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Abstracts

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ORAL PRESENTATIONS

OP 1

Physiologically variable ventilation versus pressure-controlled ventilation for COPD: a randomized experimental study

Dos Santos Rocha André[1], Sudy Roberta[1], Bizzotto Davide[2], Kassai Miklos[1], Carvalho Tania[3], Dellaca Rafaelle[2], Petak Ferenc[4], Habre Walid[1]

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Introduction: Mechanically ventilation of patients with chronic obstructive pulmonary disease (COPD) is challenging due to the potential risks of lung overdistension and increases in driving pressure with subsequent lung injury. Recently, we demonstrated the beneficial effects of physiologically variable ventilation (PVV) on lung function, a ventilation mode that mimics the spontaneous breathing by incorporating tidal variations in volume and respiratory rate. Thus, we aimed at comparing lung function and lung aeration following ventilation with PVV or conventional pressure-controlled ventilation (PCV) in an experimental model of COPD.

Methods: Main features of COPD were induced in New-Zealand White rabbits (n = 15, mean weight 3.4 kg) by a 4-week long exposure to nebulized elastase and lipopolysaccharide. After 30 days, animals were anesthetized, tracheotomized and randomized to receive 6 hours of mechanical ventilation with either PVV or PCV. The PVV pattern replicated the spontaneous breathing of awake COPD rabbits, measured by whole-body plethysmography. Blood gases, respiratory mechanics and chest X-ray fluoroscopy were assessed during the 6 hours of ventilation. After sacrifice, lungs were excised for histological analysis.

Results: Ventilation parameters, including respiratory rate and mean driving pressure, were similar between PVV and PCV groups. However, after 6 hours of mechanical ventilation, animals receiving PVV exhibited significantly higher oxygenation index (PaO_2/FiO_2 441±37 (SD) mmHg vs. 354±61 mmHg, p <0.001) and lower $PaCO_2$ (44.1±3.3 mmHg vs. 55.8±6.5 mmHg, p <0.001) than animals ventilated with PCV. Additionally, we observed less derecruitment (decrease in lung aerated area, -3.4±9.9% vs. -17.9±6.7%, p <0.01), lower intrapulmonary shunt (9.6±4.1 vs. 17.0±5.8%, p <0.05) and lower respiratory elastance (359±36 cmH_2O/L vs. 463±81 cmH_2O/L, p <0.01) in animals ventilated with PVV. Ventilation modes had no significant differences in histological lung injury scores.

Conclusion: Prolonged ventilation with physiologically variable ventilation applied in a model of COPD prevents deterioration in gas exchange, pulmonary shunt, respiratory mechanics, and lung aeration. A recruitment effect along with a global reduction in lung shear stress may explain the benefits of PVV over PCV.

Funding: Swiss National Science Foundation (32003B_169334) & Geneva Pulmonary League

OP 2

A comparison of intraoperative pain measurement with the PMD 200 in fentanyl-based and low opioid anaesthesia: a prospective monocenter pilot study

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Background: Intraoperative pain management is a challenge for the anaesthesia team. The CE-certificated Pain Monitoring Device (PMD-200) was developed for non-invasive intraoperative pain assessment using Nociceptive Levels (NOL). In this pilot study we tested the use and reliability of the PMD-200 in daily clinical practice comparing two different intraoperative analgesia regimens: a standard fentanyl-based regime and a multimodal low opioid anaesthesia approach.

Methods: Thirty-four ASA I-IV patients of either sex (18 f and 16 m), undergoing visceral, gynaecological or urological surgery with general anaesthesia were included. The patients were divided into a fentanyl-based and a multimodal (Lidocaine, Ketamin and Magnesium), low-opioid analgesia group. During anaesthesia preparation, operation and in the recovery room, the PMD-200 was attached to the patient's finger to measure the NOL.

The primary outcome of the study was the intraoperative NOL in the two analgesia groups. The secondary outcomes were non-measure/total time ratio for the NOL and the postoperative morphine consumption in the recovery room and on the ward.

Results: The mean fentanyl use was 379 µg (±119 µg) in the fentanyl-based group and 57 µg (±18 µg) in the multimodal, low-opioid group. NOL was similar and not statistically different for the two regimens. The postoperative morphine consumption in the first 24 hours after surgery was 6 (±12) mg in the low-opioid group and 6 (±11) mg in the fentanyl-based group (ns). The NOL-Index provided measures for 96% of total anaesthesia time. From these 96%, in 96% (92% in total) there was no error indication, in the other 4% there was a minor error indication. In 4% there were no data at all because of a major error indication.

Conclusions: The PMD-200 delivered reliable results for approximately 90% of the monitoring time. Most of the major error indications occurred during anaesthesia preparation. There was no indication that a low opioid technique is associated with more intra- or postoperative pain. Because of the small sample size a final conclusion is not possible, but our data support the concept, that for abdominal interventions, a multimodal low opioid anaesthesia approach may be a valid option to reduce intraoperative opioid use.

OP 3

Pancreatic adenocarcinoma surgery: No difference in circulating tumor cells and recurrence between desflurane and propofol anesthesia. A randomized controlled trial.

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Background: Several clinical trials have demonstrated the value of circulating tumor cells (CTC) to predict cancer recurrence [1, 2]. Little information is available for the perioperative phase and the impact of anesthesia on CTC. Since volatile anesthetics have immunomodulatory effects, we hypothesized that desflurane reduces the level of CTC vs. propofol anesthesia in the perioperative phase of resection of pancreatic ductal adenocarcinoma (PDAC), and thereby reduces PDAC recurrence.

Methods: A 1:1 randomization to either propofol or desflurane was performed in three Swiss centers with double blinding patients and research personal. Inclusion criteria were age 18-85 years, ASA I-III with a resectable PDAC undergoing primary surgery with the intent of complete tumor resection. Patients undergoing neoadjuvant radio- and/or chemotherapy were excluded. CTC were measured using the CellSearch® device before surgery, 3 and 7 days after surgery, prior to the start of adjuvant chemotherapy (1-3 months postoperatively), as well as at 6-and 12-month follow-up. Primary endpoint was the peak level of perioperative CTC, secondary endpoint long term levels of CTC and recurrence. This trial was registered with ClinicalTrials.gov (NCT02335151). Mixed models and cox regression with adjustments were calculated.

Results: Between October 2016 and September 2019, 83 participants were enrolled into the desflurane (n = 42) or propofol (n = 41) anesthesia arm. Patient characteristics were comparable in both groups. There was no difference in peak CTC count in the perioperative phase (incidence rate ratio (IRR) of desflurane compared to propofol 1.23 [95%CI 0.74−2.03], p = 0.40). CTC counts from pre-chemotherapy to 12-month follow-up were similar as well (IRR 0.91 desflurane compared to propofol [95%CI 0.55−1.52], p = 0.70). Time to recurrence was similar for both groups (adjusted HR 0.55 [95%CI 0.19−1.54], p = 0.30).

Conclusions: This is the first prospective randomized controlled trial addressing the impact of general anesthesia on CTC and recurrence in PDAC, obviating the need for further retrospective data with a higher level of bias. Further prospective studies should address which anesthetic interventions actually impact CTC.

References
1 Sci Rep. 2017 Jul 3;7(1):45102.
2 Clin Cancer Res. 2018 Jun 15;24(12):2844

OP 4

Influence of high-flow nasal cannula therapy on airway pressure during apneic oxygenation: a randomized controlled trial

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Background: The use of high-flow nasal cannula therapy to prevent desaturation during airway management is a well recognized procedure. An almost linear relationship between flow rate and positive airway pressure in the nasopharynx of spontaneously breathing patients has been shown. This increased airway pressure was stated as the beneficial effect of high-flow nasal cannula therapy. Nevertheless, there is no data on pharyngeal and subglottic pressures generated during high-flow nasal cannula therapy in apneic adults under general anesthesia.

Methods: This randomized controlled trial investigated airway pressures generated during high-flow nasal cannula therapy in anesthetized and paralyzed apneic patients, including a comparison of closed and open mouth, and using different oxygen flow rates (80, 60, 40, 20, 1 L min^{-1}). With ethics committee approval and written informed consent, following standard anesthesia induction and neuromuscular blockade, we applied jaw thrust to ensure upper airway patency. We measured airway pressure in the right main bronchus, the middle of the trachea, and the pharynx, using fiber optically placed 11-Fr catheter connected to a pressure transducer. We randomized each measurement according to closed and open mouth with the different catheter positions and flow rates.

Results: We included twenty patients undergoing elective surgery (38±18 years; body mass index 25±3 kgm-2; females 9 (45%); American Society of Anesthesiologists physical status I (35%), II (55%), III (10%). During closed mouth and increased flow rates a non-linear increase in airway pressure could be demonstrated, which was not to observe with open mouth. The different catheter positions showed no significant differences in pressure in all comparisons.

Conclusions: These results challenge the proposed generation of positive airway pressures generated during high-flow nasal cannula therapy with open mouth as an important physiological mechanism for oxygenation during apnea. Nevertheless, we could demonstrate that airway pressures remained below 10 cmH_2O even with flow rates up to 80 L min^{-1} with closed mouth, which supports high-flow nasal cannula therapy as a safe oxygenation option even with closed mouth.

OP 5

Smartphone-based optical blood pressure monitoring in the acute care setting: Accuracy compared to invasive blood pressure measurement.

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Background and goal of study: Arterial pressure (AP) monitoring is mandatory in the acute care setting. Technological improvements are opening new paths beyond oscillometric or invasive solutions. Smartphones may play a role, providing access to simplified and accurate monitoring beyond the operating room, thus impacting the management of hypertensive diseases. The main goal of this study was to assess the performance of a smartphone-based optical AP measurement to estimate and track changes of AP compared to invasive measurements.

Materials and methods: Study population consisted of 120 patients aged >17 years, scheduled for an elective surgery requiring general anesthesia and invasive AP monitoring at the Lausanne and Geneva University Hospitals. Blood pressure values were acquired simultaneously through a radial arterial catheter and a smartphone camera positioned at the patient's finger. Signals were recorded during induction of general anesthesia and compared offline by a dedicated pulse wave analysis algorithm (oBPM®) designed to estimate AP values on optical signals following an initial 1-point calibration procedure.

Results and discussion: We provide the preliminary results from the first 100 patients for systolic (SAP), diastolic (DAP) and mean AP (MAP). We observe strong coherence of our estimations with a concordance rate (CR) over 90% (CRSAP = 92.0%, CRDAP = 91.5%, CRMAP = 91.7%). Pearson's correlation reflects a good trending ability with coefficients over 0.80 (P <0.001) (SAP: 0.83, DAP: 0.88, MAP: 0.86).

Conclusion: This study demonstrates the potential for accurate estimation of AP through a smartphone-acquired optical signal in adults undergoing induction of general anesthesia. These preliminary results compared to invasive measurements could lead the way for mobile devices to leverage the monitoring AP in the near future. Such results may impact health assessment capabilities in developed and third world countries with devices widely available.

OP 6

Comparison between tablet computer and nitrous oxide for decreasing anxiety related to intravenous catheterization in children: a single-center randomized controlled trial

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Background: Nitrous oxide (N_2O) in an equimolar mixture of 50% oxygen (O_2) is commonly used for sedation for painful procedures. However, recent concerns on the potential deleterious effect of N_2O on health providers in addition to the environmental impact encourage the implementation of new tools for alleviating anxiety and pain in children. Thus, we aimed at comparing the efficacy of "active" distraction with 50% O_2-N_2O gas mixture during insertion on an intravenous line (iv) on anxiety (assessed by the Modified- Yale Preoperative Scale (m-YPAS) [1], pain and parental and health care satisfaction. Ethical approval of the study (CER-2017-01557).

Material and methods: Children aged 3 to 9 years who needed an iv-line were included following parental consent. We excluded children with cognitive disorders, epilepsy or a contra-indication for the use N_2O. All children had EMLA® cream 5% (Lidocaïne-Prilocaïne 25 mg), applied at the puncture site and baseline m-YPAS score was obtained. One hour later, children were randomized to either active game playing on the tablet computer (iPad®) or inhalation of 50% O_2-N_2O and iv-line was placed 3 minutes afterwards. Anxiety and pain scores were assessed during the iv placement, and 1 hour afterwards. Data are presented as mean and [95% CI].

Results and discussion: Intermediate analysis was performed on 33 children (23 boys) with 18 having the active distraction and 17 the N_2O. No difference in age (71.2 [59.6-82.8] vs 79 [66.2-91.8] months), basal mYPAS (5.5 [5-6] and 6.3 [5.2-7.4]) and pain scores was evidenced between children with active distraction and those having N_2O, respectively. Failure in securing the iv line was similar in both groups. Time for successful insertion was shorter with the active distraction (9.5 [5.8-13.2] vs 13.9 [9.8-18.1] min). One-way analysis of variance revealed comparable changes in mYPAS within and between groups. Conversely, pain scores were significantly higher during iv-line insertion in children having active distraction (4.7 [2.9-6.4] vs 2.3 [0.6-4.0]). No difference was noted in the parental and health care satisfaction scores.

Conclusion: Preliminary results failed to demonstrate the superiority of active distraction over inhalation of 50% N_2O in a mixture of 50% O_2 to alleviate anxiety and pain induced by iv-line insertion in children.

Reference
1 Kain ZN, et al. The Yale Preoperative Anxiety Scale: how does it compare with a "gold standard"? Anesth Analg. 1997; 85(4): 783-8.

OP 7

Correlation between cardiac output and microcirculation: a randomized crossover experimental study

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Background: Coherence between macro and microcirculation is of paramount to optimize hemodynamics and ensure peripheral tissue perfusion. Thus, we evaluated the correlation between cardiac output (CO) and microcirculation indices (MCI) in unstable hemodynamic situations.

Methods: We studied 11 anesthetized and mechanically ventilated piglets. CO values were assessed by transpulmonary thermodilution (PiCCO), and MCI by red blood cell velocity (RBCV) with a sidestream dark-field imaging at the sublingual region, jugular cerebral venous saturation in oxygen ($SjvO_2$) and arterial lactate. Hypotension was induced with sevoflurane (SEVO 6%) phase 1, and intravenous sodium nitroprusside 0.5-1 µg/kg/min, phase 2. Measurements were collected simultaneously before, during hypotension, and following restoration of blood pressure by administration in a random order of 4 vasopressors: dopamine 10 µg/kg/min, ephedrine 0.6 mg/kg, noradrenaline 0.1-0.5 µg/kg/min, neosynephrine 10 µg/kg. The relationship between CO and MCI was evaluated with a Pearson correlation test.

Results: Overall, a weak but significant correlation was obtained between relative changes in CO and all MCI, with the following correlation coefficients (r), r RBCV = 0.318, r $SjvO_2$ = 0.321, and r lactate = 0.23 ($p < 0.05$). The absolute values were also significantly correlated except for lactates. Analyzing the results separately revealed a mild relationship between MCI and CO during the phase 1, for absolute values r RBCV = 0.368, and r $SjvO_2$ = 0.49 and relative changes r $SjvO_2$ = 0.406 and r lactate = 0.336 ($p < 0.05$). During phase 2 the only correlation found was between CO and $SjvO_2$. Studying the outcomes step by step in each phase, showed a high association in absolute values at baseline 1 (BL 1) and when hypotension was induced with SEVO between CO and RBCV (r BL1 = 0.636, r SEVO = 0.802), as well as lactate (r BL1 = 0.665, r SEVO = 0.709) ($p < 0.05$). This high correlation was also found in the relative changes between CO and $SjvO_2$ only after SEVO induced hypotension (r = 0.827, $p < 0.002$). However no relationship was observed between CO and MCI following administration of vasopressors.

Conclusion: Invasive CO monitoring reflects the microcirculation in a hemodynamically stable state, and in cases of hypotension induced by anesthesia deepening. However, in the presence of hemodynamic instability requiring the administration of vasopressors, monitoring microcirculation in addition to macrocirculation is essential to guide management.

OP 8

Physiology in Anaesthesia Regarding Apnoeic Oxygenation during Nasal-Cannula Therapy at Different Gas-Flow Rates – A Randomized Cotrolled Trial

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Introduction: Oxygenation via high-flow nasal cannula (HFNC) postulates a ventilatory effect and thus increased elimination of CO_2. Recently, we demonstrated the absence of significant differences between high- and low-flow oxygen in children regarding the rates of increase of CO_2 ($mmHg*min^{-1}$) and the apnoea time. This study investigates apnoeic oxygenation and the effect of different oxygen flow rates on the rate of increase of CO_2 in adult patients undergoing general anaesthesia.

Methods: With ethics committee approval and written informed consent, this randomised controlled trial compares five groups (25 patients each) of different oxygen flow regarding CO_2 elimination.

1) Minimal-flow group: 0.25 $L*min^{-1}$ of oxygen via tracheal tube;
2) Low-flow group: 2 $L*min^{-1}$ using jaw thrust;
3) Medium-flow group: 10 $L*min^{-1}$ using jaw thrust;
4) High-flow group: 70 $L*min^{-1}$ of oxygen using jaw thrust;
5) Control group: high-flow 70 $L*min^{-1}$ using continuous laryngoscopy.

After induction of standardised anaesthesia, including preoxygenation and deep neuromuscular blockade, groups were randomly allocated to the intervention. Every 2 min we analysed arterial blood gases. The study intervention ended with either SpO_2 <92%, $PtCO_2$ >100 mmHg, or if 15 minutes of apnoea were reached.

Results: To date, data of 98 patients have been included (minimal-flow 10 patients; low-flow 20; medium-flow 21; high-flow 22; control 23). The patients were (median [IQR]) 49 [30-62] years old, weighed 71 [64-85] kg, and 45 (46%) were female.

We calculated the increase of arterial CO_2 ($PaCO_2$) in relation to the body surface. In the control group, the model revealed an arterial CO_2 slope of 1.15 $mmHg*min^{-1}$/KOF. None of the four intervention groups showed significantly different slopes: minimal-flow 0.96 $mmHg*min^{-1}$/KOF, low-flow 0.82 $mmHg*min^{-1}$/KOF, medium-flow 0.91 $mmHg*min^{-1}$/KOF, and high-flow 0.91 $mmHg*min^{-1}$/KOF.

Conclusion: Our preliminary results show no significant difference between the 5 groups regarding arterial CO_2 increase. This challenges the "ventilatory effect", the idea that the clearance of CO_2 is linearly dependent on oxygen flow rates during HFNC.

OP 9

Hypoventilation in the PACU is Associated with Hypoventilation on the Surgical Ward? Post-hoc Analysis of a Randomized Clinical Trial

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Background: Postoperative respiratory depression is common and dangerous. Monitoring all patients throughout their postoperative course remains challenging. It is therefore valuable to identify patients at greater risk of postoperative respiratory depression. We aimed to evaluate the association between early postoperative hypoventilation in the last hour of the post-anesthesia care unit (PACU) stay and hypoventilation during the rest of the first 48 postoperative hours in the surgical ward.

Methods: This is a sub-analysis of a clinical trial in which adults having abdominal surgery under general anesthesia were monitored with a respiratory volume monitor (ExSpiron®, Respiratory Motion Inc., Watertown, MA, USA) from admission to PACU until the earlier of 48 hours after surgery or discharge. The exposure was having at least one low minute-ventilation (MV) event during the last hour of PACU stay, defined as MV lower than 40% the predicted value lasting at least 1 minute. The primary outcome was the rate of low MV events lasting at least 2 minutes during the rest of the first 48 postoperative hours, while in the surgical ward.

Results: Data of 292 patients was analyzed, of which 20 (6.8%) patients had a low MV event in PACU. Low MV events in the surgical ward were found in 81 (28%) patients. All patients who had low MV events in PACU had events again in the ward, while 61/272 (22%) had an event in the ward but not in PACU. Using PACU low MV events as a predictor, the sensitivity was 0.25 (95% CI: 0.16, 0.36), and the specificity was 1.00 (0.98, 1.00). The positive and negative predictive values were 100% and 78%, respectively.

Conclusion: In adults recovering from abdominal surgery, events of hypoventilation during the first postoperative hour are associated with similar events during the rest of the first 48 postoperative hours, with positive predictive value approaching 100%.

OP 10

No ventilatory effect during very high-flow THRIVE in apnoeic children – a Randomised Controlled Trial

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Background & goal of study: A ventilatory effect of high-flow nasal cannula therapy (HFNC) in adults has been suggested. Our previous paediatric study with $2Lkg^{-1}min^{-1}$ showed a prolongation of the safe apnoea period without improvement of CO_2-clearance. The study was criticised for having used lower gas flows than necessary to objectify a ventilatory effect. For this reason, we investigated the effect of HFNC with very high-flow rates on CO_2-clearance in toddlers during an apnoea of

10 min. Our primary hypothesis assumed no difference between the two flow rates regarding CO_2-clearance.

Materials & methods: With approval from the Bern Cantonal Ethics Committee we obtained written informed consent from the parents. This randomised controlled trial compared 30 children (10-15 kg body weight) in 2 different groups: HFNC 2 L $kg^{-1}min^{-1}$ vs. 4 L $kg^{-1}min^{-1}$, administering 100% O_2, using jaw thrust, under standardised anaesthesia including full neuromuscular blockade. Transcutaneous CO_2 ($PtCO_2$) and near-infrared spectroscopy (NIRS) were measured and added to standard non-invasive monitoring. The study was stopped when one out of four endpoints were reached: 1) O_2-saturation dropped below 95%; 2) $PtCO_2$ reached 70 mmHg; 3) NIRS dropped below 20% from baseline or 4) apnoea time reached 10min.

Results & discussion: Patients were (median [IQR]) 22.5 [14.0-30.0] months old, weighted 12.5 [10.5-13.4] kg, 13 (43%) were females. $PtCO_2$ increased (mean[±SD]) 3.43 [±0.83] mmHg min^{-1} with 2 L kg^{-1} min^{-1} oxygen, and (mean[±SD]) 3.47 [±0.9] mmHgmin^{-1} with 4 L $kg^{-1}min^{-1}$, without statistically significant difference (p = 0.91). This demonstrates that even very high-flow does not increase the CO2-elimination compared to lower flow rates, as reported earlier in children during 10 minutes of apnoea.

Conclusion: Even at a weight-adapted flow rate that exceeds the expected flow rate estimated using allometric scaling, the purported ventilatory effect of HFNCT remains absent in small children, which contradicts the postulated benefit of THRIVE for improved CO_2-removal during paediatric apnoeic oxygenation.

ABSTRACTS

A 1

Evaluation of non-invasive cardiac output monitoring in the presence of hemodynamic instability

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Background: One of the most reliable method for measuring cardiac output (CO) remains the transpulmonary thermodilution technique. However, its invasiveness and related complications fostered the development of several non-invasive methods as potential alternatives. To our knowledge, no study evaluated their accurary in unstable hemodynamic conditions. Thus we compared CO obtained by non-invasive techniques, namely electrical cardiometry (ICON) and aortic flow measurement (Cardio Q), to those measured with the femoral transpulmonary thermodilution (PiCCO) in the presence of major hemodynamic changes.

Methods: Hemodynamic impairment was established in 11 anesthetized, mechanically ventilated piglets by inducing a 25% drop in mean arterial pressure (MAP), with deepening of anesthesia (sevoflurane up to 6%) or intravenous administration of sodium nitroprusside (0.5-1 µg/kg/min). Piglets were then randomized to receive one of the 4 following vasopressor drugs: dopamine (10 µg/kg/min), ephedrine (0.6 mg/kg), noradrenaline (0.1-0.5 µg/kg/min), and neosynephrine (10 µg/kg). Measurements were obtained at baseline, under each experimental condition and at each step after administration of vasopressors. Agreement was evaluated by a Bland Altman test, and a Pearson correlation coefficient was calculated.

Results: Mean values of CO for ICON, CARDIO Q and PiCCO were respectively 0.603±0.408, 1.146±0.345 and 1.416±0.562 ml/min. The mean of differences (bias) between ICON and PiCCO was −0.813 l/min and the lower and upper limits of agreement were −2.097 and 0.471 l/min (95% CI). As for the comparison between CARDIO Q and PiCCO, the bias was −0.27 l/min, and the lower and upper limits of agreement were −1.430 and 0.89 l/min (95% CI). Analyzing absolute CO values, showed a low but significant relation between CARDIO Q and PiCCO (r = 0.219, p = 0.02), while non-significant correlation was found with ICON (r = 0.117, p = 0.21). Comparing the relative changes in CO detected by ICON and CARDIO Q to those observed by PiCCO following administration of each drug, revealed a lack of significant correlation with ICON (r = 0.145, p = 0.19) and a poor correlation for CARDIO Q (r = 0.261, p = 0.02).

Conclusion: In the presence of severe hemodynamic instability requiring the administration of vasopressors, there was a lack of correlation between non-invasive and invasive methods of CO monitoring. Therefore, relying solely on CARDIO Q or ICON in unstable pediatric patients may be hazardous.

A 2

Perioperative analgesia in children: Which variable is associated with the desire for more analgesic treatment?

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Background: Insufficiently treated pain after appendectomy (AE) and tonsillectomy (TE) in children is frequent. [1, 2] The aim of this analysis was to detect variables associated with the desire for more analgesic treatment from data retrieved in routine clinical settings.

Methods: Data source was the registry PAIN OUT infant, in which children >4 years are enrolled for quality control of pain management. We analyzed patient characteristics, data pertaining to anesthesia, analgesia, surgery, and the results of a standardized patient-outcome questionnaire (Faces Pain Scale revised [3]) filled in on the 1st postoperative day. Primary endpoint was the "desire for more analgesic treatment" ("desire" vs. "no desire"; regression analysis, elastic net regularization; OR (95% CI), level); mean (95% CI); median (IQR).

Results: Data of 472 (AE) and 426 children (TE) were analyzed (males 49%; 9.5±3.8 years; duration surgery 45±26 min). One day after AE and TE, 24.8% and 20.4% of the children indicated they would have liked more analgesic treatment. Patients with desire reported more pain (worst pain: 8 (6/10) vs. 6 (4/8); p <0.001), more sleep disorders due to pain (67% vs 29%; p <0.001), more nausea (38% vs. 27%; p = 0.002) and more vomiting (25% vs. 15%; p <0.003). Patients with desire less frequently received two or three preventive nonopioid analgesics of different substance classes before the end of surgery (17% vs. 29%; p = 0.02), and higher opioid doses during the first 24 hours (morphine equivalents 81(60-102) vs. 50(43-56) µg/kg; p <0.001). Regression analysis revealed that having woken up due to pain during the night increased the probability for the desire 2.8-fold for AE and 3.7-fold for TE, whereas an increase in pain scores by one point increased the probability 1.4-fold and 1.3-fold, respectively. For TE, receiving no or only one preventive nonopioid analgesic increased the probability for the "desire" with an OR of 3.5 (2.1-6.5) and 2.0 (1.1-3.8) compared with children receiving at least two different classes of nonopioid analgesics. For AE, this variable did not meet level of significance, as children received less preventive nonopioid analgesics.

Conclusions: The results support the regular use of at least two classes of preventive nonopioid analgesics before the end of surgery. This can be easily realized in clinical practice. The use of (high) opioid doses has to be questioned.

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A 3

Changes in right ventricular deformation during hyperoxia versus normoxaemia in patients with stable coronary artery disease and healthy controls

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Background: During anaesthesia, emergency and critical care treatment, patients with coronary artery disease (CAD) are often exposed to supraphysiologic arterial oxygen tensions. The balance between benefits and risks of hyperoxia (HO) in patients with stable CAD is controversial, with reports about reduced left ventricular contractility or increased morbidity and mortality. Effects of HO on right ventricular (RV) function are less well described. Advanced cardiovascular magnetic resonance (CMR) feature tracking software allows assessment of myocardial deformation, which may serve as early marker of ventricular dysfunction. In a CMR study we quantified the effect of HO on RV function and deformation in awake participants and patients.

Methods: Ten healthy participants and 25 patients with stable one- or two-vessel obstructive CAD were included. In a CMR study, a short-axis function stack of both ventricles was obtained first during room air (RA) breathing, then during HO induced by breathing O_2 at 10L/min for 5 minutes via non-rebreathing facemask. RV strain was analysed by a blinded reader who manually traced epicardial and endocardial contours of the RV for determining peak global circumferential strain (RVGCS), time to peak strain, systolic and diastolic strain rate parameters.

Results: In the healthy control group, RVGCS, time to peak strain, and systolic strain rate did not change significantly with HO (RVGCS: RA, -14.6±3.9% vs. HO, -13.1±4.5%, p = 0.353; time to peak strain: 282±45ms vs. 286±29ms, p = 0.540; and systolic strain rate: -0.85±0.27/s vs. -0.67±0.28, p = 0.055).

In CAD patients RVGCS worsened from -14.8±3.3% on RA to -13.9±3.6% at HO (p = 0.040). Time to peak strain became significantly prolonged from 319±40ms on RA to 329±49ms at HO (p = 0.046). This was accompanied by a reduction of systolic strain rate from -0.79±0.27/s to -0.75±0.22/s (p = 0.037). Diastolic strain parameters did not differ significantly between RA and HO in either group.

Conclusion: In our cohort of CAD patients HO significantly impaired RV systolic deformation as determined by CMR feature tracking. Hyperoxia is a potent coronary vasoconstrictor but has also profound effects on the pulmonary vascular bed, which may reduce RV afterload and improve RV function. Studies are required in a larger patient cohort and with regional analysis to assess the role of hyperoxia in CAD patients.

A 4

Novel specific therapies for selective cell removal from the blood. Presentation of a nanotechnology-based method in an ex vivo pilot study.

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Introduction: Chronic lymphatic leukemia (CLL) is the most common type of leukemia in the western world. For the majority of patients, an initial watch-and-wait strategy is appropriate. In case of a fast increase in lymphocytes, an anti-cluster of differentiation 20 (anti-CD20) antibody (directed against B-lymphocytes) in combination with chemotherapy is initiated. Severe side effects are a typical result of this treatment, particularly as antibody-induced cell death leads to the release of many degradation products. Aim of this study was to test if a nanoparticle-based cell-type-specific removal of lymphocytes is feasible.

Methods: Upon ethics approval (BASEC No. 2016-01140, Kantonale Ethikkommission, Zurich, Switzerland), blood from CLL patients with increased lymphocyte counts was collected. The anti-CD52 antibody alemtuzumab (MabCampath®) was bound to magnetic carbon-coated cobalt nanoparticles. Patient blood was incubated with nanoparticles, dissolved in phosphate-buffered saline (PBS) or with PBS alone. Nanoparticles were then removed using magnetic bead columns. The blood was run once or twice over magnetized bead columns. CD3 and CD19 positive cells (representing T-cells and B-cells, respectively) were determined by flow cytometry.

Results: In a first approach, blood of 10 patients with <20'000 or >20'000 lymphocytes/µl was tested, evaluating the effect of column passages. Anti-CD52-coated nanoparticles reduced B-cells by 38% compared to the control approach (where only PBS was used) after the first (p <0.001), and an additional 15% after the second passage (p = 0.004). Similarly, they reduced T-cells by 35% (p <0.001) and 18% (p = 0.003), respectively. Overall more than 50% of B- and T-cells were removed with this simple ex vivo model.

When focusing on the lymphocyte count, removal efficiency after the first column passage was higher in patients with <20'000 compared to >20'000 lymphocytes/µl. B-cells were reduced by 56% and T-cells by 45% as compared to 25% and 28%, respectively, in patients with <20'000 compared to >20'000 lymphocytes/µl (p = 0.018 and p = 0.200).

Conclusion: In this pilot study, B- and T-cells were successfully removed with specifically designed nanoparticles. This ex vivo approach may be a promising treatment option for specific, personalized, and therapeutic cell removal from patient blood, also in situations other than CLL.

A 5

Impact of serial transthoracic shocks on systolic and diastolic function in a healthy swine model.

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Introduction: Electric defibrillations and cardioversion are standard interventions to terminate arrhythmia. In a healthy animal model using cardiovascular magnetic resonance (CMR) our group showed that serial transthoracic shocks consistently resulted in acute myocardial edema, which was confirmed histologically. Yet, it is still unclear how this injury affects myocardial function.

Methods: Ten healthy anaesthetized pigs were scanned in a 3 Tesla clinical MRI system with a standard short axis function stack and a clinical T2 mapping sequence in three short axis slices to detect myocardial edema. Five transthoracic shocks with 200J each were applied within five minutes. Five hours post-shock the same images were acquired. Six control animals underwent the same protocol yet without shocks. Changes in myocardial deformation was evaluated by CMR feature tracking strain analysis in radial orientation. After five hours the animals were euthanized and histologic samples were obtained from regions of interest in the left ventricle determined by positive edema findings with T2 mapping. Hematoxylin and eosin (HE) stains of these samples were then assessed for interstitial edema by planimetry, while cross-sectional fiber area was measured to determine intracellular edema.

Results: The mean interstitial area was larger in pigs of the shock group than in control animals (9.4±1.7% vs. 1.1±0.2%; p <0.01). Assessment of intracellular edema also showed greater cross-sectional fiber area after transthoracic shocks (443±35 µm^2 vs. 219±26 µm^2; p <0.01). Both the formation of shock-induced interstitial and intracellular myocardial edema were correlated with worsening systolic function, demonstrated by reduced peak strain (r = -0.574, p = 0.040). T2-mapping results demonstrated that increasing tissue water content led to a delay in systolic contraction seen by an increase in time to peak strain (r = 0.679, p = 0.004). A slowing of early diastolic strain rate was correlated with increasing interstitial and intracellular area in histology (r = 0.646, p = 0.017), indicating decreased diastolic function as well.

Conclusions: Serial transthoracic shock in a healthy swine model consistently leads to myocardial edema, observed by increased intracellular and interstitial space. The extent of this injury is related to aggravation of systolic and diastolic function assessed by advanced strain analysis with CMR feature tracking. Future studies are warranted to assess these effects in clinical settings.

A 6

Effects of vasopressors on the micro- and macrocirculation: a randomized self-controlled crossover animal study

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Perioperative vasopressor administration is a key strategy during pediatric anesthesia to restore macrocirculation. Although, there is no consensus on the choice of the best vasopressor regarding their effect on the microcirculation. Thus, we assessed the differential effects of routinely used vasopressors on both macro- and microcirculation under two different experimental conditions.

Eleven piglets were anesthetized first with sevoflurane (PART-S) then by continuous infusion of propofol (PART-N). Central venous and arterial lines were secured for blood gas, blood pressure, cardiac output (CO) measurements and drug administration. Cerebral ($CrSO_2$) and renal ($RrSO_2$) tissue oxygen saturation were measured by near-infrared spectroscopy. Sublingual microcirculation was evaluated by sidestream dark-field imaging. Carotid and intrarenal arterial blood flows were assessed. Measurements were obtained under baseline conditions (BL1, BL2) and following reduction in the mean arterial blood pressure (MAP) by 25% via increasing sevoflurane during PART-S and intravenous sodium nitroprusside in PART-N. Macrocirculation was restored by noradrenaline (NA), dopamine (DA), ephedrine (EP), and phenylephrine in randomized order.

Both sevoflurane and nitroprusside lowered the MAP (-31±8% vs BL1 and ?32±10% vs BL2, respectively, p <0.05) while no changes occurred in the peak carotid and renal flows. All vasopressors restored the macrocirculation with no evidence for a difference in the central venous oxygen saturation. NA led to the highest increase in MAP (33±19% vs BL1 and 32±30% vs BL2, p <0.05). A higher-than-baseline CO could be evidenced under each vasopressor effect in PART-S. $CrSO_2$ increased significantly under DA and NA compared to the BL1 (15±5.6% and 12±3.8%, p <0.05). The lactate level increased under NA and EP (23±20% and 31±26%, p <0.05) while DA led to a significant increase in red blood cell velocity (86±33%, p <0.05) vs BL1 in PART-S.

All vasopressors used in routine clinical practice were able to counterbalance the decrease in systemic vascular resistance. Despite the significant decrease in MAP, both carotid and renal flows remained within the baseline values due to the physiological compensation. DA, EP and NA led to a detrimental effect on the microcirculation indices, which confirms the potential for a mismatch between the micro- and macrocirculation. Thus, monitoring microcirculation is essential to follow the effects of vasopressors.

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A 7

Impact of Rapid versus Gradual Changes in Arterial Partial Pressure of Carbon Dioxide on Blood Flow and Myocardial Oxygenation in an Experimental Anaesthetized Model

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Background: Hyper- and hypocapnia have known vaso-modulatory effects in the coronary circulation. Oxygenation-sensitive cardiovascular magnetic resonance (OS-CMR) detects changes in tissue oxygenation and can provide a comprehensive assessment of the impact of systemic blood gas changes on the myocardium. The purpose of this study was to compare the physiological responses to rapid blood gas changes induced by hyperventilation followed by apnea in comparison to steady-state levels of hypocapnia and hypercapnia in an experimental animal model.

Methods: Eighteen anaesthetized female swine were used in this study. A blood flow probe was attached to the left descending coronary artery (LAD). In ten animals an LAD stenosis was induced, while eight animals served as controls. In a 3 Tesla MRI, $paCO_2$ was modulated from a preset baseline (paO_2 = 100 mmHg/$paCO_2$ = 40 mmHg) to 30 mmHg and subsequently 50 mmHg by minor changes in ventilation rate. Rapid changes in $paCO_2$ were achieved by 60s of hyperventilating (30/min) from baseline followed by an apnea of up to 90 seconds.

Results: Targeting stable hypocapnia of 30 mmHg from baseline did not alter CBF or myocardial oxygenation. Stable hypercapnia ($paCO_2$ = 50 mmHg) increased CBF significantly in control (5±5%, p = 0.007) and stenosed (4±6%, p = 0.036) animals. Myocardial oxygenation rose in both post-stenotic territories (4.2±6.2%, p = 0.036) and in control subjects (6.2±6.2%, p = 0.011). Rapid hyperventilation induced a similar degree of hypocapnia (control: $paCO_2$ = 25±7 mmHg, stenosed: 27±3 mmHg) and decreased CBF. This had no effect on tissue oxygenation. Apnea resulted in a similar $paCO_2$ (control: $paCO_2$ = 52±9 mmHg, stenosed: 47±7 mmHg) compared to steady-state blood gas levels, which increased CBF significantly in controls 346±327% (p = 0.008) and stenosed 82±110 (p = 0.039) animals markedly. By the end of apnea, a rise in tissue oxygenation of 2.9±2.2% was observed in controls (p = 0.008), -2.7±5.1 (p = 0.125) was observed in the stenosed group (p = 0.011 vs. healthy).

Conclusion: Rapid hyperventilation followed by apnea results in more pronounced changes in myocardial blood flow than similar steady state deflections in $paCO_2$. Only apnea after hyperventilation induced deoxygenation in the stenotic myocardium, while steady state deviation did not compromise myocardial oxygenation. Similar breathing maneuvers may be seen in the induction phase of anaesthesia, which could potentially be a harbinger of perioperative ischemic myocardial events.

A 8

Ventricular strain is compromised outside of the coronary autoregulation zone – An assessment by cardiovascular magnetic resonance

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Background: Coronary autoregulation maintains near constant myocardial blood flow between approximately 60-140 mmHg of mean arterial pressure (MAP). Using oxygenation-sensitive (OS) Cardiovascular Magnetic Resonance (CMR), our group showed that myocardial oxygenation is compromised at MAP below the lower limit of the autoregulation range. However, above the upper limit there is luxury-perfusion leading to a slight oxygen excess. Yet, it is unknown how these changes impact ventricular function. CMR feature tracking software can quantify deformation of the myocardium and allows for strain analysis using OS images. The aim of this study was to assess the impact of myocardial oxygenation and coronary blood flow (CBF) over a wide range of MAP on myocardial function.

Methods: In ten anaesthetized swine a flow probe was surgically attached to the proximal left anterior descending coronary artery before moving them into a 3T MRI scanner. Using phenylephrine and urapidil, MAP was varied in steps of 10-15 mmHg from a baseline of 70 mmHg. At each MAP level OS cine images, CBF-readings, arterial and coronary sinus blood gases were obtained. For strain, the images were analysed by tracing endo- and epicardial contours in end-diastole with feature tracking-software and peak circumferential strain was calculated for both ventricles. The relationship of peak strain to MAP, CBF and myocardial oxygenation was established.

Results: In total 101 levels were analysed ranging from 35-196 mmHg. A curvi-linear fit showed that peak strain in both ventricles was compromised at low and higher MAP in comparison to the baseline of 70 mmHg. There was no relation of peak strain to blood flow changes. Moreover, peak strain in the left ventricle worsened with an increased myocardial oxygen extraction ratio obtained by invasive gas measures (r = 0.261, p = 0.026), and also worsened with decreasing tissue oxygenation assessed by OS-CMR in a non-linear relationship.

Conclusion: In an experimental animal model, bi-ventricular function as assessed by CMR-feature tracking is compromised at blood pressures outside of the coronary autoregulation zone. The oxygenation deficit at MAP levels below the autoregulation zone may explain the attenuated peak strain. As there is an increase in blood flow and an oxygen excess

at higher MAP the detected compromise in myocardial strain is likely attributed to other mechanisms. More research is required to understand the effects of MAP on myocardial function.

A 9

Pain-inflammation axis: Effects of the nociceptin system on the regulation of toll-like receptors

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Introduction: Nociceptin receptor (NOP) agonists have shown broad analgesic properties in inflammatory pain models.1-2 Recent clinical studies have demonstrated that the nociceptin-NOP system is a target for the treatment of pain or inflammatory diseases.3-5 However, the function of nociceptin and NOP has not been fully elucidated yet. Toll-like receptors (TLRs) are a family of pattern recognition receptors which play a central role in inflammation and pain. The aim of this study was to investigate effects of nociceptin on the regulation of TLRs in human THP-1 cells under inflammatory conditions.

Methods: Human monocytic cells (THP-1) were stimulated with or without different concentrations of lipopolysaccharide (LPS) for 24 hrs. mRNA expression of nociceptin, NOP and TLRs (TLR2, TLR4, TLR7, TLR9) were detected by quantitative RT-PCR. Cell surface TLR2, TLR4 and cellular TLR7, TLR9 protein levels were measured using flow cytometry. To investigate effects of nociceptin on the regulation of TLRs under inflammatory conditions, cells were cultured with or without LPS 10 ng/ml or LPS 1 µg/ml and with or without nociceptin 1 nM for 24 hrs.

Results: mRNA of nociceptin, NOP and TLRs (TLR2, TLR4, TLR7, TLR9) were constitutively expressed, and corresponding protein levels could be detected in THP-1 cells. LPS dose-dependently regulated TLR2, TLR4, TLR7, and TLR9 protein expression. LPS 10 ng/ml and LPS 1 µg/ml respectively upregulated cell surface TLR2 and cellular TLR7 protein levels compared to the controls without any stimulus (both $p < 0.01$). Nociceptin 1 nM partially antagonized the upregulating effects of LPS on TLR2 (MFI with IQR: 3.6E5 (3.3E5/4.0E5) vs. 3.8E5 (3.6E6/4.1E5), $p < 0.05$) and TLR7 (6.4E5 (5.3E5/ 8.8E5) vs. 8.1E5 (6.0E5/9.5E5), $p < 0.05$) compared to the cells cultured with LPS 10 ng/ml or LPS 1 µg/ml only. Nociceptin had no effect on the regulation of TLR4 and TLR9 in the LPS-treated THP-1 cells.

Conclusions: Activation of the nociceptin-NOP system regulates TLR2 and TLR7 proteins in THP-1 cells stimulated by LPS. Elucidating effects of nociceptin and NOP on TLRs in human blood leukocytes under inflammatory conditions may lead to new insights in the treatment of pain and/or inflammation.

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A 10

Glucose—Insulin—Potassium (GIK) morbidity and mortality effects in cardiac surgery: a systematic review and meta-analysis of randomized trials

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Background: Although experimental studies strongly support the cardioprotective effects of glucose—insulin—potassium (GIK) infusion, clinical trials have yielded mixed results due to the heterogeneity of patient populations as well as varying GIK administration patterns. An updated systematic review and meta-analysis were conducted to assess the impact of GIK treatment on postoperative complications in patients undergoing on- or off-pump cardiac surgery.

Methods: We searched MEDLINE, Embase and the Cochrane Central Register without language restrictions for studies from inception to March, 2020. We included randomized controlled trials that compared GIK infusion as cardioprotective measure to conventional treatment or placebo in adults undergoing on- or off-pump cardiac surgery. Postoperative myocardial infarct (PMI) was the main study endpoint; secondary outcomes were in-hospital mortality, postoperative complications, as well as duration of mechanical ventilation, intensive care stay and hospital stay. Postoperative glycemia and cardiac index were also examined. The study was registered with PROSPERO (N° CRD42019117728). We computed risk ratios (RR) or mean differences (MD) with 95% confidence intervals (CI) and heterogeneity was estimated using I2 statistic.

Results: From 47 studies, 5'872 participants were pooled for meta-analysis. The incidence of PMI was 5.9% and 8.3% in the GIK and Control groups, respectively (n = 20, RR [95% CI] = 0.83 [0.65 to 1.04] I2 = 0). Compared to control treatment, GIK infusion was associated with lower hospital mortality (n = 19, RR [95%CI] = 0.64 [0.43 to 0.97], I2 = 0), reduced acute kidney injury (n = 6, RR [95%CI] = 0.59 [0.4 to 0.87, I2 = 0), fewer atrial fibrillation (n = 23, RR [95%CI] = 0.75 [0.6 to 0.94], I2 = 0.58), as well as a shorter duration of mechanical ventilation (n = 14, MD [95%CI] = -1.77 [-3.04 to -0.49] hours, I2 = 0.96), shorter stay in intensive care (n = 20, MD [95%CI] = -5.39 [-9.34 to -1.44] hours, I2 = 0.99) and faster hospital discharge (n = 19, MD [95%CI] = -0.84 [-1.6 to -0.08] days, I2 = 0.95).

Conclusions: Perioperative administration of GIK was associated with improved postoperative clinical outcomes as reflected by lower in-hospital mortality and morbidity as well as lesser utilization of hospital resources. Further clinical studies are warranted to ascertain the effectiveness of GIK in minimizing myocardial injuries and to explore the specific dosage and timing of GIK infusion.

A 11

Anesthetic neurotoxicity: the association between general anesthesia and the level of plasmaneurofilament light. Preliminary results.

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Background: The potential neurotoxicity of general anesthesia (GA) is a widely controversial issue. Neurofilaments Light (NF-L) are assuming importance as new marker of neuronal damage. Promising results are shown in chronic neurological disease and as predictor for the neurologic outcome after cardiac arrest. Previous findings suggest that general anesthesia and surgery may be associated with neuronal damage in the short term. Therefore, our intent is to evaluate the impact of the general anesthesia alone on the central nervous system, minimizing the surgical bias.

Materials and methods: A prospective controlled single centre study designed to determine the association between the exposure to anesthetic agents and change in plasma NF-L levels. We compare pre (t0) and postoperative (after 24 hours) plasma NF-L in patients with similar surgical interventions but different anesthetic techniques. To detect this incidence with an accuracy of±8% (α of 0.05) and power of 0.85, at least 113 patients are needed. We recruited patients undergoing electrophysiological interventions in local anesthesia (non-exposed group) and patients requiring similar procedures in GA (exposed group). We excluded patients suffering from neurodegenerative diseases and neurocognitive disorders. The NF-L concentration was measured using a Quanterix' SIMOA assay (University Hospital of Basel, Switzerland). We compared the NF-L delta plasma levels (t24-t0) between the two groups using Mann-Whitney U Test due to the limited sample size.

Results: 39 patients were enrolled, 21 (GA) and 18 local anesthesia (LA). In the exposed group, the median age is 74 years old; the median duration of operation is 90 minutes. In the non-exposed group, the median age is 78.5 years old; the median duration of operation is 65 minutes. There is a significant difference with respect to age, operation time and NF-L baseline value between the two groups. Delta NF-L value of GA vs. LA doesn't show statistical significant difference ($p = 0.121$).

Conclusion: Based on these preliminary results, we didn't find an association between GA and neuronal damage in the short term. This interesting finding suggests a limited neurotoxic impact of GA but it should be confirmed by a large sample size.

A 12

Visualizing myocardial injury from elective cardioversion

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Background: Despite everyday use of electrical interventions in cardiovascular care, the extent and type of concomitant myocardial injury is not fully understood. Current literature disagrees about the question whether and how cardioversion or defibrillation damage the myocardium, especially when serologic markers are used. Such markers are not always cardiac-specific, nor diagnostic for type and region of myocardial injury. We aimed to investigate whether the acute and long-term impact of electrical cardioversion on myocardial structure and function is detectable using CMR imaging.

Methods: Patients scheduled for elective cardioversion were enrolled to undergo three CMR exams: on the morning prior to cardioversion to assess pre-existing injury; two to five hours after cardioversion to assess the acute response; and six to ten weeks later to investigate chronic injury. The CMR exam studied left ventricular (LV) function, T2 mapping to measure edema, extracellular volume (ECV) to measure diffuse fibrosis, and quantified both degree of injury and proportion (%) of myocardial area affected.

Results: Eight patients completed the study, requiring 1-2 shocks (totalling 120-300 J biphasic energy) to achieve sinus rhythm. LV ejection fraction increased after cardioversion from 47±13% to 55±15% (p = 0.020), and was 52±16% at the third exam (p = 0.199). Even prior to intervention, some patients showed edema (baseline T2 >40 ms) afflicting 49±23% of their LV myocardium. Area affected by edema expanded to 72±18% after cardioversion (p = 0.002) and returned to 54±24% by the third exam. T2 rose from baseline (40.4±1.8 ms) after cardioversion acutely to 44.1±5.2 ms (p = 0.028) and normalized until the late exam (40.8±3.1 ms). Myocardial area affected by diffuse fibrosis (ECV >30%) was 28.3±9.4% at baseline and 38.8±18.9% late after cardioversion (p = 0.018). Pathologic T2 increases (indicative of edema) were not observed in all patients, but individuals with higher baseline ECV also experienced greater T2 increase after cardioversion (r = 0.840, p = 0.036).

Conclusion: Elective cardioversion improves left ventricular systolic function, but aggravates myocardial edema and possibly adds to diffuse fibrosis during several weeks thereafter. Such sequelae of cardioversion were observed mainly in patients with a greater burden of pre-existing myocardial injury. More data is needed to corroborate these preliminary findings and to study whether this type of myocardial injury predicts worse outcome.

A 13

Safety of sugammadex vs. neostigmine for reversal of neuromuscular blockade during non-cardiac surgery – a propensity-score matched case-control study

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Introduction: Postoperative residual neuromuscular block is a major contributor to patient morbidity and mortality. Sugammadex is effective for reversing even deep blocks, but may also provoke serious complications and clinical safety profile therefore remains controversially discussed. We tested the hypothesis that in patients having surgery with general anesthesia and requiring reversal of neuromuscular block, sugammadex is non-inferior to neostigmine on a composite of clinically important adverse short-term events.

Methods: With IRB approval, we considered 89,753 patients who had cardiac, noncardiac, or pediatric surgery, and had their neuromuscular block reversed by either sugammadex or neostigmine from 2016 to 2019 at Cleveland Clinic Main Campus. Adverse events were defined as clinical concerns for bradycardia, anaphylaxis/allergy, bronchospasm, and cardiac arrests. Events were identified by searching anesthesia records for administration of any medication (atropine, glycopyrrolate, epinephrine, ephedrine, methylprednisolone, diphenhydramine, and albuterol) or any intervention (chest compression, defibrillation) which were related to the four adverse events and then evaluated by an adjunction committee by manual chart review. The primary outcome was a composite outcome of four adverse events.

Results: Among 89,753 surgeries on 70,690 patients, 16,480 (18%) cases received sugammadex and 73,273 (82%) received neostigmine. Baseline factors were well balanced with all absolute standardized differences <0.11. The incidence of the composite outcome was 2.9% in the sugammadex group and 2.6% in the neostigmine group. Noninferiority was not found, with an estimated odds ratio of 1.15 (sugammadex vs. neostigmine, 95% CI: 1.03 to 1.28), noninferiority P = 0.22. Bradycardia was by far the most common complication (2.4% sugammadex versus 2.2% neostigmine). Severe potentially life-threatening complications like anaphylaxis (0.23% sugammadex vs. 0.28% neostigmine) and cardiac arrest (0.01% sugammadex versus 0.02% neostigmine) were similar in both groups.

Conclusions: Sugammadex was not non-inferior to neostigmine on the composite outcome Nonetheless, the absolute difference in composite complications was only 0.3%, corresponding to a number-needed-to-treat >300. There thus does not appear to be a clinically meaningful difference in the incidence of short-term complications when non-depolarizing muscle relaxants are reversed with neostigmine and sugammadex.

A 14

Comparison of the efficacy and safety of interventions for the prevention of acute and chronic pain following breast surgery: a systematic review with meta-analyses and trial-sequential analyses

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Background and objective: The aim of this review is to compare indirectly the efficacy of any intervention, administered perioperatively, on acute and persistent pain after breast surgery.

Databases and data treatment: We searched for randomised trials comparing analgesic interventions with placebo or no treatment in patients undergoing breast surgery under general anaesthesia. Primary outcome was intensity of acute pain (up to 6h postoperatively). Secondary outcomes were cumulative 24 hour morphine consumption, incidence of PONV, and chronic pain. We used an original three-step approach. First a meta-analysis was performed when data from at least three trials could be combined, secondly trial sequential analyses were used to separate conclusive from unclear evidence. And thirdly the quality of evidence was rated with GRADE.

Results: Seventy-three trials (5512 patients) tested loco-regional blocks (paravertebral, pectoralis), local anaesthetic infiltrations, oral gabapentinoids or intravenous administration of glucocorticoids, lidocaine, NMDA antagonists or alpha 2 agonists. With paravertebral blocks, pectoralis blocks, and glucocorticoids, there was conclusive evidence of a clinically relevant reduction in acute pain (>1.0 cm VAS). With pectoralis blocks, and gabapentinoids, there was conclusive evidence of a reduction in the cumulative 24 hour morphine consumption (≥5 mg). With paravertebral blocks and glucocorticoids, there was conclusive evidence of a relative reduction in the incidence of PONV of 70%. For chronic pain insufficient data was available.

Conclusions: Mainly with loco-regional blocks, there is conclusive evidence of a reduction in acute pain intensity, morphine consumption, and PONV incidence after breast surgery. For rational decision-making, data on chronic pain is needed.

A 15

Postoperative Anemia is Associated with Nonfatal Myocardial Infarction and All-cause Mortality

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Background: Myocardial infarction is a major postoperative complication and is probably mostly consequent to myocardial oxygen supply-demand mismatch. Perioperative anemia is common and strongly associated with postoperative complications and mortality. We therefore aimed to test the hypothesis that the lowest in-hospital postoperative hemoglobin concentration is associated with a composite of nonfatal myocardial infarction and all-cause mortality within the first 30 days after noncardiac surgery.

Methods: With IRB approval we conducted a retrospective cohort study as a sub-study from the POISE-2 multicenter trial. In the POISE-2 trial 10.010 non-cardiac surgical patients >45 years old at risk for cardiovascular disease were factorially randomized to aspirin versus placebo and to clonidine versus placebo from 2010 to 2013. All POISE-2 patients were enrolled. We excluded 1817 patients in whom postoperative hemoglobin concentrations were not available and 950 POISE-2 patients who were recruited from Cleveland Clinic sites since they were included in the companion analysis. Patients were stratified into four groups based on hemoglobin levels for data presentation: <8 g/dL, 8-11 g/dL, 11-13 g/dL and >13 g/dL. We assessed the association between the lowest hemoglobin concentration during the initial hospitalization and a composite of non-fatal myocardial infarction and all-cause mortality during the initial 30-days, using a multivariable logistic regression model. Potential confounders were adjusted.

Results: 7243 patients analyzed. The overall incidence of non-fatal myocardial infarction and all-cause mortality was 8.9%, ranging from 21% amongst patients with lowest haemoglobin concentrations <8 g/dL, to 2.1% in those with hemoglobin concentrations >13 g/dL. After adjusting for baseline factors, in patients with a lowest hemoglobin concentration <11 g/dL, each one g/dL reduction in lowest hemoglobin concentration was associated with a 1.51 (95% CI: 1.41, 1.61; P <0.001) increase in the odds of the composite outcome. In contrast, there was no significant relationship amongst patients with a lowest hemoglobin concentration that exceeded 11 g/dL (OR = 1.00, 95% CI: 0.90, 1.11; P = 0.95).

Conclusion: Postoperative hemoglobin concentration is an additional modifiable risk factor for nonfatal myocardial infarction and all-cause mortality, especially in patients with or at risk of cardiovascular disease.

A 16

Video-analysis of all 428 intubations performed by Rega within one year

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Background: The Swiss air-rescue helicopter emergency medical services (Rega-HEMS) introduced videolaryngoscopes for all helicopters in 2018. This offered the opportunity to film and analyse pre-hospital intubations as it has never been done before.

Methods: This prospective observational study was approved by the necessary ethical committee of Bern (2017-02104) and included all prehospital intubations performed by Rega physicians from the 12 Rega-HEMS bases throughout Switzerland from 02/2018 to 02/2019. All videos were analysed and additionally, physicians completed two different questionnaires: one with information about prior experience and a second one with information regarding the airway management of each intubation.

Results: During the 12 months study period, 428 patients were intubated by 110 individual HEMS-physicians using videolaryngoscopes (C-MAC™, Karl-Storz, Tuttlingen, Germany). Of these, 316 cases (74%) were also recorded by video. The first-pass success rate (FPS) was 87.6% and the overall success rate was 98.6%. The median duration of the successful intubation attempt was 30 seconds (22-42 s; range 11-149 s). The median overall time to successful intubation was 31s (23-44s; range 11-305 s). Time to successful intubation as well as the first-pass and overall success rate were independent of prior experience in anaesthesia. Visibility was impeded by blood (21.6%), vomitus (14,6%), saliva (24,9%), or extensive sunlight (12,7%). Fogging of the camera lens was observed in 35,3%. Arytenoid cartilage was hit during the tracheal intubation process in 24% of the intubation attempts once and in 28% more than once.

Discussion/Conclusion: Our study revealed similar success rates of Rega physicians using videolaryngoscopes, compared to reports from very experienced anesthesiologists [1]. The use of a videolaryngoscope seems to increase safety in airway management even for relatively inexperienced residents performing in the prehospital setting. Video-analysis allowed for precise measurement of intubation times and demonstrated common problems such as multiple hits on arytenoid cartilages that would otherwise remain unnoticed.

Reference

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A 17

Postoperative nausea, an unresolved anaesthesia complication?

Quality control of the evidence-based guideline on postoperative nausea and vomiting (PONV) at University Hospital Basel.

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Background: Postoperative nausea and vomiting (PONV) are among the most common and, along with postoperative pain, the most relevant postoperative anaesthetic complications. Approximately one third of patients are affected by PONV, which is why generally valid recommendations, i.e. guidelines for dealing with it have been developed. The Department of Anaesthesiology at the University Hospital Basel is applying an evidence-based guideline that defines how PONV should be handled prophylactically and therapeutically. However, the benefit of these treatment and prophylaxis regimens depends largely on the efficient and correct application. Therefore, this master thesis examined whether the guideline is applied correctly and whether it fulfils its purpose.

Methodology: To answer the research question, a random sample was taken at the University Hospital of Basel. For this purpose, postoperative follow-up checks were performed during a period of two weeks on all 535 patients who had been anesthetized. The data collection consisted of patient interviews, analyses of the preoperative and intraoperative anaesthesia protocols and the patient's medical history. Finally, data from 267 patients could be included in the sample. Considered as risk factors for PONV were female gender, age <50, history of PONV/kinetosis and non-smoking status.

Results: In the sample it was found that about 50% of the patients were treated accordingly to the guideline. In these cases patients were correctly classified according to their PONV risk and all recommended prophylactic measures were taken. PONV occurred in 26% of all patients. In the group of patients who were correctly treated according to the scheme, PONV occurred in 47%. PONV could therefore be prevented by the correct application of guideline in half of the cases.

Conclusion: Based on the analysis, compliance with the PONV guidelines is obviously a challenge in daily clinical practice in and its implementation is difficult. The used guideline for handling PONV based on the risk assessment may be too complicated for the daily clinical routine. On this basis, it would be advisable to develop a simplified, easily implementable guideline for the handling of PONV.

A 18

Pain trajectories based on routine pain scores predict chronic postoperative pain by early pain intensity, but not by the slope of pain resolution

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Chronic postsurgical pain (CPSP) is a major health issue [1]. Analysis of dynamic aspect such as trajectories of acute postsurgical pain (APSP) has been suggested as a better way to predict CPSP than APSP intensity itself [2, 3]. However, studies suggesting that the slope of the APSP trajectory often present data with relatively high initial pain scores, which should be rare when using efficient APSP therapy. The aim of this study was to assess the predictive value of the APSP trajectory and the initial APSP intensity (i.e. the intercept of the trajectory) for presence of CPSP 6 months after surgery.

Material & methods: We used data of an ongoing study (ALDO) with randomly selected patients having scheduled high risk of CPSP type surgery. Pain scores (numeric rating scale NRS) at rest for the 5 first postoperative days were fitted with a linear regression line. We performed logistic regression with the slope and intercept of the regression lines, as well as mean pain intensity on each day, as continuous explanatory variables and the probability of CPSP (intensity ≥3/10) 6 months after surgery as the dependent variable.

Results: 233 patients were included by the time we started the analysis, 100 patients were discharged before the 5th day, 15 patients had incomplete data and 19 were lost to follow-up. Analysis was therefore based on 99 patients (mean age 59 y): 33% had joint surgery, 29% spine surgery, 22% laparotomy and 16% miscellaneous. 56% of patients received postoperative analgesia orally and 44% through patient-controlled devices. Mean NRS scores were 2.5 ±1.6, 2.5 ±1.6, 2.0 ±1.5, 2.0 ±1.7, 2.0 ±1.6 (mean±SD) on the first 5 postoperative days. CPSP prevalence was

44.4%. Logistic regression analysis showed that the slope of the regression line was not predictive for CPSP. The intercept of the pain trajectory was predictive for CPSP (p = 0.01), as well as daily mean NRS scores on the 1st to 4th postoperative days.

Conclusion: We confirmed that intense APSP is predictive of CPSP. However, when using routine pain scores at rest, the absolute intensity seems to be more important than the trajectory itself. It needs to be tested whether non-linear analysis of this trend may yield additional information about the risk of CPSP.

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A 19

Duration and Timing of Intraoperative Hypotension and its Impact on Early Postoperative Acute Kidney Injury in Cystectomy Patients – A Retrospective Cohort Analysis

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Background and goal of study: Intraoperative hypotension is frequent during major non-cardiac surgery and a common side effect of anaesthesia. Mean arterial blood pressures (MAP) below thresholds of 65 mmHg have been progressively associated with acute kidney injury (AKI) in a non-urological population. The aim of this study was to confirm these findings in a homogenous population undergoing major urological surgery.

Materials and methods: In this retrospective observational single tertiary high caseload centre cohort series we analysed intraoperative data of 416 patients undergoing open radical cystectomy with urinary diversion between 2013 and 2019 and their correlation to postoperative AKI judged according to the Acute Kidney Injury Network criteria. We assessed the risk for postoperative AKI for different hypotension thresholds in form of time below a fixed threshold. Patients were divided into groups falling below MAP <65 mmHg, MAP <60 mmHg and MAP <55 mmHg. The probability of developing postoperative AKI using all risk variables as well as the hypotension threshold variables (minutes under a certain threshold) was calculated using regression method.

Results and discussion: Postoperative AKI was diagnosed in 128/416 patients (30.8%). Multiple regression analysis show that for every minute below a threshold of 65 mmHg (OR 1.010 [1.005 – 1.015], p <0.001) and 60 mmHg (OR 1.012 [1.001 – 1.023], p = 0.02) the risk of developing AKI increases by 1.0% or 1.2%, respectively. On average, 26.5% (MAP <65 mmHg), 50.0% (MAP <60 mmHg) and 76.5% (MAP <55 mmHg) of minutes below a certain threshold occurred between induction of anaesthesia and start of surgery and are thus fully attributable to anaesthesiological management.

Conclusion: With increasing time below hypotension thresholds of MAP <65 mmHg and <60 mmHg the risk for developing postoperative AKI escalates. Special attention has to be paid to the time between induction of anaesthesia and surgical incision as many episodes of hypotension occur in this period.

A 20

Futility in the emergency setting: anesthesiologists' versus surgeons' perspective

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Background: a futile intervention in the emergency setting refers to a procedure that is unlikely to benefit significantly to the patient. However, several criteria influence the decision to perform or not a procedure. These include patient, hospital and physicians' characteristics and values related factors. The latter may vary among the different categories of healthcare professionals involved in the decision, particularly anesthesiologists and surgeons. We explored differences in the perception of futility and level of autonomy regarding the final decision to intervene or not between the two categories involved in the treatment of emergency surgical patients.

Methods: the study was performed in March 2019 at the Geneva University Hospitals. All anesthesiologists and surgeons working in the emergency setting were invited to take part of a web-based survey. The clinical case of a trauma patient resuscitated for a cardiac arrest and in need of emergency surgery was presented. Participants were asked about their decision to performing or not surgery. The 46 questions survey also explored organisational, patient, family and professional-related factors leading to the decision in daily practice. Possible differences in perspective over futility and physicians' autonomy were also assessed. For descriptive statistics we used mean values with proportions. All answers were dichotomized and chi Square test used to compare groups. A p value <0.05 was considered significant.

Results: 109 physicians − 62 anesthesiologists and 47 surgeons − answered to the questionnaire (corrected participation rate of 42%). There was no difference between the two groups as to the decision to perform surgery for the patient presented. However, anesthesiologists considered previous quality of life as more important (97% vs 83%, p = 0.0134) to make a decision. Surgeons considered more often that treatments with uncertain benefit (79% vs 60%, p = 0.0349) and without garantee of a good quality of life (60% vs 39%, p = 0.0307) should still not considered as futile. Anesthesiologists felt more unfree to decide (30% vs 79%, p = 0.0001), disrespected in their opinion (83% vs 47%, p = 0.0001) and pressured to operate (91% vs 53%, p <0.0001).

Conclusions: Significant differences exist between anesthesiologists and surgeons in their perception of futility and contribution to decisional process in the emergency setting. This suggests an increased likelihood of conflict between the two categories.

A 21

The effective group size for teaching cardiopulmonary resuscitation skills – a randomized controlled simulation trial

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Purpose of the study: The ideal group size for effective teaching of cardiopulmonary resuscitation (CPR) skills is currently unknown. The limit is reached when instructors are unable to notice and correct essential errors of the participants. This study aims to define the group size where instructors are able to detect and correct a predefined 80%-threshold of errors of participants.

Materials and methods: After ethics committee approval and written informed consent of instructors, a simulated high quality single-rescuer Basic Life Support setup (incl. bag-mask ventilation and use of automated external defibrillators) was established. Medical students acted as simulated course participants and were instructed to make three pre-defined CPR-quality errors (e.g. chest compression too fast, very superficial, etc.) during the study period. Instructors were randomized to groups of 3 to 10 participants and observed the CPR-skills performance of the simulated course participants during 7 minutes. Instructors corrected errors of these participants when applicable. Predefined primary outcome was percentage of correctly identified and corrected errors.

Results: Eight instructors per group sizes from 3 to 10 simulated participants summed up to a total of 64 instructor participants. Instructors were 41±9 years old, 33% were female, had a median experience of 6 years (IQR 2-11), and taught 3 (IQR 1-5) courses during the last year before the study. The median percentage of errors corrected per group size was: group size 3: 89%; group size 4: 83%; group size 5: 80%; group size 6: 83%; group size 7: 71%; group size 8: 79%; group size 9: 76%; and group size 10: 72%. Each additional participant in a group increased the percentage of errors not detected by 2%. Assuming linear correlation, the 80%-threshold of corrected errors would then be at six participants.

Conclusions: This randomized controlled simulation trial reveals a decrease in the ability of instructors to detect errors in cardiopulmonary resuscitation skills performance with increasing numbers of participants

per group. The conservatively estimated maximum group size still enabling instructors to oversee and correct essential errors during CPR-teaching is six. These results might influence the instructor-participant ratio during CPR-education.

A 22

Epidemiology of multimorbidity in the perioperative patient population

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Background: The complexity of patients presenting for surgery has increased in recent decades and will continue to rise, as shown by the parallel increase in ASA physical status of patients over the same time period. Despite several modifications of the ASA classification, multimorbidity is still not considered. Only the single most severe systemic disease is decisive in defining a patient's ASA class irrespective of the number and the nature all other comorbidities. However, there are limited data about the prevalence of multimorbidity and the commonly occurring clusters of comorbidities in the perioperative patient population. Therefore, the aim of this cohort study is to assess the number and type of all comorbidities that might influence the perioperative management.

Methods: All patients who have been included in the multicentre prospective ClassIntra® validation study at the University Hospital Basel will be included in this cohort study. About 30 patients from each surgical discipline undergoing any type of in-hospital surgery were followed up until 30 days postoperatively. For the purpose of assessing the epidemiology of multimorbidity, the severity of all comorbidities relevant for ASA classification has been extracted from the electronic anaesthesia protocol and the electronic medical record according to a predefined list. The primary endpoint is the number of comorbidities relevant for perioperative management across all ASA classes.

Results: Of 320 enrolled patients with an average age of 56 years (SD 19 years), 54% were women. There were 27 ASA I (8%), 150 ASA II (47%), 116 ASA III (36%) and 27 ASA IV (8%) patients. The patients had a median of 5 comorbidities (range 0-17) with a significantly higher number with increasing ASA class: ASA I patients had 1 comorbidity (range 0-4), ASA II 4 (range 1-12), ASA III 9 (range 1-17) and ASA IV patients had 12 (range 5-17) comorbidities. Throughout all ASA classes, the most commonly observed comorbidity clusters were cardiovascular (n = 177, 55%), neurological (n = 150, 47%) and liver or kidney (n = 150, 47%) disorders.

Conclusion: In patients presenting for surgery, the prevalence of multimorbidity is high especially in higher ASA classes. However, multimorbidity is not yet considered in the current ASA physical status classification. In a further international multicentre cohort study, we aim to assess the impact of multimorbidity on perioperative management, outcome and costs.

A 23

Renal Injury After Open versus Laparoscopic Non-cardiac Surgery: A retrospective cohort analysis

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Background: Laparoscopic surgical approaches enhance recovery, reduce postoperative pain, and shorten hospital length-of-stay. Nevertheless, increased intra-abdominal pressure is associated with decreased renal blood flow, renal hypoxia and acute kidney injury. When combined with Trendelenburg positioning, renal function may further deteriorate. We tested the primary hypothesis that the combination of laparoscopic surgical approach and Trendelenburg position is associated with larger reductions in estimated glomerular filtration rate (eGFR) within the initial 48 postoperative hours compared to open surgery without Trendelenburg positioning. Secondarily, we tested, if laparoscopic procedures are associated with greater incidence of postoperative acute kidney injury.

Methods: Adults who had laparoscopic colorectal surgery in Trendelenburg position at the Cleveland Clinic Main Campus from 2009 to 2006 were propensity-matched to patients who had comparable open procedures. Patients with pre-existing renal impairment were excluded.

Results: Among 7,357 eligible patients, 1,846 laparoscopic cases with Trendelenburg were matched to 1,846 open cases. There was no association between laparoscopic approach and postoperative eGFR. A significant protective effect of the laparoscopic procedure on the odds of having AKI was found. Patients who had laparoscopic surgeries were an estimated 0.70 (95% CI: (0.55, 0.90), pHolm?adj = 0.006) times as likely to have AKI as open surgical patients.

Conclusion: Despite compelling potential mechanisms, laparoscopic approach with Trendelenburg position in adult colorectal surgeries did not worsen postoperative eGFR, and actually reduced postoperative acute kidney injury. Given the other advantages of laparoscopic surgery, the approach should not be avoided for concerns about renal injury.

A 24

Effects of normoxic versus hyperoxic hyperventilation followed by apnea on right ventricular strain in patients with multi-vessel coronary artery disease

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Background: Hypocapnia and hyperoxia are coronary vasoconstrictors, whereas hyper-capnia acts as a coronary vasodilator. Prior to anaesthetic induction, patients receive a FiO_2 of 1.0 and are asked to take deep breaths. Resulting hyperoxic hypocapnia may be aggravated by excessive manual ventilation. Subsequent apnea during intubation increases $paCO_2$. So far it remains unclear whether and how such rapid blood gas alterations impact right ventricular (RV) func-tion, especially so in the presence of coronary artery disease (CAD). Cardiovascular magnetic resonance (CMR) imaging is useful to assess subtle changes of myocardial function and consti-tutes the gold standard for RV imaging. The objective of this CMR study is to compare RV function of healthy persons and patients with CAD during a typical hyperventilation-apnea maneuver.

Methods: Ten healthy participants and 25 patients with stable, well-defined multi-vessel CAD underwent a CMR study. After baseline imaging at room air, subjects hyperventilated for 60 seconds (HV) and then maintained apnea for 30s. Cine images of two ventricular short axis slices were acquired at baseline and from the end of HV throughout the breathhold. After re-equilibration, participants breathed oxygen (10 L/min) for 5 minutes via a non-rebreathing mask and repeated the same respiratory maneuver under oxygen inhalation. Rapid acquisition CMR images were analyzed for RV global peak circumferential strain for each group and condition.

Results: Healthy participants showed no significant right ventricular peak strain changes within or between normoxic or hyperoxic respiratory maneuvers, although HV enhanced strain numerically. CAD patients showed significant attenuation of peak strain at the end of the hyperoxic HV-apnea sequence (baseline, -13.5±4.7% vs. hyperoxic apnea, -11.8±4.9%; p = 0.047), but not after the respective sequen-ce at room air (-13.8±4.1%, p = 0.611). In 20% of the CAD patients the hyperoxic HV-apnea sequence attenuated peak strain by more than 5% from normoxic baseline.

Conclusion: At the conclusion of an induced respiratory maneuver, which resembles a hyperoxic anesthesia induction sequence, awake CAD patients exhibit significant attenuation of RV peak circumferential strain. This response could be hemodynamically relevant during anaesthesia induction in high-risk CAD patients and needs to be investigated further in a scenario of general anaesthesia.

A 25

A systematic review of published qualitative research pertaining to the field of perioperative anaesthesia

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Background and goal of the study: Qualitative research (QR) draws on a wide range of data collection, analysis methods and theoretical frameworks to explore people's beliefs, behaviors, perspectives and experiences [1]. QR contributes to evidence-based healthcare through hypothesis generation, development and validation of research instru-

ments, intervention development and evaluation. While QR has contributed to many areas of healthcare, it appears to be underused in the field of anaesthesia. The purpose of our review is to describe the current state of QR in anaesthesia, identify topics, and highlight current limitations.

Materials and methods: We conducted a systematic mapping review of published QR studies pertaining to the field of perioperative anaesthesiology. We selected articles published between 2000 and June 2018 from 3 databases: CINHAL (241), Pubmed (520), Embase (1370). A total of 107 articles were included. Data were extracted and coded into predefined categories.

Results and discussion: We observed a 6-fold increase in the number of QR publications between 2000 and 2018, reflecting a growing interest in QR in anaesthesia. Top publishing countries are both Scandinavian (mainly Danish and Swedish) and anglophone (UK, USA, CA, AUS). Publications are balanced between medical (42%) and nursing (38%) journals. The latter publish more studies on patients' experiences and opinions than medical journals. Research teams are both interprofessional (69%) and uniprofessional (27%) and include anaesthesiologist specialists in 79% of the cases. In 55% of publications in medical journals, at least one author is a scientist outside of the classical healthcare professions. We found that methodologies were misused or misunderstood by some authors. Details regarding methodologies and author's reflections on their own cultural backgrounds, beliefs and bias were frequently missing.

Conclusions: It is encouraging to see that journals are increasingly publishing anaesthesia related QR. However, reports need better descriptions of methodologies and transparency. We advocate for a better understanding of QR theoretical concepts, involvement of QR scientists, and improved quality and exhaustivity of reporting.

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A 26

Endotracheal Intubation Success Rate in a Resident-staffed and Specialist-Physician-Supervised Urban Emergency Prehospital System: an 11-Year Retrospective Cohort Study

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Introduction: Prehospital endotracheal intubation (ETI) is sometimes required to secure the airways. Performing ETI in the field is often challenging, and success rates differ depending on the provider's training, background, and experience. In Geneva, ETI is performed by physicians working in a mobile emergency and resuscitation unit (Service Mobile d'Urgence et de Réanimation, SMUR). These SMUR units are usually staffed by an advanced paramedic and a resident physician. Whenever necessary, a senior emergency physician, acting as a supervisor, can be dispatched as a backup.

Objective: This study endeavoured to evaluate the ETI success rate in this physician-staffed and specialist-physician-supervised prehospital system.

Methods: Relevant data were electronically extracted from the Geneva University Hospitals' institutional database. Records of all adult patients taken care of between 2008 and 2018 were screened for intubation attempts. The primary outcome was the ETI success rate. Secondary outcomes were the number of ETI attempts, the rate of ETI success at the first attempt, and the rate of ETIs performed by a supervisor.

Results: A total of 3275 patients were included, 55.1% of whom were in cardiac arrest. The overall ETI success rate was 96.8%, with a 74.4% success rate at first attempt. First attempt success rate was lower in patients who were in cardiac arrest (72% vs 78%, p <0.001). Supervisors oversaw 1167 ETI procedures onsite (35.6%) but intubated in only 42% of the cases.

Conclusion: A resident-staffed and specialist-physician-supervised urban emergency prehospital system can reach ETI success rates similar to those reported in specialist-staffed system [1].

Reference

1 Crewdson et al. Crit Care 2017 Feb 14;21(1):31

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Use of nasal Nalbuphine in Prehospital Trauma Management by First-Rescue Personnel on Ski Slopes in Switzerland

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Introduction: Especially for trauma patients, pain is one of the major symptoms in the prehospital setting. Therefore, a sufficient and quick pain relief is essential but often difficult. Because of the mountainous topography of Switzerland, first rescue services (FRS) of ski resorts may have to cope with a time delay between the injury of the patient and the arrival of professional rescue personnel. One treatment strategy may be the application of "safe" opioids by non-medical specialists to improve overall treatment. Therefore, we assessed the use of nasally administered Nalbuphine for analgesic treatment by FRS at a ski resort in Switzerland.

Methods: We instructed all members of the FRS in several ski resorts in Graubunden, Switzerland, how to nasally apply Nalbuphine. We developed a treatment algorithm and distributed Nalbuphine to the rescue services, assuring they only administered the drug following a strict protocol. We collected data regarding pain scores and pain reduction after administration of Nalbuphine on-site.

Results: Average pain score was reduced from 8.1 (out of 10) before administration of Nalbuphine to 5.1 afterwards. Mean pain reduction was 3.0 points (p <0.001). Statistics showed no significant differences between genders. Five percent (n = 6) of patients developed minor side effects such as nausea. No other complications were observed.

Discussion: Nalbuphine is an opioid with a relatively good safety profile and few contraindications. It is also suitable for administration in children, pregnant and lactating women. It is a mixed agonist/ antagonist, featuring a ceiling effect regarding analgesia. Nevertheless, most patients reported a sufficient analgesic effect and good overall satisfaction with only few minor side effects. The nasal administration lead to rapid onset of drug action with the advantage of an easy appliance, especially by lay rescuers and requiring no vascular access.

Conclusion: The nasal administration of Nalbuphine by first-rescue personnel seems to be a safe and moderately effective analgesia therapy in case of severe pain and delayed arrival of professional rescuers.

A 28

Identifying and validating Entrustable Professional Activities for Swiss anaesthesiology residency training based on a task analysis

A sequential mixed-method study

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Background: Work-based learning offers an authentic and meaningful environment for residency training, but its outcome may be subject to heterogeneity without a structured curriculum. The adoption of competency-based curricula is expected to better prepare residents for independent practice. However, acquiring standard sets of competencies does not automatically ensure appropriate performance in real-life during complex tasks. Instead, the concept of Entrustable Professional Activities (EPAs) relates to authentic professional tasks that residents should be able to execute independently with distant supervision. EPAs-based curricula are therefore gaining popularity. Most studies have defined EPAs based on existing competency frameworks. In practice however, job descriptions may differ greatly across contexts and settings.

Objectives: The aim of this study was to identify and validate EPAs for anaesthesiology residency training based on what anaesthesiologists actually do in the workplace rather than what they are supposed to do in theory.

Design: A three-phase sequential mixed method design was used.

Setting: Postgraduate specialty training in anaesthesiology in Switzerland.

Participants: Thirty-three certified anaesthesiologists from 4 Swiss university hospitals participated in the various phases of the study (University Hospitals of Geneva, Zurich, Bern and Basel).

Main outcome measure: Agreement amongst participants was defined as a consensus rate of more than 80% on a final list of EPAs.

Results: A consensus was reached on a final list of 34 EPAs describing the work curriculum for anaesthesiology residency training at the Geneva University Hospitals, of which 14 apply to the first training phase and 20 to the second.
Conclusion: This study offered a context-sensitive approach for developing EPAs aligned with the learning opportunities of a training center. This congruence with the training program should favor successful implementation of curriculum reform. We think this type of study may facilitate the reform of postgraduate anaesthesiology curricula in Switzerland or beyond.

A 29

Development of secondary transports carried out by the Swiss rescue-society Rega

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Introduction: The aim of this study was to describe helicopter transfers in Switzerland in the years 2006-2016. The aim was to draw conclusions for the future and improve emergency medical care.

Methods: We analyzed the operational data of the Swiss Air Rescue Service (Rega) between 01/2006 and 12/2016. Operational data were extracted from digital systems and checked manually if necessary. Hospital categories, medical reason for transfer and times were analyzed.

Results & discussion: During the observed time, 20203 secondary transport occurred. Of these, 17947 (88.8%) were transfers from primary care to a referral hospital. Only 5.3% of transports occurred the other way around. In total, only 2.6% (n = 526) were transports from or to a specialized hospital. Analyzing the reasons for transportation, 76.8% (n = 15523) of patients were transported because of medical disease (35.2% heart/circulatory organs) and 18.4% (n = 3721) because of traumatic injuries. Further 4.8% (n = 959) could not be categorized. Most transfers were carried out during daylight hours and on Fridays before the weekend.

The large volume of transports from small rural hospital might reflect the process of centralization in the Swiss health sector, where smaller hospitals increasingly transfer patients.

Contrary to expectation, transports to a specialized clinic was not a large quantity of secondary transports by helicopter in Switzerland. The fact that medical causes, and not traumatic injuries, required more often secondary transportation may very well demonstrate a triage problem: while severe injuries are easier to diagnose and might be transported to the correct referral hospital in the first place, medical problems such as strokes still seem to be undertriaged in unnecessary high percentage.

Conclusion: This analysis shows that the type and implementation of secondary air transfer Switzerland are closely related to established hospital structures. Time-critical deployments are air-bound and mainly take place from peripheral hospitals to the hospital of central care.

New developments in medicine and aviation are increasingly making it possible to transport seriously ill patients using assist devices such as ECMO and IABP, and to use IFR in difficult meteorological conditions when a purely visual flight is not possible. The question of correct triage merits further investigations.

A 30

Intraoperative intravascular effect of Ringers lactate and hyperoncotic albumin during haemorrhage in cystectomy patients

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Background and goal of study: Crystalloids quickly equilibrate between the intravascular and interstitial volumes, consequently they are mainly used to treat temporary volume deficits. In contrast, iso-oncotic colloids induce a long-lasting plasma volume expansion. As doubts have been raised about synthetic colloids, albumin solutions have been used more extensively. The effect of 20% albumin on blood volume expansion and crystalloid kinetic in a clinical setting involving relevant intraoperative blood loss during major abdominal surgery is still unknown. We expect that fluid replacement with crystalloid will be better sustained intravascularly with the administration of 20% albumin during haemorrhage.

Material and methods: In this single-arm, single centre feasibility study, an i.v. infusion of 3 mL/kgBW of 20% albumin was administered over 30 min to 13 cystectomy patients during the bleeding phase (mean blood loss 973mL) in addition to Ringers lactate solution. Blood samples were collected at regular intervals over a period of 300 min to estimate clinical efficacy (i.e. plasma volume expansion / infused volume) which was analysed with a regression modelling equation.

Results and discussion: Mean haemorrhage was 973 mL (SD ±395). The regression method showed a strong linearity (r = 0.82) between the blood loss minus the blood volume expansion and the independent effects of the infused volume of Ringers lactate and 20% albumin solutions (all P <0.001). The mean clinical efficacy was for the Ringer solution 0.37 (95% CI 0.30 to 0.44) mL/mL and for the 20% albumin 1.77 (95% CI 1.17 to 2.37) mL/mL on an average of 5 hours. This resulted that the 20% albumin expanded plasma volume around 5 times stronger / more potent than the Ringers lactate solution.

Conclusion: The infusion of 20% albumin during haemorrhage of around 1000 mL expands blood volume by 1.8 times and its effect was long standing whereas Ringer solution expanded by 0.4 time. These results suggest that 20% albumin can be used as a potent blood volume expander in this setting, but also sustaining a pronounced longer intravascular effect of Ringers lactate solution.

A 31

Assessment of human factors after advanced life support courses – a randomized controlled simulation trial

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Purpose of the study: Human factors are an essential learning outcome of advanced life support courses. Even though human factors are taught in international life support courses, different course systems assess taught competences differently. Currently, summative assessments after life support courses only assess adherence to current resuscitations guidelines and do not specifically test human factors. The goal of this randomized controlled simulation trial was to investigate participants' perception of human factors assessment during different summative tests.

Materials and methods: After ethics committee approval and written informed consent all 5th and 6th year medical students who attended 19 life support courses during one study year at the University of Bern were invited to participate in the study. All courses followed the 2015 European Resuscitation Guidelines. Each course was randomized to one of two summative assessment types: 1 − individual assessment (one instructor simulates a team, the assessed student leads this "team" through a cardiac arrest scenario test); or 2 − group assessment (3-4 students form a team, one of them is assessed as the team leader; team-members are not assessed and act only on team-leader commands). After completing

the summative tests, students were asked to rate the tests' ability to assess human factors using a visual-analogue-scale (VAS, 0 = no agreement, 10 = total agreement).

Results: Altogether, 227 fifth year students participated in 1-day Immediate Life Support courses (mean age 25 years, 62% female), and 196 sixth year students participated in 2-day Advanced Life Support courses (mean age 26 years, 51% female). Team leadership, team membership, communication and team management was rated significantly higher in the group assessment cohort after 1-day courses. Team membership, communication and team management was rated significantly higher in the group assessment cohort after 2-day courses. Situational awareness was rated comparable after both course types.

Conclusions: Summative assessment in teams is perceived significantly better in assessing human factors as it reflects how cardiac arrest scenarios are taught during life support courses. These results might influence current summative assessment practices in life support courses. However, if these results translate into improved performance during real cardiac arrests needs to be further investigated.

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Increasing Number of Episodes of Intraoperative Hypotension is associated with Early Postoperative Acute Kidney Injury in Cystectomy Patients – Results from a Retrospective Cohort Analysis

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Background and goal of study: Intraoperative hypotension is frequent during major non-cardiac surgery and a common side effect of anaesthesia. It has been progressively associated with acute kidney injury (AKI). In a sub study of major urological procedures, we hypothesized that the number of episodes of falling below a certain hypotension threshold intraoperatively is a risk factor for postoperative AKI.

Materials and methods: We analysed data of 416 patients undergoing open radical cystectomy with urinary diversion at our high caseload centre between 2013 and 2019. We performed a probability prediction to analyse the risk of AKI depending on minutes below a certain hypotension threshold. We focused on subgroups of patients that recorded events below a given threshold and assessed the number of episodes as a grouped variable (1 to 3, 4 to 8, 9 to 15, >15 episodes) in order to improve comparability. This led to conditional probabilities with 1 to 3 episodes as the reference group. We predicted the conditional probabilities for AKI with the help of quadratic splines with knots at 20, 60 and 120 minutes.

Results and discussion: Figure 1 illustrates predicted probabilities for postoperative AKI using an average of our patient population. For a MAP below 65 mmHg, the probabilities for AKI increased with increasing number of episodes (1−3 episodes: 23.7%, 4−8 episodes: 27.3%, 9−15 episodes: 37.0%, >15 episodes: 69.2%). This leads to an OR of 5.671 compared to baseline (95% CI 1.444−25.498, P = 0.016). A similar trend was seen for a MAP below 60 mmHg (1−3 episodes: 26.0%, 4−8 episodes: 37.0%, 9−15 episodes: 47.1%) and 55 mmHg (1−3 episodes: 26.9%,4−8 episodes 61.5%), but no significance could be shown, mainly due to lack of statistical power.

Conclusion: Our results suggest that avoiding repeated episodes of intraoperative hypotension will protect postoperative renal function in cystectomy patients.

A 33

Effects of group size on learning during cardiopulmonary resuscitation courses − a focus group study

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Purpose of the study: Group sizes in cardiopulmonary resuscitation courses vary greatly and are often driven by economic reasons. Currently, the best group size for cardiopulmonary resuscitation courses is under debate. Another study by our research group investigated the group size where instructors are still able to detect and correct 80% of errors of participants and revealed six participants as the threshold. In the current focus group study, we explored the perception of the effect of different group sizes on learning during cardiopulmonary resuscitation courses.

Materials and methods: After ethics committee approval and written informed consent, we invited the instructors and students acting as simulated course participants of the previous study to join one of seven focus groups. Interviewers used open questions to explore thoughts, feelings and attitudes of study participants of the effects of group size on learning. All focus groups were video-recorded, transcribed and afterwards coded by two researchers. Qualitative analysis was performed using the thematic analysis approach.

Results: Altogether 31 participants (13 simulated course participants, 18 instructors) participated. Simulated course participants were 24±2 years old; instructors were 44±9 years old; 45% were female. Topics revealed were: Small teaching groups provide more familiar atmospheres and give course participants the chance to ask more questions and keep engaged during the course. Small courses also seem to ensure higher self-confidence in course participants to be able to transfer the newly learnt skills into practice. Larger groups bear the risk of anonymity. Participants tend to get distracted and remain more passive. Additionally, instructors feel that they are unable to allocate enough time to each student in larger groups and have to shorten their individual feedback to course participants.

Conclusions: Students and instructors prefer smaller teaching groups during cardiopulmonary resuscitation courses. Both agree that smaller groups keep participants engaged and provide the chance to ask more questions. Instructors perceive that teaching is more effective in small groups. These factors might be taken into consideration when deciding on group sizes for cardiopulmonary resuscitation courses to possibly enhance learning outcome of course participants.

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Summative assessments' ability to test human factors after advanced life support courses – a video analysis

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Purpose of the study: Advanced life support courses teach technical cardiopulmonary resuscitation skills, adherence to current resuscitation guidelines, and human factors managing cardiac arrests. However, the summative assessments after life support courses tend to only test technical skills and adherence to current resuscitation guidelines. The goal of this study was to investigate how two different summative assessment methods after life support courses are able to assess human factors.

Materials and methods: After ethics committee approval and written informed consent, medical students of the University of Bern participated in a randomized controlled trial evaluating two different summative assessment methods: 1) group assessment – the assessed student acted as team leader of a group of students. Only the team leader was assessed, but he or she guided the team through a cardiac arrest scenario; 2) individual assessment − the assessed student leads a "simulated cardiac arrest team" composed by only one course instructor mimicking an

entire resuscitation team. All assessments were videotaped, after completion of the study three experienced instructors, not involved in the initial assessment, analysed independently the videos using four different validated scores or a checklist. All of them focused on team leadership and team performance.

Results: We present the data of the "Concise Assessment of Leadership Management" form (L. Nadkarni et al., Simul Healthc 2017) as preliminary results. Each assessor analysed 20 assessment videotapes. Overall, neither announcement of the leader's role, nor engagement of team members in decision-making was observed in both assessment methods. Maintenance of the global view and the periodical assessment was rated comparable between both assessment methods. Items that were better assessable in the team leader group were: explicit addressing of people, reinforcement of closed-loop communication, assignment of roles, and balancing of workload for the team.

Conclusions: These preliminary results of the video analysis of two different assessment methods show that the group assessment might be able to better test some essential items of leadership. Especially testing communication skills and team management skills increased in the group assessment and might be beneficial. These results will probably be able to influence summative assessments after life support courses in the future.

A 35

Does summative assessment after advanced life support courses test the course content? A focus group study.

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Purpose of the study: International advanced life support courses teach regularly human factors, technical resuscitation skills and adherence to current resuscitation guidelines. Currently, human factors are not explicitly tested in summative assessments. The goal of the study was to explore subjective perceptions of assessed course content in summative assessments after advanced life support courses.

Materials and methods: With ethics committee approval and written informed consent we invited medical students and instructors, who participated in a previous study evaluating two different assessment methods after life support courses, to take part in one of five focus groups. The interview question route explored thoughts, feelings and attitudes towards the question if the summative assessment after advanced life support courses was assessing the course content. Participants with experiences in both assessment methods in each focus group discussed their impressions of the summative assessment. All focus groups were videotaped, transcribed and coded separately by two researchers. Qualitative analysis was performed following the thematic analysis approach.

Results: Altogether, 27 course participants and 5 instructors participated in the focus groups. Course participants were aged 26±2 years, 67% were female. Instructors were aged 40±14 years, 40% were female.

All participants agree that both assessment methods tested knowledge (e.g. the resuscitation algorithm, adherence to guidelines etc.) but not technical cardiopulmonary resuscitation skills. Students pointed out that the group assessment was more likely to assess communication skills. Instructors additionally addressed that the individual assessment (using an instructor as multifunctional team) was not realistic, because essential human factors cannot be tested. Instructors and students agreed that the more the assessment reflects clinical practice, the better it is. Some students suggested that the team members should also be evaluated in the summative assessment.

Conclusions: Students subjectively perceived that the summative assessments after advanced life support courses regularly assess adherence to current resuscitation guidelines, however they do not test technical cardiopulmonary resuscitation skills and human factors. Using group assessment methods, human factors could be assessed better, and also team members could be evaluated for their technical resuscitation skills.

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