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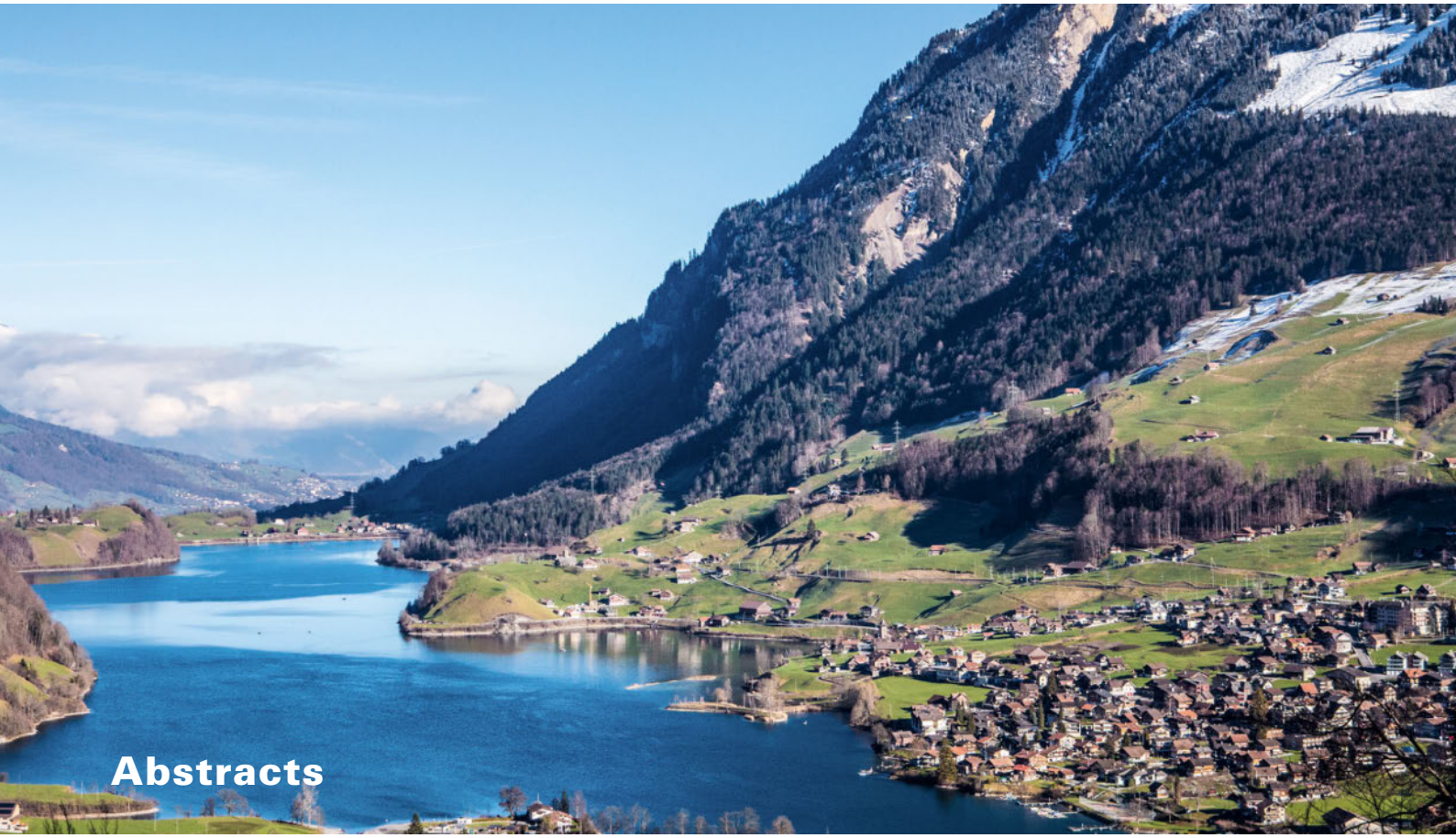

Abstracts

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INTERLAKEN (SWITZERLAND), NOVEMBER 7–9, 2019

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FREE COMMUNICATIONS

FC 1

Benefits of physiological variable ventilation during asthma exacerbations: a randomised experimental study

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Introduction and Aim
Mechanical ventilation during asthma exacerbations may be challenging with a high risk for severe complications. We recently demonstrated the protective effects of physiological variable ventilation (PVV) on respiratory mechanics in healthy lungs. Herewith, we aimed at investigating whether PVV is beneficial in the context of asthma exacerbation, using an experimental animal model.

Methods
Allergen-sensitized rabbits were anaesthetized, tracheotomized and exposed to methacholine aerosol, reaching a sustained increase in airway resistance (asthma exacerbation). Animals were then randomised to receive 6 hours of ventilation, either by pressure-controlled mode (PCV, n = 7) or PVV (n = 8). Other ventilatory parameters were kept similar during the 6h, namely, PEEP 3cm$H_2$0, I:E ratio 1:3 and FiO_2 40%. The PVV pattern was based on a recording of the rabbits' spontaneous breathing. Parameters for ventilation, blood gas and respiratory mechanics were measured hourly. Bronchial lavage fluid (BALF) was analysed.

Results
Animals in PVV group showed significantly lower ventilation driving-pressure (13.0 vs 17.2 cm$H_2$0, p <0.001), better PaO_2/FiO_2 ratio recovery during exacerbation (90 vs 75%, p = 0.01), and tended to have higher compliance than animals in PCV group. Significant differences appear as early as 2-hours of ventilation and become more prominent thereafter. Additionally, expression of inflammatory cells in the BALF was lower in the PVV group compared to PCV (2.6 vs 4.4 G/L, p = 0.02).

Conclusion
Applying physiological variable ventilation in a model of asthma exacerbation leads to an improvement in gas exchange, ventilatory pressures, respiratory mechanics and bronchoalveolar inflammation. A global reduction in lung tissue stress may explain these benefits from PVV, which became more evident over the 6 hours of ventilation.

FC 2

Value of capnography to detect asthma exacerbations during mechanical ventilation

a study in allergen-sensitized rabbits

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Introduction
Capnography is an essential monitoring modality during mechanical ventilation. The analysis of the capnographic waveform provides insight into ventilation-perfusion matching. Herewith, using a rabbit model of asthma, we investigated whether capnography has a diagnostic value during asthma exacerbations.

Methods
New-Zealand white rabbits were allergen-sensitized with ovalbumin over 1 month (n = 6), in order to incite airway hyperreactivity. Sustained bronchoconstriction was then provoked through methacholine aerosol (MCh, 250 µg/mL), under anaesthesia and mechanical ventilation. Slopes of phase 2 and 3 normalized to the end-tidal CO_2 concentration (Sn3T, Sn2T) were determined by using mainstream time domain capnography at baseline and after MCh provocation. The airway and respiratory tissue mechanics were measured by forced oscillation technique. PaO2/FiO2 ratio was calculated from blood gas samples.

Results
MCh aerosol led to decrease in $PaO2/FiO_2$ ratio (453±9 vs 303±22, p <0.01). The Sn3T was significantly higher after MCh (0.047±0.01 vs 0.034±0.01, p = 0.02), while the Sn2T was lower (5.87±0.5 vs 6.46±0.5, p = 0.03). The airway resistance (Raw, 18.3±1.5 vs 11.8±0.7 cmH_2O.s/l), tissue damping (G, 140±8 vs 108±6 cm H_2O/l) and elastance (H, 445±30 vs 406±24 cm H_2O/l) were significantly higher after MCh (p <0.05). To summarize, Sn3T increased 37±9% and Sn2T decreased 10±3% after MCh. Raw, G and H increased 55±9%, 30±5% and 13±%, respectively.

Conclusions
Heterogeneous bronchoconstriction resulting in ventilation-perfusion mismatch after MCh aerosol is reflected in the increases in Sn3T and decreases in Sn2T. These phenomena affected the respiratory system mechanics and the gas exchange alike. Thus, capnography is able to diagnose this heterogeneous ventilation, likely caused by different time constant alveoli appearing during asthma exacerbations.
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FC 3

Intraoperative remifentanil versus dexmedetomidine: a systematic review and meta-analysis

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Background
Intraoperative remifentanil is associated with increased postoperative analgesic requirements and opioid consumption. Dexmedetomidine has characteristics suggesting it may substitute for intraoperative remifentanil during general anaesthesia, but existing literature has reported conflicting results. We undertook this meta-analysis to investigate whether general anesthesia including dexmedetomidine would result in less postoperative pain than general anesthesia including remifentanil.

Materials
The MEDLINE and PUBMED electronic databases were queried up to June 2018. Only trials including patients receiving general anaesthesia and comparing dexmedetomidine with remifentanil administration were included. Meta-analyses were performed mostly employing a random-effects model.
The primary outcome was pain score at rest (analogue scale, 0-10) at 2 postoperative hours. Secondary outcomes included pain score at rest at 24 postoperative hours, opioid consumption at 2 and 24 postoperative hours and rates of hypotension, bradycardia, shivering and PONV.
Results: Twenty-one controlled trials, including 1309 patients, were identified. Pain scores at rest at 2 postoperative hours were lower in the dexmedetomidine group (mean difference [95%CI]: -0.7[-1.2;-0.2];I2 = 85%; p = 0.004; quality of evidence: moderate). Secondary pain outcomes were also significantly lower in the dexmedetomidine group. Rates of hypotension, shivering and PONV were at least twice as frequent in patients who received remifentanil. Time to analgesia request was longer and use of postoperative morphine and rescue analgesia was less with dexmedetomidine, while episodes of bradycardia were similar between groups.

Conclusions
There is moderate evidence that intraoperative dexmedetomidine during general anaesthesia reduces pain outcomes during the first 24 postoperative hours, when compared to remifentanil, with fewer episodes of hypotension, shivering and PONV.

FC 4

Obesity paradox and perioperative myocardial injury in non-cardiac surgery

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Background
The impact of obesity on mortality was shown to exhibit a paradox behavior with increased BMI being associated with better survival. The impact of obesity on the incidence of perioperative myocardial infarction/injury (PMI) following non-cardiac surgery is incompletely understood. Methods: We performed a prospective diagnostic study enrolling consecutive patients undergoing non-cardiac surgery who had a planned postoperative stay of ≥24 hours and were considered to be at increased cardiovascular risk. High risk patients were defined as patients older than 65 years old OR older than 45 years old and a history of coronary artery disease, cerebrovascular disease or peripheral artery disease. Screening is performed in patients undergoing elective, urgent or emergency visceral, orthopedics, traumatology, urology, thoracic, and vascular surgery. All patients were screened using serial measurements of high-sensitivity cardiac troponin T (hs-cTnT). PMI was defined as an absolute hs-cTnT increase of ≥14 ng/L from preoperative to postoperative measurements. Body-mass-index (BMI) was classified according to WHO classification (underweight BMI <18kg/m2, normal weight 18 – 24.9 kg/m2, overweight 25-29.9 kg/m2, obesity class I 30-34.9 kg/m2, obesity class II 35-39.9 kg/m2, obesity class III >40kg/m2). The primary endpoint was the incidence of PMI according to BMI. The secondary objective was mortality within 365-days according to BMI category.Results: We enrolled 4277 patients undergoing 5413 surgeries. The median BMI was 26 kg/m2 (IQR 23 - 30 kg/m2). The incidence of PMI showed a non-linear relationship with BMI and ranged from 12% (95% CI 9 – 14%) in the obesity class I to 19% (95% CI 17- 42%) in the underweight group. This was confirmed in multivariable analysis with obesity class I group showing the lowest risk (adjusted OR 0.64; 95% CI 0.49 – 0.83) for developing a PMI whereas other BMI Groups did not show significant differences. Mortality at one year was paradoxically lower in all obesity groups compared to patients with normal body weight. Moreover, there seems to be a protective impact of obesity for cardiovascular death. Conclusions: Obesity does not seem to be associated with a lower incidence of PMI, but seems to impact on mortality.

FC 5

Factors associated with patient willingness to participate in anaesthesia clinical trials: a cross-sectionnal study

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Background and Goal of Study
Clinical trials are essential to improve knowledge of anaesthesia and perioperative medicine. Unfortunately, many studies face participant-recruitment issues and fail to include the planned number of participants. There is limited published data about how information delivered about the study or how the experiences and attitudes of prospective participants influence willingness to participate. The purpose of this study was to identify such factors in the domain of anaesthesia care.

Materials and Methods
We performed a cross-sectional study on a sample of discharged adult inpatients admitted to a tertiary university hospital. Using questionnaires, we explored a variety of factors likely to influence willingness to participate such as patient personal factors (current health, past exposure to clinical research and anaesthesia), attitudes towards clinical research and study-related factors. Six different scenarios of anesthesia trials were assessed. Univariate and multivariate analyses were performed on questionnaires' answers. Linear regression modeling was used to assess the specific association between personal and study-related factors and willingness to participate in the studies described in the scenarios.

Results and Discussion
1318 participants having received questionnaire were eligible. Of these, 398 returned their questionnaire fully completed. Multivariable adjustment revealed that factors related to altruistic values (β, 9.6, 95% CI 3.4 to 15.7, P = 0.002), to the feeling of benefiting from a more effective treatment (β, 4.7, 95% CI 0.2 to 9.2, P = 0.041) and to the absence of fear about double blinding (β, 5.7, 95% CI 1.3 to 10.2, P = 0.012) were positively associated with willingness to participate. Conversely, concerns about drug-related adverse effects (β, –11.7, 95% CI –16.9 to –6.5, P <0.001) and anxiety about surgery (β, -5.2, 95% CI –10.0 to –0.5, P = 0.031) were negatively associated with willingness to participate.

Conclusion(s)
The understanding of factors that act as incentives or barriers to participation in anesthesia clinical trials is likely to improve patient participation by providing appropriate information and reassuring patients.

FC 6

Persistent postoperative opioid use in a Swiss university hospital: do we have to worry about an "opioid epidemic" in Switzerland?

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Worldwide use of prescription opioid analgesics is increasing (1), and this does include Switzerland (2). The rising number of drug overdose deaths in the US has triggered warnings also in Europe, and alarming figures on persistent opioid use after surgery have been published (1), suggesting a link between this and the "opioid epidemic".
In Switzerland, no data on persistent opioid use after surgery are available. Therefore, we analysed data of an ongoing study on persistent postoperative pain to answer the following questions:
How many patients use opioid analgesics 6 and 12 months after a surgery, and how many of those did not use opioids before surgery? Which type of surgery is at risk for persistent opioid use?

Methods
We used data of all patients participating in a prospective observational trial (BASEC Nr 2016-02111) with completed follow-up at 6 months. Inclusion criteria: adults having elective surgery associated with high risk of chronic post-surgical pain: total knee arthroplasty (TKA), spine surgery, thoracotomy /-scopy, sternotomy, herniorrhaphy, laparotomy, and breast surgery. Information on preoperative opioid use was collected from preanesthetic consultations, and patients were contacted by email or telephone at 6 and 12 months to inquire about persistent pain and analgesic use.

Results
Data on opioid use were available for 170 of 233 patients (73%) at 6 months and for 88 of 150 patients (59%) at 12 months. At 6 months 11 (7,1%) of the 170 patients were taking opioids. Only 1 of these 11 patients did not take opioids before the surgery. 9 of the 11 patients had spine surgery, and 2 a TKA. At 12 months, 4 (5,7%) of 88 patients were still taking opioids, and all 4 did already use opioids before surgery.

Discussion
Spine surgery and TKA are surgeries at risk for persistent opioid use. However, in our cohort almost all patients with persistent postoperative opioid use were already taking opioids preoperatively. The rate of new persistent opioid use at 6 months in our data is 1/170 (0.5%).
In comparison, the rate of new persistent opioid use after surgery in the US is >6% (3). In the US the problem exists even after minor surgery (3), whereas in our study persistent opioid use was limited to spine and major knee surgery among the types of surgery included.

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(3) Brummett CM et al: JAMA Surg 2017: e170504

FC 7

Pain Response to Open Label Placebo in Induced Acute Pain in Healthy Adult Males

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Background
Open label placebos (OLP) plus patient education are demonstratively effective in reducing chronic pain, and recent studies on their effect on pain have established interest in this field. Nevertheless, data on their effect on acute pain are scarce, and on hyperalgesia and allodynia, absent.
This study assessed the effect of OLP on acute pain in healthy adult males and the influence of placebo education.

Methods
Thirty-two healthy males were included in this prospective, randomized assessor-blinded crossover, single center study assessing pain intensities, hyperalgesia and allodynia upon intracutaneous electrical stimulation. We compared the effect of intravenous OLP on pain compared to no treatment. Further comparisons were the effect of OLP on hyperalgesia and allodynia, and the influence of education (short vs. detailed) prior to placebo application. Saliva cortisol was also assessed.

Results
Median pain levels (expressed as interquartile range) were 21% lower during OLP compared to no treatment, 4.04 (3.18 to 4.96) vs. 5.07 (4.66 to 5.36), respectively. Both, hyperalgesia and allodynia (expressed as area in cm2) were lower during OLP treatment compared to no treatment. Hyperalgesia: 29.54 (17.10 to 47.49) vs. 55.26 (41.88 to 68.44); allodynia: 24.04 (11.02 to 38.82) vs. 45.27 (31.32 to 61.68). This corresponds to reductions of 47%. All differences were significant ($p < 0.05$). The extent of placebo education had no effect on pain. Saliva cortisol was not influenced by placebo, nor cortisol influenced placebo-effect.

Conclusion
OLP reduces acute pain, hyperalgesia, and allodynia in healthy adult males. Short education is sufficient for an effect.

FC 8

Dislocation rates of catheters placed either parallel or perpendicular to the femoral nerve

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Background
Femoral nerve catheters (FNC) provide excellent analgesia after major knee surgery and ultrasound provides high success rates of FNC placement near the nerve. However, catheter displacement with unsatisfactory pain therapy is frequent in the postoperative period. A catheter placement parallel to the femoral nerve resulted in fewer dislocations compared to a placement perpendicular to the femoral nerve in a volunteer study. We designed this study to assess this finding in the clinical setting.

Methods
After approval by the Ethical Committee and written informed consent, eighty ASA I-III patients with BMI <40kg/m2 scheduled for major knee surgery were randomly allocated in one of the two studies group where the FNC was placed under ultrasound guidance and neurostimulation control: GroupIP where the FNC was placed perpendicular to the nerve, or in the GroupOOP where the FNC was placed parallel to the femoral nerve. For GroupIP the short-axis in-plane view was used. For GroupOOP the short-axis out-of-plane view was used but with the modification of rotating the transducer to the long-axis in-plane view for proper catheter placement. In both groups the catheter-over-the-needle technique was used, followed by subcutaneous tunneling. Usual active and passive mobilization protocols were allowed postoperatively. The primary outcome was the dislocation rate at 24 and 48h postoperatively; secondary outcomes were time to place the catheter, difficulty threading the catheter, pain scores and sympathetic blockade at 24 and 48h postoperatively.

Results
(Preliminary results, study ongoing) There were no block failures and correct position of the catheters could be confirmed in all patients. Considering dislocation rates, no difference between the two techniques was noted at 24 or 48 hours. Also pain scores and sympathetic block did not differ between the two groups. However, GroupOOP required more time for block performance. Moreover, this group showed a tendency for the catheter to be placed intramuscularly (iliopsoas muscle), in which case the catheter had to be pulled back.

Conclusion
Placement of the FNC parallel to the nerve does not seem to prevent catheter dislocation. Moreover, this technique needs longer performance time and seems to be technically more demanding.

FC 9

Chronic postsurgical pain, pain-related interference and use of analgesics six months after surgery

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Introduction
The ICD-11 definition of chronic postsurgical pain emphasizes that pain should have a significant impact on pain-related functional interference with its physical and affective domains. This has rarely been investigated in the past.

Methods
Patients undergoing visceral, orthopedic, gynecologic surgery or neurosurgical back surgery were enrolled in the international registry PAIN OUT.1 They completed the validated pain outcome questionnaire on the first postoperative day and the Brief Pain Inventory (BPI) as well as the DN4 (douleur neuropathique en 4 questions) six-months after surgery.2,3 Patients' pain-related interference with daily living, encompassing pain, physical and affective interference was calculated as PITS (Pain Interference Total Score). According to their PITS (NRS 0-10) patients were allocated to one of four groups: no interference (PITS = 0), mild (PITS 1-2), moderate (PITS 3-5), severe interference (PITS ≥6). A DN4 score ≥3 was assessed as presence of neuropathic symptoms. The need for analgesics to treat chronic postsurgical pain was evaluated. Approval of the local ethics committee; patients' written informed consent. Statistics: median (IQR); ordinal regression analysis (OR [95% CI]).

Results
Of 2054 patients, 59.5%, 22.0%, 13.2% and 5.3% suffered from no, mild, moderate or severe pain-related functional interference. Physical interference was more pronounced than affective interference. Pain scores were 0 (0/0), 1 (0/2), 3 (2/4) and 5 (3/6) in the four groups ($p < 0.001$). Analgesics were used by 2.7%, 17.0%, 63.8% and 76.9% with WHO-III taken by 0.3%, 0.8%, 5.8% and 18.8% of the patients allocated to the PITS groups. Preoperative use of analgesics was frequent specifically in patients undergoing orthopedic (7%) or back surgery (15%). A positive DN4 was reported by 1.6%, 21.4%, 39.4% and 58.3% of the patients ($p < 0.001$). Risk for a higher PITS group increased by 29% (OR 1.3 [1.12-1.45]) in patients with positive, compared to negative DN4, and by 190% (OR 2.9 [2.7-3.2] if average pain was ≥3.

Conclusions
The BPI provides meaningful information on pain-related functional outcome, which was significantly impaired in 18.5% of the patients six months after surgery. High pain scores were not always associated with high PITS. Neuropathic symptoms were associated with increased PITS.

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FC 10

Respiratory complications after interscalene brachial plexus block versus a shoulder block: a randomized, controlled, single-blinded trial

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Background and Aims
Interscalene brachial plexus (IS) block is associated with an 80-to-100% rate of hemidiaphragmatic paresis. A combined block of the suprascapular and axillary nerves, also called shoulder block, is an analgesic alternative; however, the respiratory complications associated with this block have never been investigated. This randomised controlled single-blinded trial tested the hypothesis that a shoulder block would result in less respiratory complications, when compared with an IS block, while providing similar analgesia.

Methods
Thirty ASA I-II patients scheduled for elective shoulder arthroscopy under general anaesthesia were randomly allocated to an IS block or a

shoulder block using a 20ml-volume of local anaesthetics administered under ultrasound-guidance. The primary outcome was rate of hemidiaphragmatic paresis (diaphragmatic excursion reduction>75%), measured by M-mode ultrasonography, before and 30 min after the procedure. Secondary outcomes were functional respiratory outcomes measured with a bedside spirometry, along with duration of analgesia and pain scores.

Results
Demographic data were similar between groups. Rates of hemidiaphragmatic paresis were 80% (95%CI: 52-96%) and 13% (95%CI: 2-40%) in the IS and shoulder groups, respectively (p <001). Functional respiratory outcomes were significantly better preserved in the shoulder group. Pain scores were reduced in the IS group at 2 postoperative hours but increased at 24 hours, when compared with the other group, while morphine consumption was equivalent.

Conclusions
A shoulder block reduces rate of hemidiaphragmatic paresis, with less impact on respiratory function. Differences in pain scores during the course of the study may probably be the result of rebound pain.

FC 11

International Multicenter Cohort Study for the External Validation of ClassIntra® – Classification of Intraoperative Adverse Events

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Background
Intraoperative adverse events are of immediate concern to patients, anaesthesiologists and surgeons, but prospectively validated systems for their reporting are lacking. ClassIntra® is a newly developed classification of intraoperative adverse events, which was derived from the CLASSification of Intraoperative Complications - CLASSIC. ClassIntra® defines an intraoperative adverse event as any anaesthesia - or surgery-related deviation from the ideal intraoperative course between skin incision and skin closure. The events are graded using 5 severity grades depending on the need for treatment and the severity of symptoms. This international multicentre prospective cohort study aimed to externally validate ClassIntra®.

Methods
In a random sample of in-hospital patients from any surgical disciplines, the anaesthesia and surgical team assessed all intraoperative adverse events according to ClassIntra® . All postoperative complications were assessed daily until hospital discharge using the Clavien-Dindo classification. The primary endpoint was the risk-adjusted association between the most severe intra- and postoperative complication assessed in a hierarchical multivariable proportional odds model. Additionally, interrater reliability and practicability was evaluated in a survey including 10 fictitious cases describing intraoperative adverse events.

Results
Of 2520 enrolled patients from 18 centres in 12 countries, 610 (24%) experienced at least one intraoperative and 838 patients (33%) at least one postoperative event. Multivariable analysis showed a gradual increase in risk for a more severe postoperative complication with increasing grades of ClassIntra® (OR (95%CI) for ClassIntra® I vs 0: 0.98 (0.69, 1.40); II vs 0: 1.45 (1.00, 2.10); III vs 0: 2.63 (1.39, 4.97); and IV vs 0: 3.62 (1.27, 10.35)). The survey (response rate 83%) showed an intraclass correlation coefficient of 0.76 (95% CI 0.59, 0.91) and a practicability of 6 out of 9 (IQR 5-7).

Conclusions
Severity of intraoperative adverse events according to ClassIntra® is strongly associated with postoperative complications. ClassIntra® therefore provides a simple, validated, standardised and reliable tool to report intraoperative adverse events in daily clinical practice and research. Moreover, it is applicable in all surgical disciplines and in anaesthesia.

FC 12

Raising blood pressure in major noncardiac surgery does not reduce major adverse cardiovascular events – preliminary results from the BBB Study (Biomarkers, Blood Pressure, BIS) [NCT02533128]

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Background
Major adverse cardiovascular events (MACE) are a leading cause of perioperative mortality following major noncardiac surgery. Intraoperative hypotension has been shown to be associated with both short and long-term morbidity and mortality.1Whether this association is of a causal nature and whether haemodynamic intervention may help prevent MACE remains unclear.

Methods
In this single-center, randomized controlled trial 451patients at cardiovascular risk undergoing major noncardiac surgery were randomized to either liberal (mean arterial pressure [MAP] at discretion of the anaesthestist, ≥60 mmHg) or tight intraoperative BP management (MAP ≥75 mmHg) with haemodynamic management guided by an institutional algorithm. The primary endpoint was a composite outcome of relevant postoperative high-sensitivity cardiac troponin I elevation (> 40 ng/l with relative increase ≥35% on postoperative days 0-3 compared to preoperatively) and MACE at 30 days.

Findings
Between 2015 and 2019 we randomized 451 patients, 225 to tight, 226 to liberal BP management. Gender (82% male), history of peripheral artery disease (45%), stroke (8%) or congestive heart failure (1%); number of Lee criteria (16% ≥3); mean age (69) and preoperative BNP (99 ng/l) was similar between the groups, however, prevalence of coronary artery disease was higher in the tight (49%) vs the liberal group (37%). The patients underwent the following procedures: vascular (67%), abdominal (12)%, urological (10%), thoracic (6%) orthopedic (3%) miscellaneous (2%). The mean intraoperative MAP was higher in the tight (81 [IQR 73 to 86] mmHg) vs. the liberal group (78 [69 to 84] mmHg; p <0.0001). The mean area under threshold below a MAP of 75 mmHg was significantly lower in the tight BP group. The primary endpoint was reached in 104 patients (46 tight [20%], 58 liberal BP [26%]) management) (p = 0.23, Chi-Square).

Interpretation
Tight BP management did not significantly reduce the incidence of relevant troponin elevation or major adverse cardiovascular events compared to liberal BP management. Further planned subgroup analyses will

reveal if specific patient groups may have profited from tight BP management. Future studies will need to elucidate the role of individualization of perioperative hemodynamic management.

References
1 Wesselink EM, et al. Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. British Journal of Anaesthesia2018.

FC 13

Prediction of long-term quality of life after severe traumatic brain injury based on variables at hospital admission

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Objectives
Early variables after severe traumatic brain injury (sTBI) could predict health-related quality of life (HRQoL). The aim was to investigate the rate of patients with a low or impaired HRQoL 4 years after sTBI and to develop a prediction model with early variables.

Methods
Adult patients with sTBI [abbreviated injury score of the head region (HAIS) >3] and an assessment with the disease-specific HRQoL instrument 'Quality of Life after Brain Injury' (QOLIBRI) were included. The outcome was the total score (TS) of QOLIBRI; cut-off for low or impaired HRQoL: <60 points. A multivariate logistic regression model and prediction model were performed.

Results
One hundred-sixteen patients [median age 50.8 years (IQR 25.9-62.8; 21.6% >65 years)] were included; 68 had a HAIS of 4 (58.6%), 48 (41.4%) a HAIS of 5. Median GCS was 13 (IQR 3-15). The median TS was 77 (IQR 60 – 88); low or impaired HRQoL was observed in 28 patients (24.1%). Two variables were associated with low or impaired HRQoL: GCS <13, working situation other than employed or retired. The prediction model had an AUROC of 0.765; calibration was moderate (Hosmer Lemeshow Chi2 6.82, p = 0.556).

Conclusion
A quarter of patients had a low or impaired HRQoL after 4 years; lower GCS and working situations were associated with low or impaired HRQoL. The model performance to predict long-term HRQoL based on early clinical variables was modest.

FC 14

Effect of ivabradine on major adverse cardiovascular events and mortality in critically ill patients: a systematic review and meta-analyses of randomized controlled trials with trial sequential analyses

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Purpose
Ivabradine is a bradycardic drug without effect on contractility or vascular tone, authorised for heart rate (HR) control in chronic heart diseases. We examined whether ivabradine could decrease major cardiovascular events (MACE) and mortality and in critically-ill patients.
Methods: We searched electronic databases for RCTs. Trial quality was assessed using the Cochrane risk of bias tool. Random-effects meta-analyses were performed if at least 3 trials or 100 patients were available. Results are reported as Weighted Mean Difference (WMD), Odds Ratio (OR), and 95% Confidence Intervals (CI). Trial sequential analyses (TSA) were performed to estimate the sample size needed to reach definitive conclusions of efficacy or futility.

Results
We included 12 RCTs (n = 1452 patients). Compared to placebo or standard care, ivabradine reduced HR (9 RCTs, 1005 patients; WMD -9.6 bpm, 95%CI [-13.7 to -5.5]). Ivabradine had no effect on MACE (3 RCTs, 819 patients; OR 0.77, 95%CI [0.53 to 1.11]) or mortality (9 RCT, 1311 patients; OR 1.13, 95%CI [0.65 to 1.95]). Sample sizes were not reached to allow definitive conclusion on both outcomes. Ivabradine was not associated with a significant risk of atrial fibrillation (3 RCTs, 315 patients; OR 3.12, 95%CI [0.63 to 15.45]). Effect on bradycardia was not established (5 RCTs, 434 patients; OR 1.2, 95%CI [0.60 to 2.38]). Risk of bias was overall high or unclear.

Conclusions
Ivabradine reduces HR, without increasing atrial fibrillation. The effect on MACE or mortality in acute care remains unclear. Further RCTs powered to detect changes in clinically relevant outcomes are warranted.

Registration
Prospero CRD42018086109.

FC 15

Does oxycarbon improve cerebral oxygenation during apnea? A mono-center randomized cross-over trial inspired by aviation-research

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Background
Several projects in aviation and high-altitude research have demonstrated improved cerebral perfusion, performance, and oxygenation by adding CO_2 in hypobaric hypoxia [1]. Hypoxia is of concern also in anesthesia, especially in patients with a decreased oxygen reserve.
This study aimed to test whether 5% CO_2 in O_2 increases the time until significant cerebral hypoxia was detected by near-infrared spectroscopy (NIRS) in bariatric patients under normobaric conditions.

Methods
After ethical approval, patients (18-65 years), BMI >35kg/m2requiring anesthesia for bariatric surgery at the University Hospital Zurich were included in this mono-centric, single-blinded, controlled, crossover proof-of-concept study.
According to the randomization, patients received first oxycarbon (5%CO_2, 95%O_2) or the comparator (95%O_2). After a wash in of 10 minutes, apnea was performed by disconnecting the ventilator from the endotracheal tube until NIRS value dropped by 20% from baseline, or until SpO_2 decreased to 80% (as a safety termination criterion). Reventilation was then performed until parameters returned to baseline. With the crossover design, the procedure was repeated with the other substance (oxycarbon or comparator). During apnea, NIRS, vital signs, and bispectral index were recorded permanently, blood samples were drawn at the beginning and the end of the apnea.

Results
Based on the power calculation, 30 patients were enrolled. Tissue oxygenation drop by 20% was not reached in this patient population, as the safety termination criterion was reached first. The time until oxygen saturation dropped to 80% was similar after both interventions (mean difference -6s [95%CI from -19 to 7] p = 0.37), but both cerebral tissue oxygenation index and PaO_2 were higher after oxycarbon administration (difference of 1.46% [95% CI: from 0,33 to 2.59], p = 0.018, and 0.6 kPa [95 CI: 0.12 to 1.09], p = 0.021, respectively).

Conclusion
This study demonstrates improved blood and cerebral tissue oxygenation upon oxycarbon administration. The possible link to a clinical scenario for improvement of cerebral oxygenation has to be investigated in future trials.

Reference
Imray CH et al, Clin Sci (Lond) 2003

FC 16

Prediction of mortality in adult patients with sepsis, using six novel biomarkers: a systematic review and meta-analysis

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Introduction
Sepsis requires rapid recognition and urgent treatment. But at the same time, the use of biomarkers to help identify patients with a high risk of mortality is appealing. The aim of our systematic review and meta-analysis was to assess the prognostic value of angiopoietin-1 (Ang-1) and 2 (Ang-2), high mobility group box 1 (HMGB1), soluble receptor for advanced glycation endproducts (sRAGE), soluble triggering receptor expressed on myeloid cells 1 (sTREM1), and soluble urokinase-type plasminogen activator receptor (suPAR) for all-cause mortality in adult patients with sepsis.

Methods
The systematic review focused exclusively on observational studies of adult patients with sepsis, any randomized trials were excluded. For the meta-analysis, only studies which provide biomarker concentrations within 24 h of admission in sepsis survivors and non-survivors were included. For pooling of the results, reported means with standard deviations (SD) were used for calculations. Results are presented as forest plots of pooled mean differences (MD) between non-survivors and survivors with 95% confidence interval for each of the six biomarkers. Studies not included in the quantitative analysis were narratively summarized.

Results
The qualitative analysis was performed with 44 studies of which 28 were part of the meta-analysis. The pooled mean differences in biomarker concentration (non-survivors – survivors), measured at onset of sepsis, are listed as follows:

Ang-1: –2.9 ng/ml (95%CI: –4.1 to –1.7, p <0.01)
Ang-2: 4.9 ng/ml (95%CI: 2.6 to 7.1, p <0.01)
HMGB1: 1.2 ng/ml (95%CI: 0.0 to 2.4, p = 0.05)
sRAGE: 1002.8 pg/ml (95%CI: 628.2 to 1377.3, p <0.01)
sTREM-1: 86.8 pg/ml (95%CI: 2.4 to 171.1, p = 0.04)
suPAR: 5.2 ng/ml (95%CI: 4.5 to 6.0, p <0.01)

ROC analyses for the prediction of mortality according to baseline (≤24 h of admission) biomarker concentration further support the utility of Ang-1, Ang-2, and suPAR, with AUCs of 0.620 to 0.778, 0.632 to 0.960, and 0.670 to 0.788, respectively. The other biomarkers had lower AUCs: 0.570 to 0.610 for HMGB1, and 0.444 to 0.827 for sTREM-1. For sRAGE, we found a single AUC of 0.660.

Conclusion
Ang-1, Ang-2, and suPAR provide beneficial prognostic information about mortality in adult patients with sepsis. The further development of standardized assays and the assessment of their performance when included in panels with other biomarkers may be recommended.

FC 17

Sevoflurane enhances iNOS expression and macrophage phagocytosis in vitro and in a murine model

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Background
It has been shown that sevoflurane decreased mortality in an animal model of sepsis.Through the release of free radicals such as NO and removal of microbes through phagocytosis macrophages are able to kill pathogens and hence play a pivotal role during early stages of sepsis. The aim of this study was to evaluate whether sevoflurane has an effect on the anti-microbial function of macrophages by assessing the expression and activity of inducible NO synthase (iNOS) and phagocytosis of E. coli in vitro as well as in vivo.

Methods
Murine bone marrow-derived macrophages (BMDM) were used to measure the expression of iNOS upon stimulation with lipopolysaccharide (LPS) in the presence and absence of 2% sevoflurane. Bactericidal effects of BMDM were examined by measuring uptake of fluorescently labeled E. coli (fE. Coli) after 8 hours of stimulation with LPS. Extracellular signal-regulated kinase (ERK), a possible sevoflurane-induced iNOS regulator, was determined by Western blot. In vivo, mice were injected intraperitoneally (IP) with LPS, followed by 2 hours of anesthesia with either sevoflurane or ketamine/xylazine. Thirty minutes before animals were sacrificed (20 hours after initial LPS injection), fE. Coli were injected IP. Peritoneal macrophages were collected and the uptake of E. coli, as well as iNOS expression, were determined by flow cytometry. Comparison between two groups was performed by two-tailored student's t-test and for 3 or more groups using one-way ANOVA with Bonferroni'spost hoccomparison.

Results
In vitro, sevoflurane amplified iNOS expression 8 hours after treatment with LPS by 466% compared to BMDMs treated with LPS alone. Uptake of fE. Coli in LPS-stimulated BMDMs increased by 70% in the presence of sevoflurane, and this was blocked in cells treated with pharmacological iNOS inhibitor 1400W. At the level of cellular signaling, pERK/ERK was reduced in the presence of sevoflurane. Additionally, we found that inhibition of ERK phosphorylation, as observed in the presence of sevoflurane, also increased iNOS expression. In vivo experiments showed that sevoflurane enhanced LPS-induced iNOS expression after 20 hours by almost 700%, and that uptake of E. coli increased by 49% compared to LPS-treated animals anesthetized with ketamine/xylazine.

Conclusion
In mice, sevoflurane enhances the bactericidal properties of macrophages, thus bolstering endogenous host-defense via an iNOS and ERK phosphorylation-dependent mechanism.

FC 18

Sevoflurane reduces apoptosis of target cells by natural killer cell inhibition

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Introduction
Natural killer (NK) cells play a significant role in tumor immunosurveillance. They are known to be primarily responsible for the elimination of circulating tumor cells. Different mechanisms in NK cells lead to tumor cell death: degranulation, release of cytokines (balance between pro-apoptotic cytokines IFNg and TNFa and anti-apoptotic IL6), as well as extracellular vesicles (EVs). Anesthesia per se has been hypothesized to interfere with NK cell activity, but previous studies analyzing the effect of sevoflurane on these cells have yielded conflicting results. Thus, this study aimed to determine the role of the volatile anesthetic sevoflurane on NK cell-induced apoptosis of tumor cells.

Methods
In vitro experiments were performed using the cell lines NK92 and K562 as effector and target cells, respectively. For each experiment NK cells were exposed to 2.2% sevoflurane in an airtight chamber (controls in room air) for 2 hours followed by incubation for 1 to 6 or 24 to 48 hours with tumor cells in a 1:1 ratio. Apoptosis in K562 cells was determined using flow cytometry (early, late apoptosis). To define degranulation, release of CD107a, a membrane marker of these granules, was measured. Real-time RT-PCR was performed determining mRNA expression of IFNg, TNFa and IL6. EVs were analyzed using Nanosight. Perforin, a protein involved in the induction of apoptosis, was determined using Western blot. The time course of apoptosis was analyzed by two, comparison of only one time-point by one-way analysis of variance (ANOVA). Multiple comparisons were corrected for by Bonferroni's post hoc test. The PCR, Western blot and Nanosight experiments were analyzed with unpaired t-Tests.

Results
Between 1 and 6 hours, no significant difference of apoptosis of K562 tumor cells between the sevoflurane and air group could be detected. At 24 hours, a significant 10% decrease of early (p = 0.02) and total (p = 0.03) tumor cell apoptosis was observed in the sevoflurane group. No significant difference in degranulation or cytokine release was detected.

Also, no significant difference in the number or size of EVs could be detected, however, perforin content in EVs was decreased in the sevoflurane group.

Conclusion
This in vitro study identified a modest impairment in NK cell activity following exposure of NK cells to 1 MAC sevoflurane. Qualitative changes of the content of EVs may be involved in the mechanism.

FC 19

The new P2Y12 inhibitor cangrelor unreliably inhibits heparin-induced platelet aggregation in the presence of HIT antibodies, an in vitro study

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Introduction
Cardiac surgery in patients with HIT puts the patient at high risk of lethal thrombotic complications if heparin is used during surgery. Two strategies exist to prevent intraoperative platelet aggregation during cardiopulmonary bypass if anti-PF4/heparin antibodies (HIT-Abs) are present. The first is to use an alternative anticoagulant, the second is to use heparin combined with an antiaggregant agent, iloprost or tirofiban. The new P2Y12 inhibitor cangrelor could be an attractive candidate in this setting and several authors report its successful use. In this in vitro study we evaluated the capacity of cangrelor to inhibit platelet aggregation induced by heparin in the presence of HIT-Abs.

Methods
Platelet poor plasma (PPP) from 30 patients with functional HIT-Abs was mixed with platelet rich plasma (PRP) from healthy donors. Heparin-induced platelet aggregation (HIPA) was measured by light transmission aggregometry (LTA) after adding heparin to achieve a final concentration of 0.5 IU ml-1 and compared to samples with normal saline only (negative control) or cangrelor (final concentration 500 ng ml-1) added prior to heparin (treatment).

Results
Heparin 0.5 IU ml-1 triggered platelet aggregation in 22 out of 44 PPP-PRP mixtures, with a median aggregation of 85.9% (IQR 69.2 to 90.9). For these 22 HIPA positive samples, the median aggregation in the corresponding negative control was 22.1% (IQR 15.9 - 29.7) ($p < 0.001$). Median aggregation in the treatment samples was 28.5% (IQR 19.5 to 51.9): significantly lower than in HIPA positive samples ($P < 0.001$) but higher than in negative control samples ($p < 0.05$). The mean percentage of inhibition of HIPA by cangrelor was 73.4 ± 34.0%. In only 10 out of 22 positive samples (45%) cangrelor reduced HIPA by more than 95%. In 5 out of 22 (22%) the inhibition by cangrelor was less than 50%, and in 3 out of 22 (14%) it was less than 10%.

Conclusion
In this in vitro study we found that cangrelor unreliably inhibits heparin-induced platelet aggregation in the presence of HIT-Abs. We conclude that cangrelor cannot be used as a standard antiaggregant agent in combination with heparin for cardiac surgery in HIT patients, unless its efficacy has been confirmed in an aggregation test prior to surgery.

FC 20

The implementation of a ROTEM® sigma-based algorithm for the management of coagulopathic bleeding in a tertiary center

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Introduction
Viscoelastic assays are used for the management of perioperative or traumatic bleeding. Recently, the manufacturer of ROTEM® has introduced the automated sigma model. The change in technology results in new normal ranges and therefore new cutoff values triggering intervention compared to previous published ROTEM® delta cutoff values. Here, we describe the analysis performed to identify new cutoff values and the specific algorithm for the ROTEM® sigma.

Methods
78 samples were obtained from 39 patients with various hemostatic defects and 12 healthy volunteers. Chosen standard laboratory test (SLT) cut-offs were fibrinogen (Fi) <1.5 g/l, platelet count (Pltc) <50 G/l or <100 G/l, prothrombin ratio (PR) <80% and activated partial thromboplastin time (aPTT) >37 sec or 1.5x the normal value. PLTEM was calculated as EXTEMA5 – FIBTEMA5. The clinically critical range (CCR) of SLT was defined as the range around the threshold that leads to treatment. Correlation was sought between SLT and ROTEM parameters. The best cut-off for the different ROTEM parameters to identify the chosen SLT thresholds (ROC analysis) were integrated in a step-by-step algorithm.

Results
Correlation between Fi and FIBTEMA5 was very strong ($r = 0.94$) but was lower in the CCR (0-2.5 g/l) ($r = 0.65$). The correlation between Fi and EXTEMA5 was weakly moderate ($r = 0.42$). PLTEMA5 showed very strong correlation ($r = 0.96$) with Pltc in the CCR (<150 G/L). INTEMCT showed very strong correlation with aPTT ($r = 0.84$). EXTEMCT correlated moderately with PR ($r = -0.58$). Cut-off based on ROC curve analysis for different parameters are showed in Table 1. A FIBTEM A5 ≤12 mm combined to a EXTEM A5 ≤44 mm could detect a Fi <1.5 g/L with a 100% sensitivity and a 77.5% specificity. EXTEM A5 ≤34 mm could detect Pltc <50 G/L with a 90.9% sensitivity and a 87.3% specificity. PLTEM A5 ≤16 mm could detect Pltc <50 G/L with a 100% sensitivity and a 96.4% specificity.

Conclusion
In-house cut-off values of key ROTEM® sigma parameters differ from the published ones for ROTEM® delta. We report the first preliminary ROTEM® sigma-based algorithm for hemorrhage. Diagnostic and therapeutic performances shall be prospectively validated.

POSTERS

P 1

Activation of toll-like receptor signaling influences nociceptin and the nociceptin receptor expression in human NB4 cells

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Introduction
The nociceptin receptor (NOP, also called opioid receptor-like 1) has been described as a target for the treatment of pain or inflammatory diseases.1-3 However, mechanisms contributing to the regulation of the nociceptin system are still not fully revealed up to date. Toll-like receptors are a family of pattern recognition receptors which play a central role in inflammation. Impact of TLR activation on opioid receptors and endogenous opioids have been reported.4,5 The aim of this study was to investigate the effects of TLR signaling on the nociceptin system in human NB4 cells under inflammatory conditions.

Methods
Human promyelocytic leukemia cells NB4 were stimulated with or without different concentrations of phorbol-12-myristate-13-acetate (PMA) for 24 hours. mRNA expression of prepronociceptin (ppNOC), NOP and TLRs (TLR2, TLR4, TLR7, TLR9) was detected by quantitative RT-PCR. Nociceptin, NOP and TLR protein levels in NB4 were determined using flow cytometry. To examine the contribution of TLR signaling to the regulation of nociceptin and NOP, cells were cultured with or without PMA 5 ng/ml and with or without agonists specific for TLR2 (LTA 10 µg/ml), TLR4 (LPS 1 µg/ml), TLR7 (imiquimod 10 µg/ml) or TLR9 (ODN 2216 1 µM).

Results
Nociceptin, NOP and TLRs (TLR2, TLR4, TLR7, TLR9) mRNA were constitutively expressed and corresponding protein levels could be measured in NB4 cells. PMA dose-dependently upregulated ppNOC and NOP mRNA after 24 hours. PMA 5 ng/ml suppressed TLR2 mRNA and increased TLR4, TLR7, TLR9, ppNOC and NOP expression compared to controls (all $p < 0.05$). TLR7 agonist imiquimod prevented PMA's effects on ppNOC and NOP mRNA (both $p < 0.05$). An antagonistic effect on NOP mRNA was observed in the group PMA+ODN 2216 compared to the cells treated with PMA only ($p < 0.05$). As for intracellular nociceptin and cell surface NOP, no changes were observed in NB4 co-stimulated with PMA and different TLR agonists compared to the PMA-treated samples.

Conclusions
Activation of TLR7 and TLR9 signaling influences nociceptin and the nociceptin receptor mRNA expression in NB4 cells under inflammatory conditions. Mechanisms contributing to these effects need to be further elucidated.

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P 2

Regional distribution of lung inflammation in an animal model of multiple-hit ARDS assessed by micro-PET-CT imaging

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Introduction
Mechanical ventilation can incite and worsen lung injury. This feature is particularly relevant in the context of Acute Respiratory Distress Syndrome (ARDS), due to widespread alveolar collapse, which concentrates mechanical stress within both poorly aerated lung due to aletectrauma, and aerated lung regions due to exaggerated stretch. It is not clear how these mechanisms contribute to lung inflammation and worsening injury during prolonged mechanical ventilation. In this experimental work, using an animal model of ARDS, we evaluated the effects of prolonged mechanical ventilation in the lung regional inflammation using micro-PET-CT imaging.

Methods
ARDS was induced in juvenile rabbits (4-5 weeks, n = 9), by combining iv endotoxin (20 µg/kg) and injurious ventilation, followed by 5 hours of protective ventilation (pressure-control, PEEP 6 cm H_2O; Pplateau 20-22 cm H_2O). Subsequently, microCT and PET imaging were performed using the Triumph II Trifoil Imaging system. Lung regions (ROI) were segmented and partitioned based on normalized CT density into Aerated, Poorly-aerated and Collapsed regions. Standardised uptake values (SUV) were calculated. Ventilation and blood gas parameters were recorded.

Results
Moderate ARDS was triggered in all animals (PaO_2/FiO_2 = 226 ± 91 [SD]). ROI volumes were 16.6±3.4; 6.8±1.7; 5.4±1.2 mL in Aerated, Poorly-aerated and Collapsed lung regions, respectively. SUV was significantly higher within collapsed (0.84±0.29, $p < 0.001$), and Poorly-aerated ROI's (0.81±0.27, $p = 0.036$) compared to Aerated (0.77±0.25) lung.

Conclusion
Despite a protective ventilation strategy, significantly higher SUV in Poorly-aerated and Collapsed lung regions suggest that atelectrauma may contribute to lung inflammation. Further study is underway to compare this outcome with healthy lung and with alternative ventilation strategies in ARDS.

Grant
FNRS32003B_169334

P 3

Identifying risk factors for perioperative transfusion in elective hip and knee arthroplasty

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Background
Blood product transfusion is associated with risks and side effects. Identification of factors that may increase the risk of blood product utilization is critical for resource allocation. Objective of this study was to identify transfusion risk factors for elective hip and knee arthroplasty patients.

Methods
This retrospective, observational study was performed in a single non-university teaching hospital in Switzerland with approval of the Ethics Committee East Switzerland (BASEC-nr. 2018-00306). Included were adult patients undergoing elective hip or knee arthroplasty. Main outcome was perioperative transfusion rate.

Results
531 patients were included (95.5% ASA 2 or 3; 321 hip arthroplasties, 210 knee arthroplasties). The transfusion rate for the entire cohort was 8.1%, of which 34 patients underwent hip arthroplasty (10.6%) and nine had knee arthroplasty (4.3%). Age, operation type, and preoperative haemoglobin levels were associated with transfusion. BMI was higher in the patients requiring a transfusion ($p < 0.001$).

Conclusion
When performing either hip or knee arthroplasty, older patients and those with lower preoperative haemoglobin could benefit from additional preventive measures to reduce the likelihood of transfusion. Since these transfusion risk factors differ, risk identification ought to be specific to the institutional setting.

P 4

Validation of the Clinical Frailty Scale (CFS) in French language

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Background
Pre-operative frailty, a state of reduced physiological reserve associated with increased vulnerability to stressors, has been associated with increased morbidity and mortality after surgery. Frailty assessment using tools such as the Clinical Frailty Scale (CFS) should be part of pre-operative assessment of elderly patients. However, after a literature search we were only able to identify the original English (EN) version of the CFS validation, thereby limiting its use by clinicians from other native languages. The use of the EN version or a non-validated translation of the CFS by healthcare personnel can result in different assessments and contribute to biases. Therefore, in order to promote the adequate use of this scale in a wider panel of countries, we aimed to develop, validate and characterise a French (FR) version of the CFS.

Methods
We included 28 patients recruited prospectively for the observational "The very old intensive care patient: A multinational prospective observation study" (VIP Study) in the Intensive Care and Peri-Interventional Intermediate Care Units at Geneva University Hospitals (FR speaking hospital). The study was approved by the Geneva Regional Ethics Committee. A FR version of the CFS was obtained by translation (EN->FR) and back translation (FR->EN). The final CFS-FR was then evaluated twice on the same patients with at least a 2-week interval by FR-speaking doctors and nurses.

Results
Inter-rater reliability was 0.87 (95%CI: 0.76-0.93) between doctors for the original CFS-EN version and 0.76 (95%CI: 0.57-0.87) between nurses for the FR version. Inter-rater variability between doctor and nurse was 0.75 (95%CI: 0.56-0.87) for the original CFS-EN version, and 0.73 (95%CI: 0.52-0.85) for the FR version. Test-retest (stability) with the original vs the FR version was 0.86 (95%CI: 0.72-0.93) for doctors and 0.87 (95%CI: 0.76-0.93) for nurses.
Differences between the evaluations of the CFS-EN and CSF-FR were not different from 0, with a mean difference of 0.06 (95%CI -0.24, 0.36) for the EN version and -0.03 (95%CI -0.47, 0.41) for the FR version. Agreement between the FR and the EN version for doctors was similar. Average original version ratings were slightly lower than FR version ratings, though this difference did not reach significance: -0.29 (95%CI -0.54, 0.04).

Conclusion
The CFS-FR version developed and validated in the present study has adequate psychometric properties for doctors or nurses to evaluate frailty.

P 5

Association between Intraoperative Fentanyl Dosing and Postoperative Nausea and Vomiting and Pain: A Prospective Cohort Study

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Background
Postoperative nausea and/or vomiting (PONV) is one of the anaesthesia-related effects most dreaded by patients and may delay hospital discharge. Although scores and risk factors are established, many were developed prior to contemporary anaesthesia regimens and without focussing on modifiable anaesthesia-related variables.

Objective
To examine whether or not there is an association between intraoperative fentanyl doses and PONV and, secondarily, pain within the first 24 h in a contemporary anaesthesia regimen.

Design
Prospective, observational cohort. As informed consent was waived, neither patients nor treating physicians were aware of the study.

Setting
Single center university hospital.

Patients
Inclusion criteria were opioid-naïve patients with a simplified Apfel score ≥2, undergoing abdominal, gynaecological, or otorhinolaryngological inpatient surgery and without chronic pain.

Intervention
none.

Main outcome measure
We examined three models of increasing complexity exploring PONV and fentanyl dosing by logistic regression (Model 1: simplified Apfel score + intraoperative fentanyl; Model 2: Model 1+ preemptive antiemetic prophylaxis; Model 3: Model 2 + postoperative morphine). Model 1 was the primary analysis. Secondarily, we explored whether or not postoperative pain scores were associated with intraoperative fentanyl dosing.

Results
Of 363 included patients, 163 (45%) experienced PONV, despite over 80% propofol-based anaesthesia maintenance and some 2/3 of patients receiving additional antiemetic agents. After adjusting for the simplified Apfel Score, higher intraoperative fentanyl was associated with PONV (OR per µg.h-1: 1.006 [95% CI 1.002-1.010]). Adding intraoperative fentanyl to the simplified Apfel score also increased the area under the ROC curve (0.601 [95%CI 0.555-0.662] vs. 0.651 [95%CI 0.594-0.707]; P = 0.016). Finally, higher intraoperative fentanyl doses were associated with higher 24 h pain scores (P = 0.001) and trended towards higher 24 h morphine requirements (P = 0.055).

Conclusion
Even when using propofol and other antiemetic agents, PONV rates at 24 h remained higher than expected. Intraoperative fentanyl – a modifiable risk factor–is associated with PONV and pain.

Trial registration
clincialtrials.gov, NCT03201315

P 6

Characteristics of a single- versus multiple-injection axillary brachial plexus block: a randomized, controlled, single-blinded trial

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Background
An ultrasound-guided axillary brachial plexus block can be either performed with a multiple-injection technique (each nerve blocked individually), or a dual-injection technique (an injection for the musculocutaneous nerve and another one for the radial, median, and ulnar nerves). When the arm is in full abduction, the musculocutaneous nerve lies close to the axillary artery and the other nerves. This randomised controlled single-blinded trial tested the hypothesis that a single-injection technique has a reduced procedure time and is as effective as a multiple-injection technique.

Methods
Fifty ASA I-III patients randomly received an ultrasound-guided multiple- or single-injection block with 32 mL of local anaesthetics. In the single injection group, the needle was positioned inferior to the axillary artery, without needle tip repositioning. In the multiple injection group, each nerve was blocked separately. The primary outcome was the performance time. Secondary outcomes included needling time, block success, oxycodone consumption and pain scores.

Results
Demographic data were similar between groups. Success rates were 96% [95%CI: 80%-100%] and 84% [95%CI: 64%-96%] in the multiple- and single-injection groups, respectively (p = 0.16). Mean procedure time was significantly reduced in the single-injection group (5.7 min [95%CI: 5.1-6.4]), when compared with the multiple-injection group (4.0 min [95%CI: 3.6.4.4]; p <0.001). Other block-related outcomes were similar between groups except needling time which was significantly reduced in the single-injection group. Total postoperative oxycodone consumption

was significantly less in the multiple-injection group (6.8 vs 15.4 mg; p = 0.03).

Conclusions
An axillary brachial plexus block performed with a single-injection technique is associated with a reduced time performance but an increased consumption of opioids at 24 postoperative hours.

P 7

The impact of nerve cross section area on sensory block onset time. A prospective, monocentric, crossover study on volunteers

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Background
Ultrasonography allows for a more precise deposition of the local anaesthetic (LA) around the nerve possibly leading to a reduction of the volume of LA needed to perform a peripheral nerve block. This could help reduce the risk for local anaesthetic toxicity (LAST) and increase patient safety according good clinical practice using the smallest dose needed to achieve a successful block.
On healthy volunteers a volume of 0.11 ml/mm^2 of LA was shown to be enough to achieve a complete sensory blockade of the ulnar nerve at the proximal forearm in 95% of the cases. However, the relationship between sensory and motor block onset time and cross-sectional area of a nerve has not yet been elucidated. Therefore, we designed this study to analyze the relationship between sensory and motor block onset time and nerve cross-section area of two peripheral nerves.

Methods
After approval by the Ethical Committee and written informed consent, 15 healthy volunteers were included in this crossover study. Each volunteer received 4 ultrasound-guided nerve blocks in total, two nerve blocks (blocks of the ulnar and median nerves) in the non-dominant forearm and two nerve blocks (blocks of the median and ulnar nerves) in the dominant forearm. As an additional safety measure peripheral nerve stimulator was used. All blocks were performed by experienced consultant anaesthesiologists. The sequence of the nerve block was randomly assigned. The ulnar and median nerves were visualised in the short axis view (transverse plane), nerve cross-section diameter of all nerves was measured, and cross-section area was calculated using ultrasound device`s software. The volume of LA was calculated using 5 times the volume required to achieve a complete sensory blockade (according to formula 5 x 0.11 ml/mm^2). Mepivacaine 1% was used for all nerve blocks. The primary outcome was to examine the correlation between the nerve cross-section areas and their respective sensory block onset times. The secondary outcomes were to examine the correlation between the nerve cross-section area and the respective motor block onset time and duration of nerve block.

Results
(Preliminary results, study ongoing) Regression analysis shows a tendency towards a faster onset of nerve block in nerves with a smaller cross-section area.

Conclusion
A nerve cross-section area-dependent LA administration seems to be feasible leading to a patient-adapted reduction of the amount of LA and potentially increasing patient safety.

P 8

Anesthesia and patients at the end of life. A new challenge? Around 3 cases

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Introduction
Anesthesiologists are increasingly confronted with requests for general anesthesia in end-of-life patients, which implies a limitation of the therapeutic project.

Clinical cases
Three patients with short-term life-threatening conditions in whom healing is no longer a primary objective, and in whom an invasive procedure or an operation requiring general anesthesia is planned. The risks of serious adverse events due to the anesthesia itself are significant.

Discussion
It is possible to see in these procedures a request for a technical intervention responded to with a technical service. Our medical education, supported by the code of deontology, is oriented more to cure diseases than to treat patients seen as a whole. Specializations tend to fragment the patient into various organs, so that medicine loses its bearings. The fear of court judgements leads physicians to practice interventions in order to protect themselves from the accusation of professional negligence. The question is whether or not there is a violation of the rules of art if not all the means available are implemented.
The informed consent and patient's directives constitute one of the basics of medical care. Patient information is an integral part of patients' rights and an obligation for caregivers. Regarding advanced directives, the new adult's protection law allows to anticipate the will of a person incapable of discernment.
The ethics of care represents an approach based more on the care to be given and received and less on technique and healing at any price. In this relationship, the value of shared intentions must be emphasized: the caregiver intends to care, the patient intends to be cared for. For these complex clinical cases, the same anesthesiologist who meets the patient and performs the anesthesia itself must organize a personalized care.

Conclusion
The best patient care lies in the collaborative practices that clarify from several points of view the intentions of each practitioner. The anesthesiologist should be integrated well upstream in the patient care to make the other professionals aware of the risks due to anesthetic management. In this way the fear of prosecution in case of intraoperative death should be reduced since shared and consensual intention is one of the best ways of respecting the rules of art. A case discussed and explored in depth would allow each caregiver to feel comfortable with the risks taken due to procedures in end of life patients.

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