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## FREE COMMUNICATIONS I – CLINICAL AND MOLECULAR EFFECTS OF PERIOPERATIVE DRUGS

## FC 1

**A novel awake mouse urodynamic model including external urethral sphincter electromyography reveals effects of anaesthetics on bladder function**

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**Background and goal of the study:** Anaesthetics affect bladder function often leading to urinary retention. Bladder catheterization intra- and post-operatively employing anaesthetics acting on  $\mu$ -receptor is of importance to prevent bladder over-distention and urinary retention. The mechanism behind this observation is not well understood. We aimed to develop an urodynamic investigation (UDI) model allowing repeated measurements in awake mobile mice and study the effects of midazolam, fentanyl and hydromorphone on bladder function.

**Materials and methods:** Female mice underwent either bladder catheter (n = 6) or bladder catheter plus electrodes (n = 11) implantation next to the external urethral sphincter. Following awake baseline UDI (including storage phase and voiding phase), the effects of midazolam (5 mg/kg (i.p.)) and opioids (fentanyl (50  $\mu$ g/kg (s.c.)) and hydromorphone (250  $\mu$ g/kg (s.c.)) on bladder function were studied. Only one drug was applied at a time and the mice were allowed to recover for at least one day before being subjected to the next drug and UDI.

**Results and discussion:** Baseline traces showed a slow increase in intravesical pressure during the storage phase followed by a sharp pressure increase (voiding phase). Under midazolam, intravesical pressure rose constantly during the storage phase at a higher rate compared to baseline followed by a sudden pressure decrease with bladder emptying followed by sphincter relaxation alone. With fentanyl, maximal detrusor pressure (Pmax) reached higher levels than baseline and remained at that level resulting in urinary retention. Under hydromorphone, intravesical pressure increased at a rate comparable to baseline, however Pmax reached a higher level, before a rapid decrease occurred. Such high pressures were observed in 100% under fentanyl, in 60% under hydromorphone and in 20% under midazolam. Pmax were significantly increased in midazolam and opioids compared to baseline. The opioids lead to either a significantly increased bladder capacity and micturition cycle duration (hydromorphone) or a complete loss of the voiding phase leading to overflow incontinence (fentanyl).

**Conclusion:** Repeated UDIs are feasible in the awake mouse model. Anaesthetics severely interfere with physiological bladder function: Fentanyl and hydromorphone disrupted the voiding phase evidenced by the reduced coordination of sphincter activity with detrusor contraction, while voiding under midazolam was achieved by sphincter relaxation only.

## FC 2

**Protective effect of sevoflurane's primary metabolite hexafluoroisopropanol in LPS-stimulated human endothelial cells is not directly mediated via the NF- $\kappa$ B pathway**

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**Background:** The primary sevoflurane metabolite hexafluoroisopropanol (HFIP) offers anti-inflammatory properties by attenuating pro-inflammatory cytokines.<sup>1,2</sup> An effect of HFIP on the inflammatory NF- $\kappa$ B pathway has been postulated, the exact interference remains poorly understood.<sup>2</sup> This study aims to investigate how HFIP interacts with pro-inflammatory pathways in human pulmonary microvascular endothelial cells subjected to an inflammatory stimulus (HPMEC).

**Methods:** HPMEC were stimulated with lipopolysaccharides (LPS) with or without 8mM HFIP. Interleukin (IL)-6 was measured by ELISA, a well-

known and crucial mediator in the inflammatory cascade. For further pathway analysis cytoplasmic and nuclear proteins were collected and NF- $\kappa$ B pathway proteins such as IKK, I $\kappa$ B $\alpha$ , and p65 by were determined by Western blot analysis, finally assessing transmigration of NF- $\kappa$ B into the nucleus. Means and standard deviations were calculated, one-way ANOVA and Dunnet post-hoc test were used to compare groups.

Phosphoproteome profiling by liquid chromatography-tandem mass spectrometry was performed to detect phosphorylation of proteins in response to LPS or LPS+HFIP. Changes were compared by fold change and student's t-test.

**Results:** LPS-induced IL-6 expression was decreased in the presence of HFIP (LPS vs. LPS+HFIP: 6563 $\pm$ 2373 vs. 1380 $\pm$ 885pg/ml, p < 0.01). Analysis of IKK complex and I $\kappa$ B $\alpha$  degradation did not explain the attenuating effect of HFIP. Nuclear translocation of p65 was similar in the two groups at 60 min with a 0% decrease in the LPS+HFIP group compared to LPS alone (p > 0.9999). Phosphoproteome profiling revealed a counter-regulation of LPS+HFIP of overall 51 proteins. The highest homology was observed in the CDC42 GTPase cycle with an upregulation in the LPS- and a downregulation in the LPS+HFIP-exposed cells.

**Conclusion:** The results presented suggest that HFIP does not directly affect NF- $\kappa$ B pathway regulation, but interferes at the transcriptional or mRNA level with CDC42 signaling, the latter being related to IL-6 expression.<sup>3</sup> Additional experiments are required to link HFIP to CDC42-dependent attenuation of IL-6 in LPS-stimulated cells.

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## FC 3

**The primary sevoflurane metabolite hexafluoroisopropanol is a key component of sevoflurane's protective effect in cardiac hypoxia/reoxygenation-induced injury in vitro**

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**Background:** Sevoflurane provides protection from cardiac hypoxia/reoxygenation (H/R) injury. The cytochrome P450 2E1 (CYP2E1) enzyme is responsible for the biotransformation of sevoflurane to its primary metabolite hexafluoroisopropanol (HFIP). If HFIP protects from H/R injury is currently unknown. We investigated the effects of sevoflurane and HFIP on necrosis and apoptosis in cardiomyocytes subjected to H/R injury.

**Methods:** Murine cardiomyocytes were exposed to hypoxia (0.2% O<sub>2</sub>) for 6h, followed by reoxygenation in air for 2h in the presence or absence of 2.2 vol% sevoflurane or 4mM HFIP with or without 1uM disulfiram, a specific inhibitor of CYP2E1. Necrosis was measured by lactate dehydrogenase (LDH) release and apoptosis by caspase activity. Exposure-outcome relationships and potential interactions with disulfiram were analyzed using linear mixed models; p < 0.05 was considered statistically significant.

**Results:** After H/R injury, LDH release increased by +124% (95% confidence interval +94 to +154%, p < 0.001). When reoxygenation was performed in presence of sevoflurane or HFIP, LDH was similar to normoxic conditions: +7% (-22 to +37%, p = 0.6) and +21% (-7 to +50%, p = 0.1). The protection was abolished by disulfiram in the sevoflurane (p < 0.001) but not in the HFIP group (p = 0.7). Compared to normoxic conditions LDH changed by +95% (+57 to +123%) and -7% (-43 to 30%), respectively.

Similarly, caspase activity increased upon H/R by +109% (+76 to +154%, p > 0.001). Caspase levels were comparable to normoxia, when reoxygenation was performed in presence of sevoflurane and HFIP: -2% (-36 to +31%, p = 0.9) and +7% (-27 to +40%, p = 0.7). Protection was mitigated by disulfiram in the sevoflurane (p = 0.01), but not in the HFIP

group ( $p = 0.5$ ). The changes compared normoxic conditions were +58% (+13 to +104%) and +15% (-30 to 60%), respectively.

Disulfiram per se did not affect LDH and caspase under normoxic or hypoxic conditions.

**Conclusion:** Our results suggest that sevoflurane's protection in cardiac H/R injury is at least partially mediated by HFIP. Further research is needed to investigate if HFIP, a water-soluble substance with no or only minor anesthetic effects, might be suitable as an intravenous drug to protect from H/R injury.

#### FC 4

##### Perioperative continuation of blood thinners did not increase intraoperative blood loss and blood transfusion rate in cystectomy patients: an observational cohort study

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**Background and Goal of Study:** Perioperative management of anti-thrombotic therapy in major surgery is unclear and evidence for decision making is limited. The inherent risk of bleeding must be balanced against the risk of thromboembolism. Objective was to assess if perioperative continuation of blood thinners affects blood loss and blood transfusion rate during cystectomy.

**Materials and Methods:** We conducted an observational single-centre cohort study of a consecutive series of 1431 cystectomy patients between 2000 and 2020. Cystectomy was performed in patients without anticoagulation, under low-dose aspirin (ASS), oral anticoagulants (OAC, with international normalized ratio of 2-2.5) or bridging with low weight molecular heparin (LWMH). Outcome measures were intraoperative blood loss (ml/kg/h, according to body weight and duration of surgery), blood transfusion rate in the first 24 hours after initiation of surgery and rate of major adverse cardiac events (MACE) at 90 days. We used propensity score matching analysis to adjust for imbalances between groups with or without blood thinners.

**Results and Discussion:** Median blood loss was 2.11 ml/kg/h [95%-confidence interval 1.48-3.04] in patients with blood thinners vs. 2.09 [1.50-2.94] in patients without blood thinners,  $p = 0.742$ . Blood transfusion rate was 30.1% vs. 26.1% respectively,  $p = 0.317$ . Subgroup analysis did not reveal any significance between ASS, OAC or LMWH. Incidence of MACE was 9.1% in the group with blood thinners versus 8.7% in those without,  $p > 0.99$ . Limitations include selection bias and retrospective analysis from prospectively assessed data.

**Conclusion(s):** Perioperative continuation of ASS, uninterrupted OAC with low INR goal or bridging with LMWH had no impact on blood loss and transfusion rate in cystectomy patients. Therefore, there is no need for discontinuation of blood thinners.

#### FC 5

##### Crosstalk between the nociceptin and the toll-like receptor system

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**Background:** Nociceptin and the nociceptin receptor (NOP) have been described as targets for the treatment of pain and inflammatory diseases.<sup>1,2</sup> However, mechanisms contributing to the regulation of the nociceptin system are still not fully revealed. Toll-like receptors (TLRs) play key roles in the immune response and impact the expression of opioid receptors and endogenous opioids.<sup>3</sup> The aim of this study was to investigate interactions between TLR signaling and the nociceptin system.

**Methods:** Human monocytic THP-1 cells were cultured with or without phorbol myristate acetate (PMA) 5 ng/ml for 24 hrs. Nociceptin precursor (prepro-nociceptin, ppNOC), NOP and TLR mRNA were detected by quantitative RT-PCR. Corresponding proteins were measured using flow cytometry. To investigate effects of TLR signaling on nociceptin and NOP, cells were co-stimulated with or without agonists specific for TLR2 (lipoteichoic acid, LTA 10 µg/ml), TLR4 (lipopolysaccharide, LPS 100 ng/ml), TLR7 (imiquimod, IMQ 10 µg/ml) or TLR9 (oligonucleotide (ODN) 2216 1 µM) with or without PMA for 24 hrs. To examine nociceptin effects on TLRs, cells were cultured with or without different concentrations of nociceptin (10 pM-100 nM) for 24 hrs. Statistics: Median (interquartile range); Kruskal-Wallis test and Mann-Whitney U test; level of significance  $p < 0.05$ , corrected for multiple testing.

**Results:** PMA upregulated ppNOC mRNA, intracellular nociceptin and cell membrane NOP proteins (all  $p < 0.05$ ). LTA and LPS completely prevented PMA's upregulating effects on ppNOC mRNA and intracellular nociceptin protein (all  $p < 0.05$ ). PpNOC expression in PMA+IMQ and PMA+ODN 2216 was decreased to 24.2 (20.3-29.1)% and 82.9 (70.1-95.8)% compared to PMA-treated samples, respectively (both  $p < 0.05$ ). As for NOP, expression of cell membrane proteins increased after stimulation with PMA, LPS, IMQ or ODN 2216 (all  $p < 0.05$ ). In contrast, NOP proteins did not change in cells treated with PMA+TLR agonist compared to PMA controls. Nociceptin dose-dependently suppressed cell surface TLR2 and TLR4 proteins as well as intracellular TLR7 and TLR9 proteins (all  $p < 0.01$ ).

**Conclusions:** Regulation of nociceptin and NOP by TLR signaling as well as inhibitory effects of nociceptin on TLR expression in THP-1 cells suggests mutual anti-inflammatory effects of the nociceptin and TLR systems.

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## FREE COMMUNICATIONS II – PAIN AND THE PERIOPERATIVE PERIOD

## FC 6

**A score based on 3 simple questions does not predict severe post-caesarean pain in an external validation study**DEREU D.<sup>1</sup>, SAVOLDELLI G.L.<sup>1</sup>, MERCIER Y.<sup>2</sup>, MATHIVON S.<sup>1</sup>, COMBESURE C.<sup>3</sup>, REHBURG-KLUG B.<sup>1</sup><sup>1</sup>Department of Anaesthesiology, Geneva University Hospitals, Switzerland; <sup>2</sup>Department of Anaesthesia, Jura Hospital, Delémont, Switzerland; <sup>3</sup>Division of Clinical Epidemiology, Geneva University Hospitals, Switzerland

**Background:** Severe pain after caesarean delivery (CD) remains a common problem and clinicians need tools to identify patients at higher risk. Patient-specific psychological factors, such as anxiety or anticipation, have been described as significant risk factors. The tools initially proposed - time consuming questionnaires or quantitative preoperative sensory testing - are difficult to implement in routine. A simplified test based on 3 questions has been previously developed to predict patients at very high risk of developing severe pain. The goal of our study was to assess the external validity of this simple score in a similar population.

**Methods:** The validation cohort included 176 participants undergoing elective CD. A preoperative score was computed using three simple questions related to anxiety, anticipated pain, and anticipated pain medication. We compared the score with clinical observations of postoperative pain at 24 hours and at movement, measured on a visual 0-100 scale. The association between observed pain and pain predicted by the score was evaluated by linear regression. The performance of the score in discriminating patients at very high risk of severe post-caesarean pain was assessed by area under the receiver operating characteristic curve (AUC) and sensitivity, specificity, positive and negative predictive values were calculated.

**Results:** In our cohort, the mean 24-h evoked pain VAS was 53.4 ± 22. A total of 57 of 176 patients (32.4%) described a severe pain (defined as ≥ 70). Mean predictive score in the group of patients without severe pain was 51.4 ± 13.9, versus 55.1 ± 13.1 in the group with severe pain ≥ 70 ( $p = 0.10$ ). In the linear correlation analysis between predicted score and observed 24-h evoked pain in the validation cohort, determination coefficient  $R^2$  was 0.01,  $p = 0.14$ . The best sensibility and specificity (77.8% and 43.6% respectively) were achieved with the model at an optimal cut-off of 46.9. The positive predictive value of the test was 38.9% (29.7-48.7) and the negative predictive value was 81.0% (69.1-89.8). Discrimination performances of the score in predicting pain ≥ 70 (AUC) was 0.58 (0.49-0.67).

**Conclusion:** In our cohort, a previously developed score based on three simple questions yielded insufficient prediction of severe pain after CD. Our results highlight the necessity of conducting external validity studies and question the generalizability and the utility of this simple preoperative predictive score.

## FC 7

**The new ICD-11 definition of chronic postsurgical pain: Impact on incidence of CPSP and clinical measures**Hofer D.<sup>1</sup>, Lehmann T.<sup>2</sup>, Harnik M.<sup>1</sup>, Meissner W.<sup>3</sup>, Stüber F.<sup>1,4</sup>, Stamer UM.<sup>1,4</sup><sup>1</sup>Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; <sup>2</sup>Department of Biostatistics, University Hospital of Jena, Jena, Germany; <sup>3</sup>Department of Anaesthesiology and Intensive Care, University Hospital of Jena, Jena, Germany; <sup>4</sup>Department for Bio-Medical Research, University of Bern, Bern, Switzerland

**Background:** In the new ICD-11, chronic postsurgical pain (CPSP) is defined as pain at the surgical site that develops or increases in intensity after surgery and significantly influences quality of life.<sup>1,2</sup> Previous trials considered only pain intensities. We evaluated the incidence of CPSP as defined by a composite measure of patient-reported outcomes (PROs) including pain-related physical and affective functional interference.

**Methods:** Ethics approval was obtained for analysis of PAIN OUT registry data. Composite PROs for the 1st day and 12 months after surgery were analysed (PRO1 and PRO12 score; NRS 0-10). Based on pain intensity and pain-related physical and affective interference with function, patients were allocated to the group No CPSP (no symptoms), Mixed

(mild symptoms), or CPSP (moderate to severe pain and interference). To compare the endpoint "incidence of CPSP" to published results, previously used definitions were also applied. Variables associated with high PRO12 scores were analysed by multivariable linear regression analysis (regression coefficient (95% CI)).

**Results:** Of 2319 patients, 58.9%, 32.5% and 8.6% were allocated to the groups No CPSP (PRO12 score: 0), Mixed (1.0 (0.5-1.8)) and CPSP (4.3 (3.3-5.3)), respectively. When diagnosis was extended to include the new ICD-11 requirement for an increase in pain intensity at the surgical site, only 3.3% of the patients were categorized as having CPSP. In patients without any pre-existing chronic pain, 4.2% developed CPSP. Using previous definitions with cut-offs for pain NRS >0, ≥3 or ≥4, rates amounted to 37.5%, 9.7% and 5.7%. Opioid intake before admission and pre-existing chronic pain increased PRO12 scores by 0.97 (0.7-1.0) and 0.4 (0.2-0.5) points, orthopaedic compared to general surgery by 0.5 (0.3-0.6), spinal procedures by 0.5 (0.1-0.8). Use of postoperative opioids, the desire to have received more pain treatment, and increasing PRO1 scores showed a positive association, and postoperative use of nonopioid analgesics a negative association.

**Conclusions:** Using a more stringent definition of CPSP led to a lower incidence of CPSP than previously reported. Measures of pain-related functional interference more specifically describe the patient cohort, which has implications for an individualised treatment approach in patients suffering from CPSP. Variables associated with high PRO12 score should be carefully evaluated, to provide preventive care to patients at risk of CPSP.

## FC 8

**Discrepancy in reporting of perioperative complications**Gomes\* NV<sup>1,2</sup>, Polutak\* A<sup>3</sup>, Steiner LA<sup>1,2</sup>, Weber WP<sup>2,4</sup>, Rosenthal R<sup>5</sup>, Dell-Kuster S<sup>1,2,6</sup>, \*Both authors contributed equally<sup>1</sup>Department for Anesthesia, Prehospital Emergency Medicine and Pain Therapy, University Hospital Basel, Basel, Switzerland; <sup>2</sup>Department of Clinical Research, University of Basel, Basel, Switzerland; <sup>3</sup>Clarunis, Department of Visceral Surgery, University Centre for Gastrointestinal and Liver Diseases, St. Clara Hospital and University Hospital Basel, Switzerland; <sup>4</sup>Department of Surgery, University Hospital Basel, Basel, Switzerland; <sup>5</sup>Medical Faculty, University of Basel, Basel, Switzerland; <sup>6</sup>Basel Institute for Clinical Epidemiology and Biostatistics, University Hospital and University of Basel, Basel, Switzerland

**Background:** Perioperative complications contribute to patient morbidity and high cost of medical care. Standardized reporting of perioperative complications supports decision-making regarding perioperative care. The aim of our study was to assess the discrepancy in reporting of perioperative complications, prospectively recorded within a cohort study, versus a retrospective assessment based on all available health records.

**Methods:** This observational study included 320 patients undergoing any type of surgery at the University Hospital Basel, who were included in the validation study for ClassIntra®, a classification for intraoperative adverse events. All intra- and postoperative complications were prospectively graded by the treating physicians according to ClassIntra® and Clavien-Dindo. Additionally, two physicians independently recorded all intra- and postoperative complications based on health records, blinded for each other's assessment and the prospective self-assessment. The number and severity of the retrospective recordings were compared with the prospective records.

**Results:** Inter-rater agreement between the two double-blinded physicians provided an intraclass correlation coefficient of 0.89 (95% CI 0.86-0.91) for intraoperative and of 0.88 (95% CI 0.85-0.90) for postoperative complications. The incidence rate in observing any intraoperative adverse event was almost twice as high after health records review than in the prospective study (IRR 1.79, 95% CI 1.50-2.13). The grading of the most severe intraoperative complication was the same in 180, higher in retro- than in the prospective data collection in 71, and lower retrospectively than prospectively in 69 patients. The incidence rate in retrospectively observing any postoperative complication was more than double than in the prospectively collected data (IRR 2.21, 95% CI 1.90-2.56). The grading of the most severe complication was the same in 195 patients, while the grading was higher in 106 patients in the retrospective data collection and lower in 19 patients.

**Conclusions:** There is a noticeable discrepancy in the number and severity of reported perioperative complications comparing retrospective with prospective data collection. Gold standard of data collection method remains uncertain. However, based on the double-blinded-assessment of two independent raters, our study renders prospective under-reporting in the ClassIntra® validation study more likely than over-reporting in the retrospective chart review.

## FC 9

### Withdrawal from Chronic Opioid Use for Non-Cancer Pain: Results of a Two-Phase Inpatient Program

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**Aims:** Opioid withdrawal in long-term opioid use for chronic pain is a challenge. We assessed the success rate in a cohort of patients undergoing a new two-phase inpatient opioid withdrawal program from 2018 to 2019.

**Methods:** Patients were eligible for the program if they had been using opioid medication for >6 months, if their morphine equivalent dose (MED) was ≥100 mg/day or if they had failed an outpatient withdrawal attempt. Phase 1 of the program included opioid withdrawal on an internal medicine ward. We rotated opioid medications to oral morphine and then tapered stepwise over 10 days. Phase 2 consisted of a 3-week inpatient multimodal pain therapy on a psychosomatic ward. The primary outcome was the number of opioid-free patients upon completion of the program. Secondary outcomes included the number of patients who were opioid-free 3 months after completion of the program, and change in pain level on a numeric rating scale (NRS 0 to 10) when compared to the start of the program.

**Results:** Among 18 patients included in the cohort, the MED at entry ranged from 80 to 630mg per day. Sixteen patients (89%) successfully stopped using opioids after completion of the program; these encompassed all 14 patients who completed the program according to the protocol. Follow-up information after 3 months was available for 17 patients, 14 of whom were opioid free (82%). Of those, 11 reported moderate to substantial pain reduction 3 months after completing the program (decrease in NRS -1.5 to -9 points).

**Conclusions:** Sixteen out of 18 patients were opioid-free after completing a two-phase inpatient opioid withdrawal program and the majority remained without opioids up to 3 months. More importantly, a substantial proportion of patients reported an improvement of their pain after opioid discontinuation.

## FC 10

### Impact of multimorbidity on perioperative outcome and costs – a single centre cohort study

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**Background:** Multimorbidity is a growing global health problem, resulting in an increased baseline risk of patients undergoing surgical procedures. Data on both the prevalence of multimorbidity and its impact on perioperative outcome are limited. The ASA classification only uses the single most severe systemic disease to define the ASA class and ignores multimorbidity. This study aims to assess the number and type of all anaesthesia-relevant comorbidities and to analyse their impact on outcome and hospital costs.

**Methods:** This study is a nested cohort study including all patients enrolled in the ClassIntra® validation study at the University Hospital Basel. In this study, approximately 30 patients per surgical discipline undergoing any type of in-hospital surgery were followed until hospital discharge to record all intra- and postoperative adverse events. In addition, the type and severity of all perioperatively relevant comorbidities were extracted from the electronic medical record according to a predefined list. The primary endpoint was the number of all perioperatively relevant comorbidities across all ASA classes. Using structural equation models, the direct and indirect effects of comorbidities on costs were estimated after adjustment for the ASA class and further relevant confounders and mediators.

**Results:** Of 320 enrolled patients 27 were ASA I (8%), 150 ASA II (47%), 116 ASA III (36%) and 27 ASA IV (8%). The median number of comorbidities per patient was 5 (range 0-18), significantly increasing with higher ASA class, with 1 comorbidity (95% CI 0.0 to 2.0) in ASA I, 4 comorbidities (3.8 to 4.2) in ASA II, 9 (8.1 to 9.9) in ASA III and 12 (10 to 14) in ASA IV patients. Independent of ASA class, each additional comorbidity increased hospital costs by 1,361 CHF (95% CI 327 to 2,395 CHF) with almost identical proportions of direct and indirect effects. Each additional perioperatively relevant comorbidity also had an increasing effect on postoperative complications and postoperative length of hospital stay.

**Conclusion:** In patients undergoing surgery, the prevalence of multimorbidity is high especially in higher ASA classes. Multimorbidity has a relevant impact on hospital costs. Extending the ASA classification by integrating multimorbidity might be warranted to improve its predictive framework and guarantee adequate reimbursement.

## FREE COMMUNICATIONS III – VENTILATION AND HEMODYNAMICS

## FC 11

**Benefits of physiologically variable ventilation over pressure-controlled ventilation: a randomised study in a model of pulmonary fibrosis**DOS SANTOS ROCHA Andre<sup>1</sup>, PETAK Ferenc<sup>2</sup>, HABRE Walid<sup>1,3</sup>, BALOGH Adam<sup>1,2</sup><sup>1</sup>Unit for Anaesthesiological Investigations, Department of Acute Medicine, University Hospitals of Geneva and University of Geneva, Geneva, Switzerland; <sup>2</sup>Department of Medical Physics and Informatics, University of Szeged, Szeged, Hungary; <sup>3</sup>Pediatric Anesthesia Unit, Geneva Children's Hospital, Geneva, Switzerland

**Introduction:** Mechanical ventilation in the presence of pulmonary fibrosis is challenging as it may require high inspiratory pressure to ensure gas exchange, increasing the risk for ventilator-induced injury. Physiologically variable ventilation (PVV), a mode that mimics the variability of spontaneous breathing, has proven beneficial in various models of pulmonary disease, but its potential advantages in lung fibrosis have not been investigated. We assessed the benefits of PVV over conventional pressure-controlled ventilation (PCV) using an experimental model of lung fibrosis.

**Methods:** Lung fibrosis was induced by nebulized bleomycin in rabbits. After 50 days, animals were randomized to receive 6 hours of PCV ( $n = 10$ ) or PVV ( $n = 11$ ). The PVV pattern was pre-recorded in spontaneously breathing rabbits. Respiratory mechanics and blood gases were assessed hourly, end-expiratory lung volume and shunt fraction were measured before and after the 6-hour ventilation.

**Results:** The application of 6 hours of PCV increased respiratory tissue elastance ( $H$ ,  $58 \pm 14\%$  [mean  $\pm$  half-width 95% CI]) and damping ( $G$ ,  $36 \pm 13\%$ ), as well as decreased end-expiratory lung volume (EELV,  $-26 \pm 7\%$ ), oxygenation ratio ( $PaO_2/FiO_2$ ,  $?14 \pm 5\%$ ) and elevated intrapulmonary shunt ( $Q_s/Q_t$ ,  $85 \pm 71\%$ ). The time-matched changes after the application of PVV were significantly lower for  $H$  ( $41 \pm 6\%$ ),  $G$  ( $22 \pm 9\%$ ), EELV ( $-13 \pm 6\%$ ),  $PaO_2/FiO_2$  ( $?3 \pm 5\%$ ) and  $Q_s/Q_t$  ( $20 \pm 22\%$ ,  $p < 0.05$  for all).

**Conclusions:** Prolonged application of PVV, in comparison with PCV, prevented the deterioration of gas exchange, respiratory tissue mechanics and intrapulmonary shunt by reducing lung derecruitment in a model of lung fibrosis.

## FC 12

**Hemodynamic stability between spinal and general anesthesia in patient undergoing primary total knee arthroplasty: a retrospective study**Jeandin T<sup>1</sup>, Albrecht E<sup>1</sup>, Wegrzyn J<sup>2</sup>, Cachemaille M<sup>1</sup><sup>1</sup>Department of Anesthesia, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland; <sup>2</sup>Department of Orthopedics and Traumatology, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

**Background:** Total knee arthroplasty is a very common surgical procedure in daily practice and its number is constantly increasing. Some studies have reported that general anesthesia was associated with greater hemodynamic instability, but this paradigm has since been disputed. The aim of this study is to evaluate intraoperative hemodynamic stability during total knee arthroplasty according to the type of anesthesia. The hypothesis is that hemodynamic stability is better preserved during spinal anesthesia (SA) compared to general anesthesia (GA).

**Methods:** Adults undergoing primary total knee arthroplasty were retrospectively selected over a period of 10 years. Primary outcome was the presence of a hemodynamic instability defined by a norepinephrine infusion started when the variation of patient's blood pressure exceeded 30% of its baseline value for more than 5 minutes. Secondary outcomes included mean intraoperative dose of phenylephrine and ephedrine, mean blood loss, mean volume of fluid administered and the hospital length of stay. Demographic data and anesthetic strategy were extracted. Patients receiving SA versus GA were compared for the different variables.

**Results:** The analysis included 1669 patients; 59% (984) of them received a SA. Patients under SA required less often a norepinephrine infusion (3.8% vs 10.2%,  $p < 0.0001$ ). Mean dose of ephedrine administered was lower in the SA group (19mg [95%CI: 18–20] vs 31mg [95%CI: 30–33],  $p < 0.0001$ ) while there was no significant differences between mean doses of phenylephrine injected (SA group: 414µg [95%CI: 358–470]; GA group: 481µg [95%CI: 436–526];  $p = 0.07$ ). Blood loss was identical in both groups (SA group: 402ml [95%CI: 386–419]; GA group: 416ml [95%CI: 397–436];  $p = 0.29$ ), while the GA group received more mean fluids compared to SA (866ml [95%CI: 842–891] vs 734ml [95%CI: 715–753],  $p < 0.0001$ ). Mean hospital length of stay was lower in the SA group (8 days [95%CI: 8–9]) compared with the GA group (10 days [95%CI: 10–10]),  $p < 0.0001$ .

**Conclusions:** Patients under SA have a better intraoperative hemodynamic stability, as they required less vasopressors than under GA. Patients under SA have also a reduced hospital length of stay.

Keywords: Arthroplasty, replacement, knee, hemodynamic, anesthesia, general anesthesia, peripheral anesthesia, spinal, injection, nerve block.

## FC 13

**Decreased Vasopressor Requirements with Co-Administration of Dexmedetomidine to TIVA for Carotid Endarterectomy (CEA)**Vetter Christian<sup>1</sup>, Meyer Eva<sup>1</sup>, Bervini David<sup>2</sup>, Krejci Vladimir<sup>1</sup><sup>1</sup>Department of Anaesthesiology and Pain Therapy, Inselspital, University Hospital of Bern, 3010 Bern, Switzerland; <sup>2</sup>Department of Neurosurgery, Inselspital, University Hospital of Bern, 3010 Bern, Switzerland

**Background:** Patients undergoing endarterectomy of the Internal Carotid Artery (CEA) at the Department of Neurosurgery, University Hospital of Bern, receive total intravenous anaesthesia (TIVA). Functional cerebral integrity is routinely monitored with motor (MEP) and somatosensory (SEP) evoked potentials. Cerebral perfusion pressure must be kept in a predetermined range at all times to achieve optimal outcome. Dexmedetomidine (DEX) is a centrally acting  $\alpha_2$  agonist that decreases requirements of propofol during induction and maintenance of general anesthesia. In addition to being a centrally active  $\alpha_2$  agonist, DEX also acts on peripheral  $\alpha_1$  receptors. A lesser degree of vasodilatation due to propofol-sparing effects of Dexmedetomidine, plus peripheral  $\alpha_1$  agonism may result in decreased requirements of norepinephrine (NE) and other vasopressors to achieve hemodynamic goals.

**Methods:** This prospective controlled trial was approved by the local ethics committee. Patients were randomised in two groups of 23 each. The control group received TIVA only. The study group received Dexmedetomidine before induction of anaesthesia as a bolus of 0.4 mcg/kg BWT over 10 min, followed by an infusion of 0.4 mcg/kg/h. Propofol was titrated according to EEG-endpoints using a target controlled infusion pump (Schnyder Model). Intravenous norepinephrine was mainly used to achieve hemodynamic goals. Arterial Blood Pressure (ABP) was kept within 20% of preoperative measurements. Before cross clamping of the internal carotid artery, Cef of Propofol was increased until EEG-Burst Suppression (1 burst every 10 sec), and ABP was increased by 20 mmHg. Before reperfusion, Cef of Propofol was decreased to pre-crossclamp levels, Dexmedetomidine was discontinued, and ABP was decreased ( $< 140$  mmHg systolic).

**Results:** There were no differences in demographics, duration of surgery and anaesthesia. Total amount of Propofol was 1185 (1016;1500) mg in the study group compared to 1438 (1232;1733) mg ( $p = 0.035$ ) in the control group. We found no differences in Arterial Blood Pressure between groups. The study group received a total of 482 mcg NE vs. 949 mcg in the control group ( $p = 0.023$ ). Bradycardia was observed in 3 patients in the study group vs. 1 patient ( $p = 0.399$ ).

**Conclusions:** Co-administration of Dexmedetomidine in addition to TIVA decreased requirements of Propofol to reach EEG-endpoints, as well as the amount of norepinephrine for maintenance of hemodynamic stability.

## FC 14

**Preliminary Experience with Continuous Negative Pressure Ventilation (CNEP) in Covid-19 patients requiring respiratory support**Diaper J<sup>1</sup>, Bendjalid K<sup>2</sup>, Neto Da Venda E Silva I<sup>3</sup><sup>1</sup>Department of Anesthesia, University Cantonal Hospital, Geneva, Switzerland;<sup>2</sup>Department of Intensive care Medicine, University Cantonal Hospital, Geneva, Switzerland; <sup>3</sup>Department of Respiratory and Physiotherapy, University Cantonal Hospital, Geneva, Switzerland

**Background:** The recent pandemic has forced hospitals to explore alternative ways of providing respiratory support, to prevent intubation or reduce time on mechanical support. Continuous negative pressure therapy (CNEP) using a simple thoracic shell, (-5 to -25 cmH<sub>2</sub>O), applied to the thorax has been purported to increase FRC, reduce atelectasis and improve oxygenation. Electrical Impedance Tomography (EIT) used concomitantly can allow for the visualization of the recruitment of lung zones in real-time by the bedside (thoracic belt) during CNEP. We sought to assess the feasibility of CNEP-EIT, whether it allowed for periods of pause during CPAP mask therapy, and any improvements in oxygenation during mechanical ventilation.

**Methods:** A negative pressure shell was applied to 20 patients (10 intubated patients/10 non-intubated patients with CPAP). Therapy lasted from 30 mins to 2 hours. EIT images were visualized in real-time, (baseline measures compared to CNEP). In non-intubated patients, compliance and comfort during CNEP was assessed. For intubated patients, interference with mechanical ventilation and ease of application were evaluated.

**Results:** There were no complications related to CNEP-EIT in any patients. All non-intubated patients tolerated CNEP well. Therapy lasted from 1-2 hours, twice daily. CPAP mask time was reduced by approx. 3-4 hours /day. Lung zone aeration shifted from the apical zones to basal zones during CNEP sessions, (>15-20% increase in EIT quadrants 3-4). A moderate increase in oxygen saturations (90.3%-93.4%) was observed.

**Intubated patients:** CNEP allowed for improvements in oxygenation saturations (90.1-93.4%) and reduction in airway pressures (35.7; 30.2 cmH<sub>2</sub>O Paw) without interfering with mechanical ventilation (triggering). P/F ratios increased from 19.2 to 21.2 during CNEP-EIT. In patients where oxygen saturations or P/F ratios increased minimally, (n = 2), there was also little change visualized in EIT lung zone images (<5%). CNEP reduced esophageal pressures in 2 obese patients (BMI 64, BMI 30: 18 to 10 cmH<sub>2</sub>O, and 15 to 10 cmH<sub>2</sub>O respectively).

**Conclusion:** Our first experience with CNEP-EIT in Covid-19 patients requiring respiratory support appears promising. The use of EIT as a feedback system during CNEP therapy allows for the immediate visualization of the benefits of the therapy for that particular patient. Trials should determine whether CNEP can prevent intubation, or reduce time on mechanical respiratory support.

## FC 15

**Tracheal intubation through intubating laryngeal tube iLTS-D® and Fastrach®: a multicentric randomised study.**Zuercher Mael<sup>1</sup>, Casso Gabriele<sup>2</sup>, Krugel Vincent<sup>3</sup>, Potié Arnaud<sup>1</sup>, Pathé Mamadou Pathé<sup>1</sup>, Schoettker Patrick<sup>1</sup><sup>1</sup>Department of Anesthesiology, CHUV University Hospital of Lausanne, Switzerland; <sup>2</sup>Department of Anesthesiology, CardioCentro, Lugano, Switzerland; <sup>3</sup>Department of Anesthesiology, Hôpital Riviera-Chablais, Renaz, Switzerland

The intubating laryngeal tube suction – disposable (iLTS-D®) (VBM Medical Inc., Sulz, Germany) is a new laryngeal tube that has been designed as a conduit for tracheal intubation, providing furthermore a gastric access. Effective ventilation through a laryngeal tube has already been demonstrated. The Fastrach® (Teleflex, Buckinghamshire, UK) is an established laryngeal mask and is still recognized as the Gold Standard for intubation in case of difficult airways. Many studies have compared other supraglottic devices (SGD) and showed the superiority of Fastrach. The aim of this prospective multicentric randomised study of non-inferiority was to establish if iLTS-D was as effective as Fastrach for tracheal intubation with the advantage of a gastric access and quicker ventilation achievement.

After ethical approval was granted, patients requiring general anaesthesia with orotracheal intubation were recruited in two primary centres and one secondary centre in Switzerland. They were randomized to one of the two study groups: iLTS-D or Fastrach. After anaesthesia induction, the assigned device was inserted and success rate and time for successful ventilation were measured. The main investigator then proceeded to tracheal intubation through the device under fiberoptic control by a second anaesthetist. Success rate after one and two attempts and time for intubation were recorded.

Ninety-nine patients were included in the study. Fifty and forty-nine patients were respectively recruited in each study group. The overall success rate for tracheal intubation was 70% with iLTS-D and 92% with Fastrach (P = 0.006). The successful tracheal intubation rate after one attempt was also lower with iLTS-D (43% vs 82%, P = 0.001). Time for intubation was identical in the two groups (44 seconds vs 50 seconds, P = 0.59). Successful ventilation was achieved in 94% of patients in iLTS-D group and 100% in Fastrach group (P = 0.829). Time for ventilation was also similar in the two groups (31 seconds vs 36 seconds, P = 0.15). The success rate for the placement of a gastric tube with iLTS-D when intubation was successful was 100%. No major complication was recorded in both groups.

The iLTS-D had an overall successful tracheal intubation rate significantly lower than the Fastrach. Ventilation success rate and time were identical. Even if the iLTS-D bears the advantage of a gastric access and effective ventilation, it should require modifications to become suitable for SGD-assisted intubation.



## POSTERS

### P 1

#### Efficacy and safety of intrathecal morphine for analgesia after lower joint arthroplasty: a systematic review and meta-analysis with meta-regression and trial sequential analysis

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**Background:** Widespread adoption of intrathecal morphine into clinical practice is hampered by concerns of its potential side-effects. We undertook a systematic review, meta-analysis and trial sequential analysis with the primary objective of determining the efficacy and safety of intrathecal morphine. Our secondary objective was to determine the dose associated with greatest efficacy and safety.

**Methods:** We systematically searched the literature for any trials comparing intrathecal morphine with a control group in patients undergoing hip, knee arthroplasty under spinal anaesthesia. Our primary efficacy outcome was rest pain score (0–10) at 8–12h; our primary safety outcome was the rate of PONV within 24h.

**Results:** Twenty-nine trials including 1814 patients were identified. Rest pain score at 8–12h was significantly reduced in the intrathecal morphine group with a mean difference (95%CI) of -1.7(-2.0,-1.3),  $I^2 = 71\%$ ,  $p < 0.0001$ , without subgroup difference between doses ( $p = 0.35$ ). Intrathecal morphine increased postoperative nausea and vomiting with a risk ratio (95%CI) of 1.4(1.2,1.6),  $I^2 = 4\%$ ,  $p < 0.0001$ . However, a subgroup analysis according to doses revealed that rates of PONV within 24h was similar between groups with doses of 100µg, while the risk significantly increased with doses above ( $p$  value for subgroup difference = 0.03). The quality of evidence for our two primary outcomes was high and moderate-to-high for the secondary outcomes.

**Conclusions:** There is high level evidence that intrathecal morphine provides effective analgesia after lower limb arthroplasty but at the expense of an increased profile of side-effects. However, a dose of 100µg represents a ceiling dose for analgesia and a threshold dose for increased rate of PONV.

### P 2

#### Predictors for perioperative blood transfusion in patients undergoing cystectomy and urinary diversion and development of a nomogram: An observational cohort study

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**Objective:** Cystectomy is associated with a substantial rate of perioperative blood transfusion, which is known to increase early postoperative morbidity and worsen cancer related outcomes. Early detection of potentially modifiable perioperative factors could reduce the need for early perioperative blood transfusion in cystectomy patients and thus positively impact outcome.

**Patients & Methods:** We conducted an observational, single-center cohort study on a consecutive series of 1168 patients undergoing cystectomy. Perioperative blood transfusion was defined as the need for packed red blood cells and/or fresh frozen plasma units within the first 24 hours after the beginning of surgery. Patients were evaluated for risk factors for blood transfusion. Multiple logistic regression analysis was performed to model the association between variables and blood transfusion, and a nomogram was developed.

**Results:** Blood transfusion occurred in 370/1168 patients (31.7%). Significant predictors were age (OR: 1.678, [95% CI: 1.379-2.042];  $p < 0.001$ ), blood loss ratio (6.572, [4.878-8.853];  $p < 0.001$ ), preoperative hemoglobin (0.316, [0.255-0.391];  $p < 0.001$ ), tumor stage (2.067, [1.317-

3.244];  $p = 0.002$ ), use of oral anticoagulants (2.70, [1.163-6.270],  $p = 0.021$ ), and interaction between female sex and blood loss ratio (1.344, [1.011-1.787];  $p = 0.042$ ). Relevant factors not reaching statistical significance, but included in the model and nomogram were administration of norepinephrine (0.722, [0.503-1.037];  $p = 0.078$ ) and duration of surgery (1.201, [0.981-1.470],  $p = 0.076$ ).

**Conclusions:** Of the major predictors found to affect perioperative blood transfusion, two can be positively influenced: blood loss ratio by meticulous surgery and hemoglobin by preoperative optimization. Others such as age or advanced disease are not modifiable. This emphasizes the importance of optimal management of patients prior to surgery.

### P 3

#### Characterisation of the spontaneous breathing variability in healthy children at rest: a prospective observational study

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**Introduction:** Spontaneous breathing demonstrates appreciable breath-by-breath variations in rate and volume, even at rest. This natural variability is beneficial for lung structure and function, and is often disrupted in pulmonary diseases or mechanical ventilation. Despite the recognition of its importance, the variability of breathing in children is not well characterized. We aimed at describing the characteristics of breathing variability in healthy children at rest.

**Methods:** 47 healthy children aged 1 to 12 years old were recruited during pre-anaesthesia visits, prior to minor elective surgeries. Children with respiratory tract diseases or a history of snoring or sleep apnoea were excluded. Breathing was recorded overnight at home for 16 hours using respiratory inductance plethysmography (RIP).

**Results:** Forty-one cases were analysed in 3 age groups (group 1: 12 to 23 months,  $n = 9$ ; group 2: 2 to 6 years  $n = 15$ ; group 3: 6 to 12y,  $n = 17$ ). Six cases were excluded because of RIP band misplacement. Respiratory rate (RR) presented a mean coefficient of variation (CV) of 21.1% (14.9–27.3, 95% conf. interval), 19.6% (15.9–23.4) and 16.6% (13.8–19.3) in groups 1, 2 and 3, respectively. The CV of tidal volume (VT), derived from respiratory inductance, was 17.6% (11.9–23.3), 14.9% (11.9–17.9) and 15.3% (12.3–18.2) in groups 1, 2 and 3, respectively. There was no evidence for statistical differences between groups.

**Conclusions:** Spontaneous breathing RR and VT vary considerably in healthy children at rest, independently of age. These aspects of pediatric respiratory physiology provide healthy reference values for the assessment of lung diseases or mechanical ventilation strategies.

### P 4

#### Postprocedure delirium and time point of assessment after electroconvulsive therapy: a prospective clinical service evaluation audit

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**Background & Goal:** Postprocedure delirium after electroconvulsive therapy (ECT) occurs in up to 68%, leading to agitation and erratic behaviour. Optimal time for delirium assessment in order to compare preventive interventions remains unclear. Aim was to verify recovery time (time from induction to obeying commands) and to find the optimal time for delirium assessment.

**Materials & Methods:** We conducted a prospective, 8-week clinical service evaluation audit (21.09.-16.11.2020) in 21 adult patients scheduled for elective ECT. Anaesthesia was induced with etomidate 0.2mg/kg and suxamethonium 1mg/kg, prolonged seizure duration or agitation were terminated using propofol. Induction with propofol, concomitant use of

alfentanil or preventive administration of clonidine was possible. We assessed patients' alertness using the Richmond Agitation-Sedation Scale (RASS) and presence of delirium using the Confusion Assessment Method for the ICU (CAM-ICU) at 10, 15, 20 and 30 min after muscle relaxation.

**Results & Discussion:** Data were completely recorded in 85 of 94 sessions (90.4%). ECT was performed in 16 of 21 patients (76.2%) for major depressive disorder. Clonidine was given in 40 of 94 sessions (42.5%), alfentanil in 52 (55.3%) and propofol for induction in 14 (14.9%). Rescue medication for agitation had to be used in 17 sessions (18.1%).

Ten minutes after administration of suxamethonium, patients had a RASS score of below -3 in 67 of 85 sessions (78.8%), unable to undergo further assessment. This decreased to 35 (40.7%) at 15 min; 17 (19.8%) at 20 min; and 2 (2.4%) at 30 min. The rate of resolved delirium increased from 2 in 89 sessions (2.2%) at 15 min; to 8 (8.9%) at 20 min; respectively 30 (33.7%) at 30 min.

For each time point, we calculated a detection rate as proportion of awake patients (RASS > -3) multiplied by incidence of delirium. The optimal time to assess patients for postprocedure delirium was 20 minutes, balancing the increase in alertness versus the decrease in delirium incidence over time when short-lived delirium resolves.

Overall, postprocedure delirium was present in 65 of 89 sessions (69.1%), agitation (RASS ≥1) in 9 of 94 sessions (9.6%). 19 patients (90.5%) had at least one episode of delirium, 4 patients (19%) had at least one positive RASS score.

**Conclusion:** After ECT, optimal time for delirium assessment was 20 minutes after muscle relaxation. Preventive measures need further investigation, as postprocedure delirium remains a significant problem.

## P 6

### Assessment of next of kin's decisional regret concerning relatives undergoing surgery, a cross-sectional analysis of systematically searched literature

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**Importance:** The implication of next of kin in the medical decision-making processes is increasingly recognized and encouraged, particularly when decisions concern elderly and frail patients undergoing high-risk surgery. It remains unclear to what extent next of kin may regret their decisions.

**Objective:** To systematically review the literature on decisional regrets of next of kin concerning relatives undergoing surgery, to describe the surgical populations studied and the assessment tools used.

**Evidence Review:** We included interventional or observational, quantitative or qualitative studies that reported on the assessment of decisional regret of next of kin concerning relatives undergoing surgery. We searched a variety of databases without restriction publication year. We also checked bibliographies of relevant articles. We assessed the quality of included studies using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (quantitative studies) and the Critical Appraisal Skills Program Checklist (qualitative studies).

**Findings:** Eleven cross-sectional, five prospective cohort and four qualitative studies matched our inclusion criteria. Sample sizes ranged from 14 to 1235 next of kin (median 110, IQR 20 – 708). In 15 studies (75%), relatives were children, in five (25%) they were adults. No study included elderly or frail patients. Eleven studies (55%) used the original Decision Regret Scale that has been validated for patients but not for next of kin. Two studies (10%) used a modified Decision Regret Scale that was adapted by the authors for next of kin. The remaining studies used single open or closed questions, or structured interviews. The quality of 3 of 16 (19%) quantitative studies and of one of four (25%) qualitative studies was rated as good.

**Conclusions and Relevance:** There is only a limited number of high-quality studies assessing the decisional regret of next of kin regarding relatives undergoing surgery. None of the retrieved studies examined this issue in elderly or frail patients. A specific, validated tool to assess decisional regret of next of kin regarding relatives undergoing surgery is lacking.

## P 7

### Designing a free-breathing oxygenation-sensitive cardiovascular magnetic resonance sequence to allow for imaging of peri-operative ischemia

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**Background:** Perioperative myocardial ischemia is associated with increased morbidity and mortality. General anesthesia bears many possible triggers for myocardial ischemia including acute blood gas changes. While cardiovascular magnetic resonance (CMR) is not feasible in an everyday intra-operative setting, its ability to measure myocardial oxygenation using oxygen-sensitive (OS) imaging provides a novel possibility to quantify tissue ischemia during the induction of general anesthesia in a research setting. However, OS-CMR is acquired with a breath-hold to reduce chest motion and is not ideal for continuous monitoring. Thus, we optimized a free breathing OS-CMR sequence and aimed to test it in an awake healthy control population performing voluntary hyperventilation and apnea. The intent of this analysis is to develop and validate this new CMR sequence for future studies implementing OS-CMR to measure myocardial oxygenation during general anesthesia.

**Methods:** Twenty awake healthy participants underwent a CMR study and performed two breathing protocols. First a maneuver representing anesthesia pre-induction protocols was performed with paced breathing at 15bpm for 150s followed by 5 deep breaths and then apnea. Controls were then asked to perform a rapid paced maneuver consisting of 60s of deep hyperventilation at 30bpm for 60s, followed by a second apnea phase. During the procedure images were acquired with either the original breath-hold (BH) OS-CMR sequence, or the new free-breathing (FB) sequence. Myocardial oxygenation was statistically compared at baseline, post hyperventilation and at the 30s timepoint in apnea.

**Results:** For the first breathing pacing protocol representing anesthesia induction, hyperventilation significantly reduced myocardial oxygenation with both sequences (FB: -12.1±10.6%, p <0.001, BH: -4.2±3.7% p <0.001) and apnea resulted in a rise in myocardial oxygenation (FB: 6.2±7.3% p = 0.002, BH: 6.9±5.7% p <0.001). With the rapid pacing maneuver similar results were observed with hyperventilation (FB: -4.4±8.2% p = 0.047, BH: -4.3±6.2% p = 0.008) and apnea (FB: 9.2±6.5% p <0.001, BH: 4.5±5.0% p = 0.001). The new FB sequence performed as well as the gold-standard for each stage.

**Conclusion:** In awake controls, alterations in myocardial oxygenation through hyperventilation and apnea can be observed by a novel free-breathing OS-CMR. It is now warranted to implement this new technique for studies investigating peri-operative myocardial ischemia.

## P 9

### Smartphone based blood pressure measurement: accuracy of the OptiBP mobile application according to the AAMI/ESH/ISO universal validation protocol

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**Background:** Auscultatory and automated sphygmomanometers or arterial catheters are the current reference techniques to measure blood pressure (BP). New technologies have emerged including cuffless approaches using smartphone-based optical signal acquisition processes. In this context, OptiBP® mobile app has been developed thanks to a collaboration between the Department of Anesthesiology, the Service of Nephrology of Lausanne University Hospital (CHUV), the CSEM (Swiss Center for Electronics and Microtechnology) and the start up Biospectral. OptiBP® provides a BP estimation using a pulse wave analysis

algorithm applied to photoplethysmography (PPG) signals derived from images acquired with a smartphone's camera. The underlying algorithm is based on the analysis of the morphology of the recorded PPG waveforms to estimate BP. A recent publication demonstrates accuracy when applied to PPG signal acquired with an oximeter fingerclip and tested against an invasive reference during a general anaesthesia induction. In the present study, measurements were carried out in a hospital ambulatory setting and follow the standards of the Association for the Advancement of Medical Instrumentation (AAMI), the European Society of Hypertension (ESH) and the International Organization for Standardization (ISO). The objective of the study was to determine the accuracy of OptiBP® smartphone app against an auscultatory reference.

**Methods:** 100 participants were recruited at the hypertension clinic of CHUV. The protocol was based the opposite arm simultaneous method as described in the ISO norm (81060-2:2018). Reference auscultatory BP values were measured using a dual-head stethoscope on one arm and OptiBP® optical signals were acquired simultaneously on the fingertip of the opposite arm. BP values were compared offline.

**Results:** A total of 353 paired recordings from 91 subjects could be analyzed. The mean  $\pm$  SD between OptiBP® and reference BP recordings was respectively  $0.5 \pm 7.7$  mmHg and  $0.4 \pm 4.6$  mmHg for SBP and DBP. The SD of the averaged BP differences between OptiBP® and reference BP per subject was 6.3 mmHg and 3.5 mmHg for SBP and DBP.

**Conclusion:** The smartphone embedded OptiBP® cuffless mobile application fulfills the validation requirements of AAMI/ESH/ISO universal standards in a general population for the measurement of SBP and DBP and represents a promising alternative to cuff-based BP measurements. Further work is ongoing in various settings, including anaesthesia and acute care

## P 10

### Alpha EEG oscillation frequency slows with increasing brain isoflurane concentrations

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**Introduction:** During anaesthesia for surgery, electroencephalogram (EEG)-based 'depth of anaesthesia' monitors commonly show a plateau in index values at minimum alveoli concentration (MAC) ranges after loss of consciousness but before the brain transitions to burst-suppression<sup>1</sup>. This insensitivity can limit their usefulness for titration. Clinical observations suggest that the frequency of the alpha (7 – 12 Hz) oscillation in the EEG may be a sensitive marker of anaesthesia dose over this MAC range.

**Methods:** We retrospectively analysed EEG data from 388 patients from the EPOCAS study, who were receiving isoflurane anaesthesia for cardiac surgery. From the period prior to cardiopulmonary bypass we measured the peak alpha frequency from spectra created from 20 second moving windows of EEG using Matlab. Brain effect-site MAC (CeMAC) was estimated from end-tidal MAC using a simple diffusion model with a diffusion half-life of 120 seconds. We used a mixed effects model to estimate the dose-response slopes of alpha frequency against CeMAC.

**Results:** Of the 388 patients, 342 (88%) had a negative dose-response slope, indicating that the alpha oscillation slows to increasing effect-site isoflurane concentration. Six patients (<2%) showed a positive dose-response slope, and 40 patients (10%) had dose-response slope confidence intervals including zero, indicating a plateau response.

**Discussion:** The alpha oscillation during anaesthesia is thought to originate from a resonance between the thalamus and cortex. The slowing of this oscillation may be due to lengthened inhibitory post-synaptic potentials, and act as a marker of hyperpolarisation in the thalamocortical system. Visual checking of the positive dose-response slopes indicated that these recordings were likely due to an absent alpha oscillation.

**Conclusion:** The frequency of the alpha oscillation can be consistently used as titration marker of hypnotic effect following loss of consciousness and before burst-suppression, and does not often show a plateauing dose-response effect.

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## P 11

### Compliance with an anaesthesia pre-induction checklist aiming to improve patients' safety during airway management: a retrospective five-year analysis

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**Background:** Airway management is still considered as a high-risk procedure and about 10% lead to fatal patients' consequences with lifelong impairment or death (NAP4). Despite clinicians' technical skills and expertise, human factors (e.g. situational awareness, communication) contribute to successful airway management. Human factors can be influenced by cognitive aids like checklists (structural approach for users to prevent human errors). In 2016, a local pre-induction checklist before start of general anaesthesia was implemented containing four items: equipment, patient, communication and feasibility. This retrospective observational study measures the compliance to the checklist over 5 years.

**Methods:** Study period: 01 May 2016 until 31 May 2021

Inclusion criteria: all procedures with airway management (general anaesthesia)

Exclusion criteria: procedures without airway management

Primary endpoint: percentage of completed pre-induction checklists

Secondary endpoints: standard working hours (7:00h – 16:59h) vs. on-call hours (17:00h – 6:59h), area of induction, urgency of the procedure and difficult airway

**Results:** Of the total 122,456 included procedures, 48.4% had a complete pre-induction checklist and compliance improved significant from 39.3% in 2017 to 53.7% in 2020 ( $p < 0.001$ ).

During the study period, pre-induction checklist was complete:

In 50.4% during standard working hours vs. 34.4% in on-call hours ( $p < 0.001$ )

In 52.5% in the operating rooms vs. 35.2% in non-operating rooms ( $p < 0.001$ )

In 53.1% of elective procedures vs. 33.3% in emergency procedures ( $p < 0.001$ )

Difficult airway was encountered in 3.6% ( $n = 4,404$ ) of all procedures:

4.1% during on-call hours vs. 3.5% standard working hours ( $p > 0.001$ )

4.2% in non-operating-rooms vs. 3.4% in operating rooms ( $p < 0.001$ )

4.1% in emergency procedures vs. 3.4% in elective procedures ( $p < 0.001$ )

**Conclusion:** This retrospective analysis showed an increase of the usage of the pre-induction checklist over the five years up to 54%. Compliance was higher for procedures during standard working hours, in the operating rooms and for non-emergency procedures. Procedures with a difficult airway occurred more frequently during on-call hours, in non-operating-room anaesthesia, and during emergency procedures. As such pre-induction checklists aim to reduce potential human errors, we will investigate barriers and facilitators for the checklist use to close the large gap in cases without application of this safety tool.

## P 12

**Nasogastric tube in critical care setting: combining ETCO<sub>2</sub> and pH measuring to confirm correct placement**

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**Introduction:** nasogastric tube (NGT) placement is a common procedure performed in critical care setting. Chest X-Ray is the diagnostic gold-standard to confirm correct placement, with the downsides of both the need for critical care patients' mobilization and intrinsic actinic risk. Other potential methods to confirm NGT placement have shown a lower accuracy compared to chest X-ray; ETCO<sub>2</sub> and pH analysis have singularly yet investigated as an alternative to the gold standard. Aim of this study was to determine thresholds in combine measurements of ETCO<sub>2</sub> and pH values, at which correct NGT positioning can be confirmed with the highest accuracy.

**Material & Methods:** this was a prospective, multicenter, observational trial; a continuous cohort of eligible patients was allocated to two arms, to identify clear cut-off threshold able to detect correct NGT tip positioning with the maximal accuracy. Patients underwent general anesthesia and orotracheal intubation; in the first group difference between tracheal and esophageal ETCO<sub>2</sub> values were assessed. In the second group difference between esophageal and gastric pH values were determined.

**Results:** from November 2020 to March 2021, 85 consecutive patients were enrolled: 40 in the ETCO<sub>2</sub> group and 45 in the pH group. The ETCO<sub>2</sub> ROC analysis for predicting NGT tracheal misplacement demonstrate an optimal ETCO<sub>2</sub> cutoff value of 25.5 mmHg, where both sensitivity than specificity reach 1.0 (AUC 1.0,  $p < 0.001$ ). The pH ROC analysis for predicting NGT correct gastric placement demonstrated the optimal pH cutoff value at 4.25, with a mild diagnostic accuracy (AUC 0.79,  $p < 0.001$ ).

**Discussion:** A device capable of combining the presence of a negative marker with a positive marker could be accurate enough in identifying the correct NGTs positioning. Further studies are required to validate the reproducibility of these results by a specific device, whose accuracy also ought to be compared with standard chest X-ray.

## P 13

**Sugammadex versus neostigmine for reversal of residual neuromuscular blockade after surgery: a retrospective cohort analysis of postoperative side-effects**

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Approved by Ethics Committee: Cleveland Clinic Foundation Review Board approval and waived consent (identifier 20-062, January 22<sup>nd</sup> 2020, Primary investigator Kurt Ruetzler, MD)

**Background:** Sugammadex and neostigmine given to reverse residual neuromuscular blockade can cause side-effects including bradycardia, anaphylaxis, bronchospasm, and cardiac arrest. We tested the hypothesis that sugammadex is non-inferior to neostigmine on a composite of clinically meaningful side-effects.

**Methods:** We analysed medical records of patients who had general, cardiothoracic, or paediatric surgery and were given neostigmine or sugammadex during 2016.06 and

2019.12. Our primary outcome was a collapsed composite of bradycardia, anaphylaxis, bronchospasm, and cardiac arrest occurring between administration of the reversal agent and departure from operation room. We *a priori* restricted our analysis to side-effects requiring pharmacologic treatment, and therefore presumably clinically meaningful. Sugammadex would be considered non-inferior to neostigmine if the odds ratio for composite of side-effects did not exceed 1.2.

**Results:** Among 89,753 surgeries in 70,690 patients, 16,480 (18%) were given sugammadex and 73,273 (82%) neostigmine. The incidence of composite outcome was

3.4% in patients given sugammadex and 3.0% in patients given neostigmine. The most common individual side-effect was bradycardia (2.4% sugammadex group vs. 2.2% neostigmine). Non-inferiority was not found, with an estimated odds ratio of 1.21 (sugammadex vs. neostigmine, 95% CI, 1.09-1.34, non-inferiority  $P = 0.57$ ).

**Conclusions:** The incidence of severe adverse events — anaphylaxis and cardiac arrest — were so rare that even with more than 89,000 cases we had little precision for estimating the incidence, much less power for a valid comparison between neostigmine and sugammadex. In contrast, there were many episodes of bradycardia and bronchospasm, both of which are transient side-effects that are easy to treat and not especially serious. Our composite was therefore driven by bradycardia and bronchospasm, and from a practical perspective was essentially a composite of just these two side-effects.

Neuromuscular blockade reversal with neostigmine was associated with slightly fewer adverse events than sugammadex (3.0 vs. 3.4%). This difference of just 0.4% corresponds to a number-needed-to-treat of 250 patients. So, 250 patients would need to be given neostigmine rather than sugammadex to avoid one episode of minor complications like bradycardia or bronchospasm. We therefore conclude that sugammadex and neostigmine are comparably safe although inferiority was statistically significant.

## P 14

**A retrospective study comparing different operating room times between hypnosedation and general anesthesia for a dressing wound intervention**

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**Background:** Hypnosedation (HS) is an anesthetic technique that has been shown to be safe and effective, it is useful with some surface surgery instead of general anesthesia (GA). There are few data on the effect of hypnosis on the length of occupancy of the operating room. In 2018, at the Cantonal Hospital of Fribourg, we started this technique (HS) with Vacuum Assisted Closure (VAC) dressing changes.

**Method:** For this non-randomized retrospective pilot study, we collect the operating times from 77 hospitalization records for VAC dressing change interventions. Interventions under HS, Hyp group (10 patients, 12 interventions) (2018-2020) are compared to a general anesthesia group separated into contemporary GAc group (42 patients, 243 interventions) (2018-2020) and historical GAh group (25 patients, 101 interventions) (2014-2016).

The primary outcome concerns four durations of the anesthetic treatment: D1: the duration of anesthetic preparation before the surgical postponement, D2: the duration of the intervention, D3: the duration of awakening in operating room, D4: the duration of monitoring in the recovery room. The Kruskal Wallis test is used. The secondary outcome concerns the difference in GA technique between the GAc and the GAh: we note the techniques of general anesthesia with intubation (GA T), use of a laryngeal mask (MLGA) or general anesthesia without ventilatory support (MAC).

**Results:** The surgical duration did not differ significantly between the groups ( $p = 0.8059$ ). The time spent in the recovery room was significantly shorter for the Hyp group than for the other two groups ( $p = 1.061e-07$ ). The time spent in the recovery room was also significantly shorter for the GAc group than for GAh ( $p = 1.105e-07$ ). The different types of

anesthesia in the GA groups showed a significant trend towards an increase in the proportion of monitored anesthesia care (MAC) for the GAc group ( $p = 0.02508$ ).

**Interpretation:** For the same operation, HS is possible instead of GA and reduces the stay in the recovery room. This allows a faster recovery for the patient who returns to his room but also a saving in terms of time spent in the recovery room. The reduction in the time spent in the recovery room by patients undergoing HS suggests a better tolerance to HS than to GA with a better postoperative recovery. MAC anesthesia also reduces the time spent in the recovery room. For the care structure, it could also represent a potential saving in human and financial resources.

## P 15

### Using frontooccipital EEG-differences as gauged by “Reduced alpha-beta-power”-algorithm to assess hypnotic states during general anaesthesia (GA), a retrospective study

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**Background:** Current practice for monitoring the hypnotic component of anaesthesia relies, other than clinical patient’s response to noxious stimuli, on processed EEG-devices. During GA, various specific EEG changes have been observed, such as a shift of the alpha band (7.7-12.5 Hz) from the occipital to the frontal area, defined as anteriorization. The use of only frontal electrodes in neuromonitoring during general anaesthesia

provides an oversimplified vision of the cerebral network interactions. A priori we proposed that a comparison of frontal and posterior alpha and beta ( $>12$  Hz) activity could improve the quality of neuromonitoring during general anaesthesia.

**Methods:** Intraoperative EEG data recorded with the Narcotrend monitor using a frontal and occipital lead during GA in the ophthalmic surgery department of the University hospital Bern were retrospectively analysed. The Reduced Power Alpha Beta (RPAB) value, designed to evaluate EEG-differences between hemispheres was applied to this frontooccipital montage. The RPAB was analysed for different periods of the (wake, maintenance, emergence) as well as before and after the administration of a ketamine bolus. RPAB was additionally compared with the Spectral Edge Frequency 95 of the frontal and occipital channels.

**Results:** A significant shift of the RPAB to the frontal regions was observed in all the 32 patients after induction of general anaesthesia. The combined alpha and beta power stayed reduced in the occipital channel during GA and was again reduced in the frontal channel after emergence. The administration of ketamine, used as coanalgesic during GA did not lead to a change of RPAB, whereas the SEF 95 of the occipital channel led to a significant rise during the observed 10 minute period after the ketamine administration.

**Conclusions:** The concept of incorporating occipital electrodes for monitoring the hypnotic state seems promising. RPAB as processed index seems to indicate reliable GA in patients with healthy frontal alpha activity unperturbed by SEF 95 or DoA index-changes after ketamine bolus. To establish RPAB as reliable index reflecting physiological frontooccipital activity-differences during GA beckons further research.

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