning prognostic parameters and specific treatments, remain vague. We aimed to link the dysregulated cellular immune response and lipid mediator profiles to the outcomes and clinical presentation of critically ill CoV2 patients. Doing so we performed the first study to describe the impact of the SarsCoV2 infection on the cell species lipid mediator signaling of classical and non-classical monocytes and their correlation with the survival of the disease.

Leukocytes were isolated from 31 critically ill Cov2 patients and 11 healthy controls. PBMCs were then analyzed by FACS and sorted into CD4, CD8 T cells, CD14+ and CD16+ monocytes, CD19 B cells, and granulocytes and performed HPLC-MS/MS.

FACS immunophenotyping revealed increased TNF α levels throughout all monocyte populations (control vs. covid) and of surviving patients, which met significance in CD16+ non-classical and CD14+/CD16+ intermediate monocytes. In monocytes, HLA-DR was significantly deprived in Covid patients compared to controls in the cell populations: CD14+ Monocytes, CD14+/CD16+ monocytes, T Helper Cells, and Neutrophils. In contrast, a higher expression of HLA-DR receptors was observed in surviving patients' classical CD14+ and non-classical CD16+ cells. The cellular source of pro-inflammatory and resolving lipid mediators SPMs shifted from non-classical to classical monocytes. Increased prostaglandins (TXB2 and PGF2a) in classical CD14 monocytes positively correlated with better clinical scores and organ function. On the other hand, non-classical CD16 monocytes exhibited a general decrease in lipid mediator levels. These decreased CD16 monocyte prostaglandins correlate with diminished clinical scores, mainly liver function.

Suppression of TNF α , lipid mediator class switch, and diminished HLA-DR expression were associated with a poorer prognosis for severely ill Covid-19 patients. A substantial TNF α response and a higher expression of TNF α in monocytes may be necessary, to overcome the infection. Concluded cytokine levels may be clinically relevant in predicting the disease's outcome. Further, lipid mediators and the induced class switch in monocytes during Covid19 infection are tightly regulated and correlate with the clinical parameters.

P 20

Effects of positive and negative end-expiratory pressures on gas exchange and haemodynamics during flow-controlled ventilation: an experimental study

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Background: Scenarios with increased intracranial pressure or haemodynamic instability often require mechanical ventilation applying the lowest possible pressures. The benefits of flow-controlled ventilation (FCV) on respiratory mechanics and gas exchange have been demonstrated previously, however, the effects of a possible setting with negative end-expiratory pressure has yet to be explored. We aimed at comparing gas exchange and haemodynamic parameters applying FCV with negative and positive end-expiratory pressures (EEP).

Methods: Fourteen pigs were anaesthetized and assigned in a random order to FCV with increasing positive EEPs (3, 6, 9 cmH₂O) and decreasing negative EEPs (-3, -6, -9 cmH₂O). Airway pressures (Paw), arterial partial pressures of oxygen and carbon dioxide along with hemodynamic parameters were assessed following 20 min ventilation at each EEP step (EEP 3-6-9).

Results: Applying negative EEPs during FCV resulted in significantly lower Paw than with positive EEPs (9.2 \pm 1.5 vs. 14.5 \pm 1.6 and cmH₂O at EEP 3; 8.7 \pm 1.6 vs 17.2 \pm 2.0 cmH₂O at EEP 6; 7.5 \pm 1.4 vs. 20.0 \pm 2.5 cmH₂O at EEP 9; p <0.05 for all). No differences in gas exchange were evidenced between the application of positive and negative EEPs. At EEP 6 and 9, increased mean arterial pressure and cardiac output was observed with negative EEP compared to positive EEP (p <0.05 respectively).

Conclusions: FCV applied with negative EEP improved haemodynamics and required lower Paw to maintain equal gas exchange as provided with positive EEP. Therefore, FCV with negative EEP may be a promising alternative in patients with increased intracranial pressure or haemodynamic instability.

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Comparison of intratracheal and extrathoracic high-frequency percussive ventilation in an experimental model of capnoperitoneum

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Background: Providing adequate mechanical ventilation during laparoscopic surgeries by abdominal inflation with CO₂ is of major importance during anesthesia management. We characterized whether high-frequency percussive ventilation provide an alternative to protect from the gas exchange and respiratory mechanical impairments during capnoperitoneum. We also aimed at assessing the differences in oxygenation, CO₂ clearance and respiratory mechanics between conventional mechanical ventilation (CMV) with modalities generating the high-frequency percussive ventilatory signal intratracheally (HFPVi) or extrathoracally (HFPVe).

Methods: Anesthetized rabbits (n = 16) were mechanically ventilated by random sequences of CMV, HFPVi and HFPVe. A custom-made blower-driven ventilator superimposed the high-frequency signals (5 or 10 Hz) over the conventional waveform during HFPVi, while the same intratracheal oscillatory pressure amplitude was provided extrathoracally (5 or 10 Hz) via a sealed chest cuirass shell during HFPVe. Lung oxygenation index (PaO₂/FiO₂) and arterial partial pressure of carbon dioxide (PaCO₂), intrapulmonary shunt (Qs/Qt) and respiratory mechanics were assessed before abdominal inflation, during capnoperitoneum and following deflation of the abdomen.

Results: Compared to CMV, HFPVi with 5Hz added oscillations during the capnoperitoneum resulted in higher PaO₂/FiO₂ (462 ± 34 vs. 405 ± 40 mmHg, p <0.05) and lower PaCO₂ (44 ± 4 vs. 54 ± 6 mmHg, p <0.05) and decreased Qs/Qt. These improvements were smaller but remained significant during HFPVi with 10 Hz and under HFPVe with either 5 or 10 Hz. Ventilation modes did not protect against capnoperitoneum-induced deteriorations in respiratory tissue mechanics.

Conclusions: Applying high-frequency oscillations combined with conventional pressure-controlled ventilation revealed benefit on improving lung oxygenation and CO₂ removal in a model of capnoperitoneum. Intratracheal generation of the oscillatory pressure bursts appears more effective than extrathoracic pressure oscillations. These findings may contribute to the optimisation of mechanical ventilation during laparoscopic surgery.

P 22

Triple block vs spinal anaesthesia vs General anaesthesia for total knee replacement in high risk patients: perioperative hemodynamic stability, complication and costs

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Objectives: This study compares perioperative and postoperative complications of patients undergoing general anaesthesia (GA), spinal anaesthesia (SA) or isolated peripheral triple nerve blocks (NB) for total knee replacement surgery in high risk patients.

Methods: In this retrospective single center study, 329 patients (ASA≥III), scheduled for elective total knee replacement between 2014 and 2020 were included. The data extraction was conducted according to the Strengthening Reporting of Observational Studies in Epidemiology (STROBE) initiative for cohort studies. All patients received a femoral catheter and a proximal sciatic nerve block for perioperative analgesia. Patients in the NB group received an additional obturator nerve block. Due to failure resulting from insufficient block or patients expressing their wish for a general anaesthesia due to intraoperative anxiety, patients were assigned according to the definitive anaesthesia method. There were 22 individuals in the NB-, 171 patients in the SA – and 136 patients in the GA group. Perioperative parameters, events and costs were compared. Differences between groups were compared using the chi-square test.

Results: The NB group showed a significantly better haemodynamic stability intraoperatively with less vasopressor consumption compared to the SA and GA groups, respectively (ephedrine-bolus: 14% vs 48% vs 64% <0.001, noradrenalin/phenylephrine infusion: 0% vs 4% vs 16% p = 0.001) and less relevant hypotension events (decrease in MAP >20%: 10% vs 40% vs 77% p <0.001). In 73% of patients in the NB group a PACU-Bypass (Aldrete Score >9) was achieved compared to 34% in SA group and just 13% in the GA group. Remarkably, during the initial 24 hours following the surgical procedure, no episodes with severe pain (visual analog scale [VAS] score >30) were observed in the NB group. Regarding other postoperative complications we could not observe a statistically significant difference between groups.

Conclusion: In summary, the use of triple block as an isolated technique for total knee replacement surgery in specific high-risk patients appears to be a safe option with less haemodynamic complications.

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Intravenous versus Inhalational anesthetics in patients undergoing intracranial aneurysm surgery: a systematic review and meta-analysis of randomized controlled trials

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Background: Surgery for cerebral aneurysmal poses a unique anesthetic challenge. However, conscient data about the influence of intravenous and inhalational anesthetics are lacking. The study aims to evaluate the superiority of intravenous anesthetics over inhalational anesthetics used during maintenance anesthesia.

Methods: PubMed, Scopus and Cochrane databases were searched for randomized controlled trials that compared intravenous anesthetic agents to inhalational anesthetic agents in patients undergoing cerebral aneurysm surgery. Statistical analysis was completed using Review Manager 5.4.1 (Cochrane Collaboration). Heterogeneity was examined with I² statistics. A random-effects model was used for all outcomes.

Results: We included 8 RCTs with 500 patients, of whom 241 (48.2%) were subject to inhalational agents during anesthesia maintenance. The meta-analysis revealed that vasospasm (RR 1.07; 95% CI 0.62-1.84; p = 0.81), hypertension (RR 1.37; 95% CI 0.67-2.79; p = 0.38), hypotension (RR 1.01; 95% CI 0.83-1.23; p = 0.46) and heart rate (MD 1.49 bpm; 95% CI -1.46,4.44; p = 0.34) are not significantly different between groups. However, the mean arterial blood pressure (MD -9.67 mmHg; 95% CI -20.40,-1.05; p = 0.08) is significantly lower in patients undergoing intravenous anesthesia during the maintenance phase.

Regarding the degree of brain swelling, this study shows that the presence of none or mild brain swelling (RR 1.03; 95% CI 0.87-1.22; p = 0.84) and moderate or severe brain swelling (RR 0.95; 95% CI 0.63-1.43; p = 0.77) are not significantly different between the groups.

Conclusion: These findings suggest that there is not significant statistical difference regarding hemodynamic and other perioperative outcomes. However, the mean arterial blood pressure is significantly lower in the intravenous anesthesia group.

P 24

Impact of local anesthetics on bone sarcoma: an in vitro study.

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Retrospective and clinical studies on patients undergoing cancer surgery suggested the perioperative use of local anesthetic drugs might improve the outcome. Previous publications indicated that lidocaine reduced cancer metastasis by inhibiting the tyrosine kinase enzyme Src. However, there is no data investigating the impact of lidocaine in non-epithelial cancer cells. The aim of this investigation was to explore in vitro the impact of lidocaine on cancer of mesenchymal origin. For this purpose, osteosarcoma and Ewing sarcoma cell lines were used.

Adhesion assays were performed by treating the cells for 48h compared to verteporfin in 6 well plates. Migration was assessed by the Boyden chamber migration during 48h. DMSO was used as control. Wound healing assays was performed during 48h and assessed with the MRI wound healing tool in Image J in cells being treated either with or without TNF- α . Src activity was evaluated by western blotting.

Adhesion, migration and wound healing were not influenced by the presence of lidocaine with or without stimulation with TNF- α . The addition of methylnaltrexone did not modify the results. Src activity was similar to the control and not increased by the addition of TNF- α .

Contrary to what has been found with cancer originating from epithelial cells, lidocaine does not prevent adhesion and migration of osteosarcoma and Ewing sarcoma cells from mesenchymal origin. Further investigations, including Src pathway activation, would be required to identify mechanistic differences between cells of epithelial or mesenchymal origin towards anti-metastatic properties of local anesthetics.

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Parturients' hemodynamics depression evaluation comparison of remifentanyl and dexmedetomidine in cesarean delivery: A systematic review and meta-analysis of randomized controlled trialsBarreto LAL¹, Ferreira PV¹, Pinheiro APS¹, Monteiro SB²¹Universidade Federal do Ceará; ²Faculdade de Medicina da Universidade de Lisboa

Introduction: Various medications have been extensively tested for use during a cesarean surgery to provide the sedation and the analgesia required for the procedure. However, previous meta-analysis compared the effects of remifentanyl and dexmedetomidine only on the neonatal outcomes. Therefore, we conducted a meta-analysis to explore its effects on the mother during a c-section.

Methods: We searched PubMed, Embase and Web of Science for randomized controlled trials (RCT) comparing the use of remifentanyl to dexmedetomidine regarding the mothers' hemodynamic variations during elective cesarean delivery. Outcomes of mean arterial pressure (MAP) and heart rate (HR) variations from baseline during surgery were examined. Statistical analysis was completed using Review Manager 5.4.1 (Cochrane Collaboration).

Results: We included 5 RCT with 258 parturients, of whom 128 (49.6%) were given remifentanyl during cesarean section, which was found to cause a greater reduction of MAP from baseline (mean difference [MD] -6.41 mmHg; 95% CI -8.53 to -4.30 mmHg; $p < 0.00001$), while it presented an increase of HR from baseline (MD 3.08 bpm; 95% CI 0.62 to 5.55 bpm; $p = 0.01$). Moreover, a subgroup analysis of hemodynamics variations from baseline at different stages of a c-section was performed, and it was found that MAP reduced more from baseline during induction (MD -7.04 mmHg; 95% CI -9.77 to -4.30 mmHg; $p < 0.00001$), intubation (MD -10.23 mmHg; 95% CI -15.28 to -5.18 mmHg; $p < 0.0001$) and skin incision (MD -7.43 mmHg; 95% CI -12.66 to -2.20 mmHg; $p = 0.005$), while there was no MAP difference from baseline between groups during delivery (MD -4.26 mmHg; 95% CI -9.73 to 1.21 mmHg; $p = 0.13$) and extubation (MD -1.70 mmHg; 95% CI -4.07 to 0.67 mmHg; $p = 0.16$).

Conclusion: Our findings indicate that the use of remifentanyl is less likely to provoke an increase in MAP that could result in a hypertensive episode during surgery. Thus, the greater control of hemodynamics variations may be beneficial to parturients and fetuses, particularly in those cesarean of preeclamptic patients.

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