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Clinically relevant concentrations of ropivacaine and lidocaine block epithelial-mesenchymal transition of lung adenocarcinoma cells in vitro

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Background: Increasing evidence suggests the type of anesthesia administered to patients undergoing cancer surgery might influence the outcome [1]. Epithelial-mesenchymal transition (EMT) is crucial during metastasis of solid tumors: cells lose their epithelial character, cell-cell adhesions are loosened, cells are increasingly able to migrate and ultimately leave the epithelial tumor network and form distant metastatic sites. EMT is characterized by a loss of E-cadherin, a transmembrane glycoprotein, and an antipodal increase in vimentin, an intermediate filament expressed by mesenchymal cells [2]. Signaling events leading to EMT depend on activation of Akt kinase (Akt), e.g., by transforming growth factor beta (TGF-β), as well as subsequent phosphorylation/activation of mechanistic target of rapamycin (mTOR), glycogensynthase-kinase-3 beta (GSK3β), Src tyrosine protein kinase (Src) and caveolin-1 (Cav-1) [3]. As we have previously shown that amide local anesthetics are able to block Akt activation [4], we hypothesized lidocaine and ropivacaine might as well attenuate TGFβ-induced EMT.

Methods: NCI-H838 lung cancer cells were either left untreated or incubated with TGFβ (2 ng/ml) for 48 hrs or 1 h in presence or absence of 10 µM lidocaine or 1 µM ropivacaine. Whole cell lysates were subjected to Western blot analysis probing for E-cadherin and fibronectin. In vitro cell proliferation and cell migration were assayed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and a transwell assay. Statistical analysis was performed using two-way ANOVA with Bonferoni correction.

Results: Co-incubation with lidocaine and ropivacaine completely abolished a 51 ± 17% (mean ± SD) loss in E-cadherin and a 120 ± 68% increase in fibronectin. In vitro cell proliferation and cell migration were significantly reduced (20 ng/ml) in absence or presence of ropivacaine at clinically relevant concentrations ranging from 1 nM to 100 µM. Cell proliferation and cell migration were significantly reduced (20 ng/ml) in absence or presence of ropivacaine at clinically relevant concentrations ranging from 1 nM to 100 µM. Cell proliferation and cell migration were significantly reduced (20 ng/ml) in absence or presence of ropivacaine at clinically relevant concentrations ranging from 1 nM to 100 µM.

Conclusions: Clinically relevant concentrations of lidocaine and ropivacaine completely blocked the TGFβ-induced rise in phosphorylation for all proteins (p <0.05 for all respective treatments vs. TGFβ-alone). The current study therefore adds new insight into a potential mechanism by which local anesthetics might be able to attenuate metastasis.

References

Hyperoxia worsens myocardial oxygenation and ventricular function in an animal model with severe coronary artery stenosis

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Background: Current guidelines limit the use of high oxygen tension after return of spontaneous circulation following cardiac arrest. These recommendations are based on neurological outcome and increased mortality, while little is known about the impact of hyperoxia on the ischemic heart. However, oxygen is frequently administered and is generally expected to be beneficial. High oxygen tensions are also usually present during general anaesthesia. This study assesses effects of hyperoxia on coronary blood flow and myocardial strain in swine with a coronary artery stenosis.

Methods: In 22 swine, a blood flow probe was attached to the left descending coronary artery (LAD) after left-sided thoracotomy, and in 11 of these animals an LAD stenosis was induced. Arterial blood gases were targeted to a baseline with a PaO2 of 100 mm Hg and a PaCO2 of 35 ± 5%. Three hyperoxia levels were reached with a PaO2 of 300 mm Hg or a PaCO2 of 30, 40, or 50 mm Hg. At each level, coronary blood flow was measured and the entire heart was imaged with a magnetic resonance cine sequence at 3 Tesla from which left ventricular ejection fraction (EF) and myocardial peak circumferential strain were measured. Swine was assessed for global and regional changes of the LAD perfused myocardium and remote tissue. All observations at hyperoxia were compared to the normoxic baseline.

Results: Control animals, hypo- and normocapnic hyperoxia decreased blood flow by 12.7 ± 2.3 and 13.3 ± 5% (p <0.01), while hypercapnia neutralized this effect (+2.20 ± 5.5%, n.s.). In stenosed animals, all levels reduced flow by 13.1 ± 5.1 to 24.0 ± 4.5% (p <0.05). For myocardial strain, no changes were observed in the control group, and at normoxia, stenosed animals did not differ from the controls. After increase in oxygen tension, the stenosed animals showed a significant strain reduction in the LAD territory (fig.). This was seen for all PaO2 levels. For ventricular function in the stenosed group, hyperoxia decreased EF to <42 ± 6% from the baseline level (48 ± 3%, p <0.05), and no changes were observed in the controls (49–56%).

Conclusion: In the presence of severe coronary artery stenosis, hyperoxia reduces coronary blood flow, ventricular function and myocardial strain in an animal model. Further research is required and current clinical practice may have to be revised as our results indicate that hyperoxia may exacerbate myocardial ischemia.
Sevoflurane improves the cohesion of brain endothelial cells after hypoxia

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Introduction: Sevoflurane is a volatile anesthetic which has been shown to reduce brain injury and cerebral infarct size after ischemia, impacting on the blood brain barrier (BBB) [1]. The grade of brain independent predictor of unfavorable outcome for patients after brain surgery. Sevoflurane is a volatile anesthetic which has been shown to positively impact on impaired endothelial barrier function. A possible mechanism might be stabilization of junction proteins in the cellular membrane under the influence of sevoflurane during reoxygenation.

Methods: RBE4 cells were exposed for 24 hours to hypoxia 0.2% O2, followed by a 4 hour reoxygenation with 21% O2 with or without 2.2% sevoflurane. Cellular DNA content was measured. In order to assess permeability of the monolayer, RBE4 cells were cultured in Boyden chambers for 2–3 days and permeation of 40kD FITC dextran was determined. Immunostaining for ZO-1 and beta-Catenin was performed to identify tight and adherence junctions. One way ANOVA performed to identify tight and adherence junction components were shown to be better maintained in the cellular membrane under the influence of sevoflurane during reoxygenation.

Discussion: These data provide evidence for the first time that sevoflurane positively impacts on impaired endothelial barrier function. A possible mechanism might be stabilization of junction proteins through sevoflurane. Further studies are needed to test the effects of sevoflurane on the blood brain barrier in vivo.

References

The primary sevoflurane metabolite hexafluoro-2-propanol attenuates hypoxia/reoxygenation injury in cardiomyocytes in vitro

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Introduction: Recent publications have shown that the primary sevoflurane metabolite hexafluoro-2-propanol (HFIP), a water-soluble substance, beneficially modulates inflammation in experimental sepsis [1, 2]. So far it is unknown whether HFIP also positively impacts in situations of ischemia/reperfusion injury similar to sevoflurane. In this study, we therefore evaluated the effects of HFIP and sevoflurane on cardiomyocytes in a hypoxia/reoxygenation (H/R) injury model.

Methods: Murine cardiomyocytes were cultured and exposed to hypoxia (9.2% O2) for 6 h (cells grown under normoxic conditions served as a control). During reoxygenation (2 h), cells were exposed to room air, HFIP (4 mM), or sevoflurane (2.2 Vol%). Cytotoxicity was monitored measuring lactate dehydrogenase (LDH) release. Caspase-3/7 and 8 activity as a representative apoptosis marker, was determined using a selective fluorogenic caspase substrate. Intracellular formation of reactive oxygen species (ROS) was detected by oxidation of 2’,7’-dichlorofluorescein-diacetate (DCF-DA) to the DCF. Cell viability and NADPH oxidase-related metabolic activity were measured in MTT assays. Linear mixed models were used for analyzing the data. \( p < 0.05 \) was considered significant.

Results: Hypoxia/reoxygenation (H/R) provoked increased LDH release of cardiomyocytes by 72% \( (p < 0.001) \), an 18% rise in caspase activity \( (p < 0.001) \), and 38% elevated formation of intracellular ROS \( (p < 0.001) \). MTT was attenuated by 11% \( (p = 0.006) \), HFIP or sevoflurane reduced H/R-induced LDH release by 52% and 42%, both \( p < 0.01 \). An attenuation of the rise in caspase activity and intracellular ROS formation was observed with HFIP or sevoflurane \( (p < 0.001) \). Lowered MTT levels almost regained levels of control values by sevoflurane \( (p = 0.514) \), but not by HFIP treatment.

Conclusion: The results suggest that a treatment with HFIP attenuates H/R-induced damage in cardiomyocytes – an effect, which is comparable to the effects sevoflurane in H/R injury. The protection might be mediated through an attenuation of intracellular ROS formation. HFIP might therefore be a promising intravenously applicable protective drug molecule in procedures such as percutaneous coronary revascularization in the near future.

References

Chronic postsurgical pain: risk factors and characteristics

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Background: Severe chronic post-surgical pain (CPS/P) resulting in clinically relevant functional impairment is reported by 5–10% of the patients [1, 2]. It is considered as an iatrogenic chronic pain, thus, identification of mechanisms and risk factors are pivotal to develop strategies to prevent CPS/P [1].

Methods: Prospective observational trial in 21 hospitals of 11 European countries, with 833 Swiss hospitals participating [3]. After ethics approval and informed consent patients undergoing elective surgery were enrolled in the registry PAIN OUT [4]. Outcome was evaluated on the first postoperative day (D1) using a validated questionnaire. Follow-ups at 6 and 12 month via email or telematic telephone interview used the Brief Pain Inventory (BPI) and the DN4 (Douleur Neuropathique en 4 questions). Primary endpoint: incidence of at least moderate CPS/P (NRS 3) at M12; secondary endpoints: role of neuropathic pain, risk factors for CPS/P.

Statistics: Univariate analysis, multivariate logistic regression analysis; Hosmer-Lemeshow test; Odds Ratios (OR/95%–CI).

Results: Complete data of 494 and 889 patients could be analysed after 6 and 12 months. One year after surgery 9.6% (7.7–11.7) complained of moderate (NRS 3-5), 2.2% (1.2–3.3) of severe CPS/P.
Intrathecal hyperbaric prilocaine 2% versus plain ropivacaine 0.4% for same day arthroscopic knee surgery: A prospective, randomized, double-blind, controlled study

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Background: Short duration spinal anesthesia is a good alternative for ambulatory day case surgery: Hyperbaric prilocaine 2% has a short onset time and a rapid recovery, and may therefore be well suited in this setting. Our primary objective was to determine the times to reach motor block, resolution, and discharge from the PACU, between hyperbaric prilocaine 2% and plain ropivacaine 0.4%.

Methods: In a prospective, randomized and double-blind design, 140 18–80 year old ASA I-II patients, scheduled for elective, unilateral, arthroscopic knee surgery lasting less than 45 min, were allocated to either the prilocaine 2% (60 mg/3 ml) or the plain ropivacaine 0.4% (12 mg/3 ml) group. Exclusion criteria were contraindications for spinal anesthesia, pregnancy, and known allergy to the study drugs.

Results: Complete recovery of motor block was faster in the prilocaine 2% group: 195 ± 67 vs 225 ± 81 min. Time to reach discharge criteria was similar in both groups: 334 ± 55 and 346 ± 73 min for prilocaine 2% and ropivacaine 0.4%, respectively. The incidence of side effects was low and similar in both groups. No case of transient neurologic symptoms occurred in either group.

Conclusions: Recovery of motor block was faster after intrathecal application of hyperbaric prilocaine 2% compared to plain ropivacaine 0.4%. However, discharge time was similar. Both drugs showed a similar risk profile.

Tramadol pharmacokinetics and genetic variants of the Organic Cation Transporter OCT1

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Background: Genetic variants in the metabolizing enzyme CYP2D6 (cytochrome P450 2D6) are well known to affect pharmacokinetics and efficacy of tramadol. Recently, also genetic polymorphisms in the liver organic cation transporter OCT1 (solute carrier family 22 member 2 member; SLC22A1) were shown to affect plasma concentration of (+) O-desmethyltramadol ([+DODT], the active metabolite of tramadol [1]. In this study the influence of OCT1 polymorphisms on tramadol analgesia and pharmacokinetics was analyzed in patients recovering from surgery.

Methods: After approval of the ethics committee and written informed consent 205 patients receiving tramadol via patient-controlled analgesia after surgery were enrolled. OCT1 genotypes (zero, one or two active alleles) and genotype dependent CYP2D6 activity scores representing no (FM), intermediate (IM), extensive (EM) or ultra-rapid metabolism (UM) were determined. Plasma concentrations of (+)-DODT were measured by (mean AUC (95%-CI)). Primary endpoint: Tramadol consumption up to 48 hours after surgery depending on OCT1-genotype (repeated measures ANOVA).

Results: Zero, one and two active OCT1 alleles were carried by 19, 82 and 104 patients (age 57.3 ± 12.6 years). The average [+DODT] plasma concentrations (AUC) were 99.3 (53.9/144.7), 80.2 (65.1/95.3) and 64.5 (51.7/72.2) ng/ml in carriers of zero, one and two active OCT1 alleles (p = 0.03 for zero versus two active alleles). In line with this, the cumulative tramadol consumption was lowest in carriers of no active OCT1 allele (p = 0.025). This finding was confirmed in the subgroup of CYP2D6 EM (p = 0.01). OCT1 effects were most pronounced in CYP2D6 EM and UM, suggesting limiting effects of OCT1-mediated hepatic uptake only in the presence of active hepatic metabolism.

Conclusions: In addition to CYP2D6, OCT1 polymorphisms responsible for variance of carrier-mediated (+)-DODT-uptake in the liver affect the efficacy and pharmacokinetics of tramadol in postoperative patients.

Reference
Results: The rate of hemidiaphragmatic paresis was 95% in group SF and 25% in group EF (p < 0.0001). Other respiratory outcomes were significantly preserved in group EF (table 1). Acute pain-related outcomes were worse between groups (table 2).

Conclusions: IS block with an extradural injection reduces respiratory complications and provides similar analgesia compared to a subclavicular injection.

Nociceptin receptor activation modulates toll-like receptor 2 expression in human peripheral blood
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Introduction: Nociceptin is an opioid-related peptide and may play a role in peripheral blood during inflammation and pain [1, 2]. Toll-like receptors (TLRs) are pattern-recognition receptors which play a key role during innate and adapted immune response. Cross-talk between opioids and TLRs has been discussed recently [3, 4]. However, no data on the influence between nociceptin and TLRs are available so far. The aim of this study was to investigate effects of nociceptin on TLR2 mRNA expression in human peripheral blood under inflammatory conditions.

Methods: After approval of the ethics committee and written informed consent, healthy blood donors were enrolled in this ex vivo study. Whole peripheral blood was cultured with or without nociceptin 10^{-6} M or phorbol-12-myristate-13-acetate (PMA) 10 ng/ml for 6 and 24 hours. mRNA expression of PNoc and TLR2 was detected by quantitative RT-PCR. To investigate possible influences of nociceptin on TLR2 mRNA expression, blood was pretreated with UFP-101 100 nM, a specific antagonist of the nociceptin receptor, for 1 hour prior to co-culture with PMA 10 ng/ml. Nociceptin protein levels in culture supernatants were measured using fluorescent-enzyme immunoassay.

Statistics: Median (95% CI), Mann-Whitney U test and Wilcoxon signed-rank test with subsequent post hoc analysis.

Results: Exogenous nociceptin enhanced TLR2 mRNA expression in human blood leukocytes after 6 hours compared to the control without any stimuli (normalized ratio: 1.0 (0.6/2.3) vs. 0.7 (0.3/2.3), p = 0.007). Both PNoc and TLR2 mRNA were up-regulated in PMA-induced blood cells after 24 hours compared to the respective controls (PNoc: 1.7 (0.5/10.5) vs. 0.2 (0.0/7.0); TLR2: 1.3 (0.7/14.8) vs. 0.7 (0.3/1.6), both p < 0.0001). Nociceptin peptide levels were increased in supernatants of blood cultured with PMA compared to the control (8.3 (4.1/24.0) vs. 5.0 (2.5/9.1) pg/ml, p = 0.02). Pretreatment with UFP-101 partially prevented the up-regulating effects of PMA on TLR2 expression with its mRNA declining to 8.18 (38.6/135.0)% of the blood treated with PMA only (p < 0.001).

Conclusions: Activation of the nociceptin-NOP system enhances TLR2 mRNA expression in human peripheral blood leukocytes. Elucidation of the function of nociceptin in human peripheral blood under inflammatory conditions could reveal new insights in the treatment of pain and inflammation.

References
Safety of Airtraq® vs. fiberoptic intubation in patients with an unstable cervical spine fracture: a neurophysiological study

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Introduction: Tracheal intubation in patients with an unstable cervical spine is challenging. The airway must be secured while the cervical spine is immobilized. Numerous airway devices and techniques exist and generate specific cervical spine movements with a potential for secondary injury. Fiberoptic intubation is described as the preferred technique by experienced anesthesiologists. The Airtraq® has been shown to perform well in patients with a simulated difficult airway. We compared the success rate, time and neurophysiologic modifications associated with tracheal intubation performed randomly by an Airtraq or a fibrescope in patients with a trauma related unstable cervical spine fracture immobilized by a cervical collar.

Methods: 38 patients were randomly assigned to tracheal intubation using the Airtraq or the fibrelescope. Neurophysiological monitoring (somatosensory evoked potentials with amplitude and latency measures after median nerve stimulation) was performed before airway management (baseline), during ventilation, during and after intubation and after definitive patient positioning for surgery. A 50% reduction in amplitude or a 10% increase in latency were defined as intubation and after definitive patient positioning for surgery. A 50% decrease in amplitude or latency where found in either group. A 1.5% increase in latency for the left arm during intubation was found in the Airtraq in signal distribution as well as intubation times. The number of attempts necessary for intubation were compared. The system automatically records the duration of the procedure, number and sequence of bronchial segments inspected, and number of collisions with tracheobronchial wall. Anaesthetists attending a Swiss difficult airway course were recruited to assess the CASS. Objective performances were assessed with participants performing a bronchoscopy from mouth to the right superior lobar bronchus (RSLB). We used an assessment tool of bronchoscopic performance [1], combining a number of wall collisions, ease of pass through vocal cords, image centering and "red-out time" (0 = bad to 8 = very good). Subjective criteria (bronchoscope proxy handling, graphic quality of the model, anatomy fidelity, reactivity of the system and usefulness for teaching) were assessed using a Likert scale (1 = bad to 5 = very good).

Results: 22 physicians were enrolled (5 residents (22.7%), 2 fellows (9.1%) and 15 senior specialists (68.2%)). Seventeen (77.3%) had 10 years of clinical experience and 13 (59.1%) had performed >50 bronchoscopies. Mean time to reach the RSLB was 92 ± 35 sec, mean number of wall collisions during procedure were 12 ± 15. Bronchoscopic performance of participants in the R-group was significantly shorter with the Airtraq (median [25th;75th] 45 seconds [39;55]) than a fiberoptic bronchoscope (121 [86;154]), (p <0.001). Bronchoscopic performance was 4.7 ± 0.7; anatomy fidelity 4.5 ± 0.6; reactivity of system 3.6 ± 1.1, usefulness for teaching 4.9 ± 0.3 and ease of use 4.3 ± 0.8.

Conclusion: Subjective assessment by participants of the simulator was excellent, especially as a tool for teaching and with regards to the graphic quality. Reactivity of the system should be improved in future. Bronchoscopic performance of participants was acceptable.

Reference

The impact of a near-infrared spectroscopy based protocol on the neurobehavioral outcome after shoulder surgery in beach chair position.

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Background: Cerebral hyperperfusion related to beach chair position and to the often performed controlled hypotension has been suggested by case reports describing poor neurological outcomes in patients without high risk for cerebrovascular events. Near-infrared spectroscopy (NIRS) offers a non-invasive tool to monitor cerebral perfusion. The impact of the NIRS based treatment protocol for the general anesthesia (G-group) and regional anesthesia (R-group) group with interscalene catheter (ISC) for postoperative analgesia were evaluated.

Methods: Eighty ASA I-III patients scheduled for shoulder surgery were divided according to our clinical standard in 2 groups: 40 patients in the general anesthesia (G-) group with propofol/remifentanil TCI and ISC for postoperative analgesia. Anesthesiologists in the R-group were blinded to the rScO2 values. Baseline data the day before surgery included neurological and neurobehavioral tests the first day after surgery. The baseline data for NIRS / bispectral index (BIS) / CO2, non-invasive blood pressure at heart level and correction for brain level and non-invasive cardiac output monitoring (esCO2 Technology) were taken prior anesthesia, after induction, after beach chair positioning and at 20 minutes after start of surgery until discharge to the PACU. A rScO2-based treatment protocol for the G-group including corrections for head position, SaO2, et CO2, mean arterial pressure, hemoglobin level and cardiac function was applied.

Results: (Preliminary, study ongoing) Patients in the R-group showed more stable values of rScO2, and blood pressure with similar neurobehavioral test results after surgery compared to baseline. In the G-group the treatment protocol was effective correcting rScO2 levels compared to baseline values leading to similar results in the neurobehavioral tests the first day after surgery compared to the R-group.

Conclusions: Regional anesthesia offers more stable cardiovascular conditions for shoulder surgery in beach chair position compared to general anesthesia. However, a rScO2-based treatment protocol allows for cerebral oxygenation correction leading to similar results in the postoperative cognitive function tests.
Which anesthesia regimen is best to reduce morbidity and mortality in lung surgery? A multicentre randomized controlled trial

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Background: One-lung ventilation (OLV) allows isolation of the individual lungs under anesthesia; however, it is associated with hypoxia-reoxygenation injury in the deflated and subsequently re-ventilated lung. Numerous studies have reported beneficial effects of volatile anesthetics on inflammatory mediators in this type of injury model. If volatile anesthetics are potent enough to impact not only on surrogate biomarkers, but also on clinical outcome still has to be determined. Therefore, a multicenter randomized controlled trial (RCT) was designed comparing propofol with desflurane anesthesia in patients undergoing lung resection surgery with OLV to detect major complications.

Methods: Five centers in Switzerland (University Hospitals of Zurich, Bern and Basel and the Kantonsspital of St. Gallen and Münsterlingen) participated in the RCT. Patients scheduled for elective lung surgery were randomly assigned to receive either propofol or desflurane as general anesthetic with pre-stratification for study site, major diseases (coronary heart disease, COPD, diabetes, chronic kidney disease) as well as pneumonia. Major complications according to the Clavien-Dindo score were defined as primary (hospitalization) or secondary (6 month follow up) endpoint comprising of re-interventions without (grade IIIa) or with anesthesia (grade IIIa), single-organ failure (grade IV), or multi-organ failure (grade V) as well as all-cause mortality (grade V). Cox regression model was used, adjusting results for study site, age, pneumonia and major diseases.

Results: 486 patients were enrolled (6 drop outs, n = 230 for each arm, randomized and analyzed). Demographics were similar in both groups. 111 patients (48%) had major surgery (thoracotomy, pneumonectomy) in the propofol, and 97 (42%) in the desflurane group. Duration of OLV, anesthesia and surgery were comparable in both groups. Incidence of major complications during hospitalization was 16.5% in the propofol while 13.0% in the desflurane group (HR for desflurane 0.95, 95%CI 0.67–1.35, p = 0.74). Incidence of major complications within six months from surgery was 40.4% in the propofol while 39.6% in the desflurane group (HR for desflurane 0.95, 95%CI 0.71–1.28, p = 0.71). Conclusion: This is the first adequately powered multicenter RCT addressing the effect of volatile anesthetics on major complications after lung surgery. No significant difference between the two anesthesia regimens could be observed.

Sevoflurane postconditioning might reduce severity of cardiac and non-cardiac complications after elective cardiac valve surgery. Results of a 6 month follow up

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Background: Anesthetic conditioning with volatile anesthetics has been linked to a significant decrease of surrogate markers. However, it is still less clear if this translates into clinical benefit. The primary aim of this study was to assess the clinical implications of these findings, we performed a 6-month follow up, including the effect of volatile anesthetics on major complications after surgery. No significant difference between the two anesthesia regimens could be observed.

Methods: All patients who successfully completed the postconditioning trial were included into this follow-up study. Primary and secondary endpoints were assessment of cardiac events (dysrhythmias, congestive heart failure and cardiac ischemia) and non-cardiac events (pulmonary embolism, bleeding, infection, cerebral events and chronic kidney failure) resulting in diagnostic or therapeutic interventions. Statistical analysis was performed in R (R Foundation for Statistical Computing). Mixed linear models with propofol as reference group were chosen.

Results: Ninety-four of the 102 patients from the primary study were evaluated in this 6-month follow-up. Sixteen out of 41 (39%) patients in the sevoflurane and 19 patients out of 53 (36%) in the propofol group suffered from one or several cardiac events during the first 3 months after participating in the primary study (p = 0.75). In 4 (9%) patients treated with sevoflurane vs. 9 (17%) patients treated with propofol non-cardiac events were reported (p = 0.61). Thus, an additional medical intervention was required only in 12 patients in the sevoflurane compared to 20 patients in the propofol group (OR: 0.24, CI: 0.040–1.43, p = 0.12). Eight patients in the propofol arm compared to only 2 patients in the sevoflurane group were re-admitted to the hospital due to complications (OR 0.233, CI: 0.042–1.293, p = 0.01).

Conclusion: We documented a similar number of adverse events in patients treated with sevoflurane vs. propofol. Despite not reaching statistical significance, we observed less severe complications in the sevoflurane group (less need for treatment, fewer admissions to the hospital).


Glucose-insulin-potassium reduces the incidence of major complications in patients undergoing open cardiac surgery

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Background: Cardiac surgery with cardiopulmonary bypass (CPB) may result in myocardial injury associated with major adverse cardiac events (MACE) and non-cardiac complications. Besides the classical cardiopulmonary bypass surgery with evidence of left ventricular hypertrophy or with a Bernstein-Parsonnet score >4 were randomly assigned to GIK or placebo. After anesthesia induction, each patient using a 60 ml solution containing either 2 g of glucose, 10 UI of regular insulin and 40 mEq of potassium (GIK group) or normal saline (placebo group) was administered over 45–60 min. The primary outcome was incidence of MACE including low cardiac output syndrome, myocardial infarction and arrhythmias requiring treatment. Secondary endpoints were requirement for inotropic support, peak serum troponin-I concentration, incidence of non-cardiac complications, length of stay (LOS), and in-hospital mortality.

Methods: In this single-center, double-blind, randomised, placebo-controlled trial, patients undergoing valve replacement or coronary bypass surgery with evidence of left ventricular hypertrophy or with a Bernstein-Parsonnet score >4 were randomly assigned to GIK or placebo. After anesthesia induction, each patient using a 60 ml solution containing either 2 g of glucose, 10 UI of regular insulin and 40 mEq of potassium (GIK group) or normal saline (placebo group) was administered over 45–60 min. The primary outcome was incidence of MACE including low cardiac output syndrome, myocardial infarction and arrhythmias requiring treatment. Secondary endpoints were requirement for inotropic support, peak serum troponin-I concentration, incidence of non-cardiac complications, length of stay (LOS), and in-hospital mortality.

Results: Over a 6-year period, 225 patients were randomised to GIK solution (n = 111) or placebo (n = 114). Patient characteristics were similar in both groups, except for a lower preoperative left ventricular ejection fraction in the GIK group (43.9% vs. 47.1%, p = 0.005). Treatment with GIK was associated with reduced incidence of MACE (52 patients [46.8%] vs. 100 patients [87.7%], p = 0.001), lower requirement for inotropic support during weaning from CPB (28.8% vs. 64.0%, p < 0.001) and in the intensive care unit (21.6% vs. 56.9%, p < 0.001), reduced peak serum troponin-I concentration (median 2.9 ng/l [interquartile range 1.5–6.2] vs. 4.3 ng/l [2.4–8.4], p = 0.038), reduced incidence of respiratory complications (42.3% vs. 70.2%, p = 0.001), reduced LOS (median 14 days [IQR 11–18] vs. 16 days [13–23], p = 0.014), and lower in-hospital mortality (0.0% vs. 8.7%, p = 0.002).

Conclusion: In patients undergoing cardiac surgery with CPB, addition of GIK solution to standard myocardial protective treatments results in improved clinical outcome.

High Sensitivity Troponin T and its Association with Mortality and Morbidity after On-Pump Cardiac Surgery at 12 Months

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Background: Troponin is a predictor of cardiac morbidity and mortality after cardiac surgery with most data examining 4th generation troponin assays. We hypothesize that the higher of the two concentrations of high sensitivity troponin T (hsTnT) on the first and second postoperative day is also an independent predictor of mortality and morbidity.
Methods: In this preliminary analysis of prospectively collected data, we included all patients undergoing on-pump cardiac surgery from 02/2010 to 03/2012 with measurements of hsTnT, which were recorded at 6 am of both the first and second postoperative day. Our primary endpoint was all-cause mortality and/or major adverse cardiac events (MACE) defined as acute coronary syndrome, cardiac arrest, congestive heart failure, or revascularization at 12 months. The secondary endpoint was all-cause mortality alone at 12 months. The optimal cut-offs were determined using a receiver operating characteristics (ROC) curve with a 1:1 weight of sensitivity and specificity. Using a Cox regression model, we adjusted the association of the higher of the two hsTnT concentrations with adverse events for the EuroSCORE II.

Results: We included 1123 of 1153 potentially eligible patients (75.6% male, mean age 66 ± 11 years) and observed and 175 (15.6%) composite events including 94 (8.4%) deaths. The cut-offs determined by the ROC curve were 0.889 µg/L for mortality and/or MACE and 0.667 µg/L for mortality alone with an AUC of 0.723 (95%CI 0.688–0.766) and 0.667 µg/L for mortality alone with an AUC of 0.741 (95%CI 0.685–0.798). In total, 302 (26.9%) and 397 (35.4%) patients were above these cut-offs, respectively. After adjusting for the EuroSCORE II, an increase in hsTnT by 0.1 µg/L was associated with a hazard ratio of 1.013 (95% CI: 1.014–1.020; p <0.001) for mortality and/or MACE and a hazard ratio of 1.017 (95% CI: 1.014–1.020; p <0.001) for mortality alone.

Conclusion: This preliminary analysis suggests that higher postoperative hsTnT concentrations are associated with higher mortality and morbidity rates in patients undergoing on-pump cardiac surgery. This association was independent of the preoperative risk assessment as embodied by the EuroSCORE II.

Figure 1
Kaplan Meier curves for MACE-free survival and survival alone by optimal ROC cut-offs at 12 months

MACE-free survival and survival alone by optimal ROC cut-offs at 12 months.
Temporal changes in lung function following haemodilution under stable hemodynamic conditions in pigs
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Since little is known about the effect of decreased haematocrit (Hct) on lung function, we assessed the acute effects of haemodilution during stable haemodynamic condition on respiratory mechanical parameters and lung volume changes on anaesthetized intubated minipigs (n = 8). After control condition, stepwise 10 ml/kg blood withdrawals were compensated with 30 ml/kg of crystalloid to maintain stable haemodynamics. Forced oscillation technique was used to measure airway resistance (Raw), respiratory tissue damping (G) and elastance (H). Effective lung volume (ELV) was measured from the CO2 elimination traces. Extravascular lung water (EVLW) was determined by thermodilution. Respiratory and haemodynamic measurements were made before and following each step of haemodilution. Haemodilution led to an increase in Raw (up to 20%) and decrease in G (up to –40%), with significant correlations with Hct levels (R = –0.67 and 0.67 for Raw and G respectively, p <0.0001). ELV decreased in parallel with a slight but significant increase in H (r = 0.66, p <0.0001) and EVLW.

Our data suggest that haemodilution affects the lung function and these changes correlate with the Hct values. The increase in EVLW indicates that this regimen leads to overcompensation, which may explain the increases in Raw and the loss of ELV. The decreases in G with Hct may be due to the altered blood rheology affecting the lung tissue viscoelasticity.

Are miRNAs involved in HLA-DR expression on the cell surface? – a miRNA screen
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Introduction: MHC class II molecules (MHC-II) help to present antigenic fragments on the cell surface of antigen-presenting cells (APCs) like B-cells, dendritic cells or macrophages to T-helper cells enabling immune responses, and are strongly linked to autoimmune diseases. Cell surface expression of peptide-loaded MHC-II (HLA-DR) is not yet completely understood and is regulated by transcriptional regulators and the intracellular storage/transport that finally leads to cell surface expression. Clinical studies revealed that cell surface-expression of HLA-DR is down-regulated in patients undergoing surgery what is thought to indicate a suppression of the immune system. Especially, in critical conditions such as severe sepsis, the amount of HLA-DR available for presenting antigen to T-cells is a crucial factor for the probability of survival and, therefore, plays an important role.

Objectives: A better understanding of HLA-DR surface expression is of importance to possibly interfere with perioperative HLA DR downregulation. The question whether miRNAs are involved in CLIP-loaded- and peptide-loaded MHC-II expression shall be unraveled.

Method: A flow cytometric based high throughput screen with miRNA mimics was done. The most important miRNAs (2048) were transfected into a melanoma cell line (MelJuSo) and analyzed by flow cytometry using the monoclonal antibodies CerCLIP to detect CLIP-loaded MHC-II molecules and L243 for detection of HLA-DR molecules on the cell surface.

Results: The High Throughput Screen identified 45 miRNAs that lead to an up-regulation of HLA-DR surface expression, and 7 miRNAs that are involved in down-regulation of HLA-DR surface expression. 16 selected miRNAs with strongest impact on HLA-DR surface expression were verified successfully. No screened miRNA did change the amount of CLIP loaded MHC-II molecules on the cell surface. Current research investigates the mechanism how these miRNAs lead to changes in HLA-DR surface expression.

Conclusion: miRNAs seem to have no influence on incorrect peptide loading of MHC-II molecules but strongly impact HLA-DR surface expression. Understanding the mechanisms behind could help to define new possible methods to tune the immune system in critically ill patients.

Functional analysis of beta-defensin 2 gene copy number variations in peripheral blood mononuclear cells
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Background: Beta-defensins are cationic antimicrobial peptides which also display immunomodulating effects by activating other immune cells. Beta-defensins are mainly expressed in skin and mucosa and can be strongly induced by invasive pathogens. The 8p23 beta-defensin genes (DEFBs) are affected by copy number variations (CNVs). The gene copy number (CN) is variable from 2 to 12. This study is aimed at investigating the impact of beta-defensin 2 gene CNV on expression in peripheral blood mononuclear cells (PBMC).

Methods: DEFB CN will be screened in 1000 healthy blood donors by paralog ratio test (PRT) and 10 donors for each CN group will be selected (totally around 100 donors). DEFB CN for these 100 donors will be accurately quantified by Multiplex Ligation-dependent probe amplification (MLPA). PBMC from these 100 donors will be cultured with lipopolysaccharides (LPS) or lipoteichoic acid (LTA) or beta-glucan. Beta-defensin 2 mRNA in PBMC will be quantified by real-time PCR. Beta-defensin 2 protein in supernatant from PBMC cultures will be quantified by ELISA. The correlation between beta-defensin 2 gene CN and mRNA and protein levels will be analyzed.

Results: The pilot study using a whole blood culture model showed beta-defensin 2 was not expressed in leucocytes without stimulation and only can be induced by LPS in a time- and dose-dependent manner. In addition, the mRNA levels varied largely among 6 individuals after 24 hours stimulation with 100 ng/ml LPS.

Conclusion: Beta-defensin 2 gene CN may have an impact on expression in leucocytes.
Neutrophil extracellular trap (NET) formation in the perioperative setting – A pilot-study
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Neutrophil granulocytes can release Neutrophil Extracellular Traps (NETs) after stimulation. These traps are comprised of networks of DNA and antimicrobial peptides and may, therefore, influence the innate immune response by immobilization of different pathogens such as e.g. Staphylococcus aureus. Moreover, this formation might be involved in the formation of deep vein thrombosis. Imbalance of this effector of the innate immunity might contribute to perioperative complications. The mechanisms of NET formation and the meaning of the involved factors are not well understood. This project was designed as a pilot study to investigate the influence of a surgical trauma on the capability of neutrophilic granulocytes to form NET-structures in vitro after stimulation with or without PMA. After ethical approval, seven “Trans Catherter Aortic Valve Replacement” (TAVI, mild surgical trauma) and nine “Aortic Coronary Bypass” (ACB, severe surgical trauma) patients were included. Blood was collected before, during, 24 h and 48 h after surgery and granulocytes were isolated by gradient centrifugation and stimulated in vitro with 50 nMol PMA for 2 h. NET-formation rate was examined by microscopic procedures and number of HLA-DR surface molecules on monocytes was determined to define general changes in the immune status. The patients’ perioperative characteristics did not differ significantly with regard to ASA category but with regard to gender and age. The ACB group contained more males and patients were younger 66.3 ± 8.1 years (mean ± Standard deviation) versus 81.1 ± 5.0 years. HLA-DR levels on monocytes did not significantly change over time in the TAVI-group but number of molecules was significantly down regulated at 24 and 48 h after surgery in the ACB group. This indicates that there is, as expected, a stronger immune modulation in the ACB group. In contrast, no significant difference could be observed for the induction of NETs for samples stimulated with PMA at all timepoints. Rate of NET-formation in non-stimulated granulocytes did not change in the TAVI group. Interestingly, there was a significant down regulation of NET-formation rate in non-stimulated granulocytes from ACB-patients at 24 and 48 h after surgery.

Conclusion: Surgical trauma seems to influence the basal NET-formation rates in patients. However, the NET-formation following PMA stimulation showed no differences between patients with a mild or severe surgical trauma.

High copy number of the 8p23 beta-defensin gene cluster is associated with mortality of severe sepsis due to respiratory tract infection in Caucasian males
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Background: Sepsis is a systemic inflammatory response after infection. Beta-defensins are a group of small cationic antimicrobial peptides which are effective against bacteria, fungi, and enveloped virus. They are mainly expressed in skin and mucosa and they are strongly inducible by invasive pathogens. In addition, beta-defensins have cytokine-like effects to modulate immune response. 8p23 beta-defensin genes (DEFB) were found to be variable in copy number (2 to 12 per diploid genome) which impact function of the genes. Thus, the gene copy number (CN) was reported to be proportional to DEFB4 mRNA expression in a variety of cells. Significant association between higher DEFB CN and risk of sepsis were reported. This study investigates the association between DEFB CN and the predisposition to and the clinical course of severe sepsis.

Method: A case-control study containing 721 patients with severe sepsis and 283 healthy controls was performed. DEFB copy number (CN) was determined by Multiplex Ligation-dependent Probe Amplification (MLPA). The association of DEFB CN with the susceptibility to and the outcome of severe sepsis before and after stratification by gender and source of infection was analyzed.

Result: DEFB CN is not associated with the incidence of severe sepsis. Increased DEFB CN is associated with mortality in male patients with severe sepsis due to respiratory tract infection (P = 0.0049). Furthermore, a linear regression between DEFB CN and mortality was established (R² = 0.76, P = 0.0023), which suggests that each increase by 1 copy from 2 copies adds 11.27% (95% confidence interval: 2.55–19.99%) to the mortality rate. Logistic regression analysis also showed DEFB CN to be an independent factor for non-survival (odds ratio [OR], 1.57 [95% CI, 1.19–2.06], P = 0.001, for each copy increase of DEFB CN). In addition, increased DEFB CN is very likely associated with death in male patients with severe sepsis due to intra-abdominal infection. However, DEFB CN is not associated with the outcome of severe sepsis in female patients.

Conclusion: High DEFB CN is associated with increased risk of death from severe sepsis due to respiratory tract infection in Caucasian males. DEFB CN could be used as a genetic marker to predict outcome of severe sepsis in male but not in female patients.
Anesthesia during Nepal earthquake: Immediate lessons

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An Earthquake magnitude 7.8 hit Nepal on Saturday 25 April 11:56 local time. Epicenter was close to the city of Gorkha. Quickly more than 6000 victims were counted and more than 15000 wounded expected. The Swiss Agency for Development and Cooperation deployed a Foreign Medical Team type 2 “Mother&Child” with the goal of mainly treating pediatric, surgical and obstetric patients. Five days after the earthquake, the team with anesthesiologists and basic material to perform spinal and ketamine anesthesia arrived in the District Hospital Gorkha. The local resources and structure of this regional hospital were assessed by a Swiss engineer, one of the two operating rooms available was declared safe for surgical procedure. Available to us at our arrival was functional anesthesia machine, halothane, oxygen in tank and monitoring. Because of the heavy destruction, the usual recovery room was occupied by many surgical hospitalized patients. During the first week, we encountered many patients that had travelled long distances with signs and symptoms of exhaustion, pain, infection, dehydration and anemia. During the first week, 41 surgeries were performed mainly related to the earthquake including open fracture of the limbs associated with infected wounds. Ten patients were operated within the 48 hours and then re-operated several times during the next following days. Nine of the first 10 patients received a blood transfusion and 9 spinal anesthetics were also operated. During an episode of severe aftershock, the surgical team evacuated the operating room but due to halothane mask anesthesia, the patient and the anesthesiologist had to remain. Thanks to a precautionary measure of having the 70 kilos oxygen tank lying on the ground horizontally, major complications were avoided. During such severe aftershock it was apparent that evacuating a patient with regional anesthesia would be simpler than a patient under general anesthesia. Eleven ultrasound axillary blocks and 9 spinal anesthesia were successfully performed. Due to the shortage of halothane, we were only able to induce by mask a limited number of children. Thereafter ketamine was used for general anesthesia. Patient recovery was better with balanced general anesthesia than ketamine anesthesia. We did not have any major complication from anesthesia. Our concerns during such earthquake was created and deployed for the 3700 nurses. In a constructivist pedagogical perspective for skill development, the measurement of knowledge transfer into clinical practice is a major issue rarely addressed. This inquiry was achieved in a 66-beds geriatric rehabilitation unit and assessed the e-learning according to 3 dimensions: knowledge increase, participant satisfaction and participant knowledge transfer into nursing clinical practice regarding pain screening and assessment.

Objectives: To evaluate knowledge transfer into nursing clinical practice following an e-learning training about pain management.

Description & Method: This inquiry ran over 3 phases and used a pre-post audit strategy. The audits included 4 clinical indicators of best practice recommended by the Registered Nursing Association of Switzerland (RNAS) and the Joanna Briggs Institute (JBI). This project used questionnaires, focus groups and collection retrospective data from nursing clinical documentation.

Results: In total, 47 nurses followed the training. Despite significant increase in knowledge (M068% vs M085%, p = 0.000) and great participant satisfaction rate among e-learning training program (up to 80%), data collected from nursing clinical documentation showed opportunities for clinical improvements towards knowledge transfer and pain management with no statistical significant differences (pBased on a quiz pre-post, knowledge increased from 68% to 85% (p = 0.000). Satisfaction with the content and method of training was high (participation rate: n = 16; 34%). Data from nursing files showed a gap with good clinical recommendations about pain screening and assessment practices with no significant changes pre-post training. During focus groups, 10 participants identified several barriers and facilitating factors towards knowledge transfer and pain management.

Conclusion: Pain assessment is a continuous challenge for patients and healthcare providers. Strategies must be developed and tested to promote evidence based practice and lead to better quality of care.

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Measuring knowledge transfer in nursing practice following an e-learning training on pain management

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Introduction: Pain assessment is an ongoing challenge for nursing practice. At the University Hospital of Lausanne, an e-learning training on pain management consisting of 21 audio-commented videos was created and deployed for the 3700 nurses. In a constructivist pedagogical perspective for skill development, the measurement of knowledge transfer into clinical practice is a major issue rarely addressed. This inquiry was achieved in a 66-beds geriatric rehabilitation unit and assessed the e-learning according to 3 dimensions: knowledge increase, participant satisfaction and knowledge transfer into nursing clinical practice regarding pain screening and assessment.

Objectives: To evaluate knowledge transfer into nursing clinical practice following an e-learning training about pain management.

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Conclusion: Pain assessment is a continuous challenge for patients and healthcare providers. Strategies must be developed and tested to promote evidence based practice and lead to better quality of care.

P 10

A simple model to justify the use of Sugammadex economically in daily practice

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Introduction: Deep muscle relaxation is often required through out an entire surgical procedure (e.g. minimal invasive orthopedic or laparoscopic procedures). Also a complete reversion of deep muscular blockade is a safety feature in the care of patient’s postoperatively. With the use of the new but expensive drug Sugammadex (117.– CHF per 2 ml vial) even deep blockades can be reversed in due time. A simple model was developed to allow an economical and clinical realisable use of this drug.

Materials and Methods: Efficiency can be defined as the net gains due to better processes and the deduction of the costs for the reversal drug. Cost savings are realized by saving time and the generation of new opportunities for a next case or the avoidance of overtime. Cost savings can be calculated by multiplying the expected saving of time with the known costs per anesthesia hour with respect to a factor of opportunity as a variable. These calculations generate a value of the possible saving of time. For the calculations the following formula was applied:

\[ \text{Eff} = (\text{ohne} - \text{mit}) \times \frac{\text{Anä} \times \text{Fopp}}{\text{K} \times \text{Anä} + \text{Fopp} \times \text{Fopp}} \]

Results: Typical values for Fopp are between 1-2 and the costs per anesthesia hour vary between 350–450 CHF at our institution. With the developed nomograms a net gain of efficiency can easily be identified. For example applying the above values justify the use of 2 ml Sugammadex at best after gain of process time of 8–20 minutes. Side effects such as a better performance of surgical departments by a better degree of capacity utilization are not taken into account

Conclusions: Despite the costs for Sugammadex, its use is economically justified under the prerequisite that the costs per anesthesia hour and the drug costs are known.

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Confounders of NT-pro-BNP and BNP as a pre-operative cardiac risk marker in a University Anaesthesiology Clinic – a pilot study

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Introduction: Ventricular cardiomyocytes secrete brain natriuretic peptide (BNP) into the blood in response to atrial or ventricular wall stretch or myocardial ischemia. Recent investigations showed that BNP is a powerful predictor of death/major adverse cardiovascular events in patients with stable coronary artery disease, acute coronary symptoms, and congestive heart failure. The preoperative BNP plasma concentration is a good predictor of cardiovascular events in the first 30 days after noncardiac surgery. The measurement of BNP plasma levels preoperatively should be considered especially in cardiac patients undergoing noncardiac surgery to assess the perioperative cardiac risk. Different nucleotide polymorphisms were worldwide detected and are partly associated with de- or increased BNP/NT-Pro-BNP plasma levels.

Objectives: This pilot study evaluates the haplotype organization of the BNP gene in a Swiss cohort of preoperative patients. Preoperative BNP and NT-Pro-BNP plasma levels will be evaluated based on haplotype.

Methods: The prospective cohort study includes 215 patients with ASA 1/2 and 220 with ASA 3/4 classification. A blood sample was withdrawn by induction of anaesthesia and NT-Pro-BNP and BNP
plasma concentrations were measured in the clinical chemistry laboratory. Blood samples were genotyped for two described single nucleotide polymorphisms: rs198389 and rs198358. Statistical analysis was done with GraphPad Prism using t-Test and Kruskal-Wallis test with Dunn’s multiple comparison test.

Results: Preoperative BNP respectively NT-Pro-BNP levels were significantly different (p >0.0001) between ASA1/2 (15 ± 18 pg/ml resp. 40 ± 43 pg/ml) and the ASA3/4 group (48 ± 131 pg/ml resp. 146 ± 775 pg/ml). Allele frequency for rs198389 and rs198358 were as expected for different haplotypes of rs198389 and BNP and NT-Pro-BNP plasma concentrations. In contrast, the CC allele of rs198389 in the ASA1/2 group did correlate with higher plasma BNP concentrations (p <0.05) compared to CT or TT carriers and CC carriers of the ASA3/4 group had higher plasma BNP concentrations (p <0.05) compared to TT carriers. There was no genotypic specific influence on the NT-pro-BNP plasma concentration.

Conclusion: Single nucleotide polymorphisms can influence BNP expression levels. Additional polymorphisms need to be analysed to determine the impact of haplotypes on BNP and NT-Pro-BNP plasma levels.

Anesthesiologic management of urgent emergency caesarean sections
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Introduction: Urgent caesarean delivery (CD) can be time critical, which can be an argument in favour of general anaesthesia (GA). Regional anaesthesia (RA) avoids the potentially difficult airway and is associated with less bleeding, better postoperative pain control and leads to a better bonding of the mother with the neonate (1). The policy of our hospital is (i) to establish epidural analgesia in high-risk pregnancies and (ii) to perform a time-out in the operating room to confirm –or reclassify – urgency of unplanned CD. We classify CD into elective, unplanned and urgent. The target decision to delivery time in unplanned and urgent CD is 30 and 10 minutes, respectively. The aim of this quality control was to analyse urgent CD in terms of frequency, mode of analgesia (GA vs. RA) and mode of anaesthesia. Those with urgent CD were further analysed for the reason of CD, umbilical cord pH and APGAR scores.

Results: There were 887 CD, 529 (40.4%) were elective, 301 (33.9%) unplanned and 57 (6.4%) urgent. Overall there were 866 (97.6%) were performed in RA. Of the 57 urgent CD 49 (85%) were in RA (20 spinal, 29 epidural). Of these, 4 RA (8%) were insufficient (1 spinal and 3 epidural) and converted to GA. Primary GA was performed in 8 patients (14%). Two of these had satisfactory epidural labour analgesia. Difficult intubation (>3 attempts) occurred in 2 women. Analysis of umbilical cord pH and APGAR is ongoing.

Conclusion: In our hospital the vast majority of SD in 2014 was performed under RA. This was also true for urgent CD. Primary GA was rare. Our policy to establish epidural analgesia in high-risk parturient seems to work, as epidural analgesia was in place in more than half of the urgent CD. That two of these had primary GA due to time pressure has to be further analysed with a focus on indication and speed of conversion from analgesia to anaesthesia.

Reference

Multichannel near-infrared spectroscopy monitoring: feasibility during cardiac and thoracic aortic surgery
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Introduction: Near-infrared spectroscopy (NIRS) monitoring of frontal cerebral tissue oxygen saturation is a useful tool for cardiac and thoracic aortic surgery [1]. However, restricted spatial resolution is a major limitation of commercially available two-channel NIRS devices. Aim of the study was to show feasibility of multichannel NIRS measurements in the operation room.

Patients and Methods: We measured chronological changes in oxygenated and deoxygenated hemoglobin concentrations using the multi-channel NIRS device FOIRE-3000, Shimadzu, Japan. We used 16 transmitter-receiver pairs resulting in 31 NIRS channels at optode spacings of 30 (n = 11) and 42 mm (n = 20) [2]. Measurements were continuously displayed on a computer screen and stored electronically. After surgery, data were processed to generate temporospatial maps including animated video sequences.

Results: Multichannel-NIRS readings were obtained in three patients (coronary artery bypass grafting, n = 2; hernia repair with hypothermic circulatory arrest and cerebral perfusion, n = 1). Record time varied between 100 and 180 minutes. Measurements were technically uneventful in all cases. Movement artifacts occurred in some cases, however, could easily be identified. Abrupt changes in hemoglobin concentrations (e.g., hemodilution; hypothermic circulatory arrest; antegrade cerebral perfusion) were reliably detected. One episode of a short-lasting cerebral deoxygenation during cerebral perfusion could be detected in right-sided temporoparietal channels, while the other channels indicated acceptable cerebral oxygenation in the rest of the monitored brain during this episode. Beside light and rapidly reversible cutaneous impressions no adverse events were monitored.

Conclusions: Multichannel-NIRS measurement in the cardiac theater is feasible and safe. Signal quality is stable and artifacts are easily identified. Hemoglobin concentration changes can be rapidly displayed as a topographical cortical map on a computer screen, allowing for rapid recognition of temporospatial deoxygenation during surgery. However, further studies are needed to assess diagnostic accuracy of multichannel NIRS measurements during cardiac and thoracic aortic surgery.

Reference

The inflammatory response after transcatheater aortic or surgical valve replacement: a comparison between current treatment modalities
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Objectives: The perioperative inflammatory response in patients with transcatheter (TAVR) or isolated aortic valve stenosis undergoing surgical valve replacement (SAVR) was investigated.

Methods: Patients were prospectively allocated to one of the following treatment modalities: SAVR using minimized extracorporeal circulation (MECC) or conventional extracorporeal circulation (CECC) or TAVR using the transfemoral (TF) or transapical (TA) access route. Following exclusion criteria included were defined: emergency treatment, participation in another study, intake of immunosuppressive or antibiotic drugs and infection. We investigated HLA-DR, CRP and sCD62L and the cytokine IL-6, IL-8, IL-10 levels before the procedure and at 4, 24, and 48 h after aortic valve replacement.

Results: 101 of 718 patients undergoing SAVR or TAVR during the study period were eligible for the study. IL-6 showed increased intraprocedural concentration and the highest peak with TA-TAVR (p = 0.01). CECC was accompanied by the highest levels of IL-8, IL-10 and CRP (p = 0.017, 0.08, and 0.007, respectively). Only small changes in the inflammatory markers were observed in TF-TAVR. HLA-DR molecules on monocytes were significantly down regulated at 4, 24 and 48 h compared to the pre-treatment levels. Changes can be continuously displayed as a topographical cortical map on a computer screen, allowing for rapid recognition of temporospatial deoxygenation during surgery. However, further studies are needed to assess diagnostic accuracy of multichannel NIRS measurements during cardiac and thoracic aortic surgery.

Reference
Gasping is a valid predictor of ROSC and hospital discharge for in-hospital cardiac arrest occurring on the ward


Introduction: Agonal respiration has been shown to be commonly associated with witnessed events, ventricular fibrillation, and increased survival during out-of-hospital cardiac arrest. There is little information on incidence of gasping for in-hospital cardiac arrest (IHCA). Our “Rapid Response Team” (RRT) missions were monitored between December 2010 and March 2015, and the prevalence of gasping and survival data for IHCA were investigated.

Methods: A standardized extended in-hospital Utstein data set of all RRT-interventions occurring at the University Hospital Basel, Switzerland, from December 13, 2010 until March 31, 2015 was consecutively collected and recorded in Microsoft Excel (Microsoft Corp., USA). Data were analyzed using IBM SPSS Statistics 22.0 (IBM Corp., USA), and are presented as descriptive statistics.

Results: The RRT was activated for 636 patients, with 459 having a life-threatening status (72%; 33 missing). 270 patients (59%) suffered IHCA. Ventricular fibrillation or pulseless ventricular tachycardia occurred in 42 patients (16%) of CA and were associated with improved return of spontaneous circulation (ROSC) (36/72%) vs. 143 (67%; p < 0.001)), and discharge with good neurological outcome (Cerebral Performance Categories of 1 or 2 (CPC) (21 (55%) vs. 41 (19%; p < 0.001)). Gasping was seen in 128 patients (52% of CA: 46 missing) and was associated with an overall improved ROSC (99 (78%) vs. 55 (59%; p = 0.003)). In CAs occurring on the ward (154, 57% of all CAs), gasping was associated with a higher proportion of shockable rhythms (11 (16%) vs. 2 (3%; p = 0.010)), improved ROSC (62 (90%) vs. 34 (55%; p < 0.001)), and hospital discharge (25 (68%) vs. 48 (23%; p < 0.001)), and with discharge with good neurological outcome (CPC 1 or 2 (21 (56%) vs. 41 (18%; p < 0.001)). Gasping was not associated with neurological outcome. Gasping was frequently observed accompanying IHCA. The faster in-hospital patient access is probably the reason for the higher prevalence compared to the prehospital setting. For CA on the ward without continuous monitoring, gasping correlates with increased shockable rhythms, ROSC, and hospital discharge.

Performance of a rural ambulance service without physician support

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Introduction: To our knowledge, this is the first study showing altered CPM in patients with acute low back pain. Patients’ EEG demonstrated shorter SEP latencies in the control group compared to the LBP group during ice water stimulation using 128-channel electroencephalography sampled at 2 kHz. The first long latency negative component of the SEP responses from the vertex were analyzed after the 1st (N1) and the 5th (N5) pulse in each burst. Data are presented as means ± SD. Mixed-model ANOVA was used for analysis.

Results: For the N1, patients had significantly shorter SEP latencies in patients with acute low back pain (LBP group) of less than 4 weeks duration, without history of chronic low back pain, and having a pain intensity of at least 3 (numerical rating scale 0–10) were matched to eleven healthy volunteers (CTRL group). As test stimuli, bursts of five 1-ms electrical pulses with an intensity 1.5 times above pain threshold were applied percutaneously every 5 seconds onto the median nerve of the left hand for 10 minutes (baseline). Then subjects immersed their right hand in ice water (conditioning stimulus), while the same electrical stimulation was applied for the next 10 minutes to investigate CPM. SEP in response to electrical stimulation were measured before and during ice water stimulation using 128-channel electroencephalography sampled at 2 kHz. The first long latency negative component of the SEP responses from the vertex were analyzed after the 1st (N1) and the 5th (N5) pulse in each burst. Data are presented as means ± SD. Mixed-model ANOVA was used for analysis.

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CANTADO is useful for ambulatory anterior cruciate ligament reconstruction

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Background and aims: Anterior cruciate ligament reconstruction (ACLR) is often an ambulatory procedure and postoperative complication rate is the same for out- and inpatients [1]. ACLR is associated to severe pain [2] and continuous femoral nerve block provides a significant analgesia [3, 4]. In our hospital, no procedure exists for postoperative pain treatment with a perineural home catheter. The aims of the study were to assess the safety and effectiveness of this technique on ACLR’s outpatients through a homecare program (Catheter ANTAligne à Domicile [5]).

Methods: 37 consecutive patients undergoing elective ACLR were assessed for CANTADO according to surgery and anesthesis criteria. CANTADO’s stages were: 1) postoperative perineural femoral catheter (PNFC) was connected to the PCA elastomeric pump filled with ropivacaine 0.2% (basal infusion 4 to 6 ml/h, bolus dose 5 ml, bolus lockout 30 min.). Paracetamol and NSAID were included in treatment (tramadol as backup). Postoperative knee brace was placed. 2) 24h postoperative care nurse visit at home. 3) 48h knee dressing changing, PNFC ablation and phentamin phtherapy at the hospital. The anesthetist consultant could be called on phone by the patients and homecare nurses 24h/24 during CANTADO. Patient’s safety, analgesia effectiveness (NRS <4) and patient satisfaction were assessed by phone call 2–4 days after PNFC ablation.

Results: 33 of 37 patients were enrolled (4 patients don’t meet eligibility criteria). Patient’s mean age was 30 years (range 15 to 52) and 37% were female. 3 patients complain about pain. No neurological dysfunction was present after 2 months.

Conclusions: Our study suggests that CANTADO provides a safe and useful program for ACPR’s outpatients. It can be used for other operations, i.e., hand and ankle surgery. Moreover, it could contribute to cost saving by a same-day discharge.

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Analgies effects of oxytocin receptor modulation in healthy volunteers

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Background and aims: Oxytocin, a hypothalamic neuro-hormone involved in parturition and breastfeeding, may also play a role in pain modulation via descending neuronal circuits projecting to lamina I-III of the spinal cord. Activation of glutamatergic and GABAergic interneurons at this level may cause pain inhibition. Additionally to GABAergic modulation, oxytocin can selectively block A-delta and C-fibers. Intrathecally administered oxytocin prevents long-term potentiation, an important mechanism of enhanced central pain processing. The present study evaluates the analgesic effects of the oxytocin agonist carbetocin by multimodal pain testing.

Methods: This is a randomized double-blind placebo-controlled crossover study in 25 healthy male volunteers testing 0.1 mg intravenous carbetocin. The primary endpoint was intramuscular lorazepam 1mg and patient satisfaction were assessed by phone call 2–4 days after PNFC ablation.

Results: For the primary endpoint, there was no significant difference between carbetocin and placebo at any time (interaction p > 0.5). The area of secondary allodynia was significantly lower with carbetocin, compared to placebo (joint p < 0.001).

Conclusions: This preliminary analysis failed to demonstrate an analgesic effect of carbetocin on the primary endpoint, but is highly suggestive for an antiallodynic effect of this compound.
cells have not been characterized. In order to better understand the mechanisms of development of neuropathic pain it is important to be described.

Methods: SNI (spared nerve injury) surgery was performed on Sprague Dawley adult male rats. This is one of the experimental models of neuropathic pain, inducing hypersensitivity in the sural territory. BrdU injection and staining for proliferation and immunohistochemistry with antibodies to mark respectively microglia (Iba1), astrocytes (GFAP), T-lymphocytes (CD2) and cytotoxic T-lymphocytes (CD8) were performed. mRNA expression of Iba1 was also measured. A spinal cord injury model was used as a positive control for T-cell infiltration.

Results: In the dorsal horn ipsilateral to SNI, Iba1 and BrdU stainings revealed the peripheral activation and proliferation respectively, attesting neuroinflammation with various timeframe depending on the parameter analyzed. Iba1 expression peaked at D4 and D7 respectively at the mRNA and protein level. Proliferation occurred almost only in Iba1 positive cells and peaked at D2. We found no increase in GFAP signaling. There were very few CD2 or CD8 positive cells in contradoction to some published data. We therefore had to exclude a technical problem and used a spinal cord injury model as positive control for lymphocyte infiltration. We observed a pronounced infiltration of both CD2 and CD8 positive T-cells in that model validating our negative result after SNI.

Conclusions: Although we show neuroinflammation following SNI with Iba1 and BrdU, we were unable to detect a clear T-lymphocyte infiltration in the spinal cord. SNI seems not to trigger a T-lymphocyte infiltration in the spinal cord in our hands. We emphasize that various reactions of microglia are observed after SNI with different timeframe and therefore the term “activation” without specific description should be used with caution.

Optimal number of injections for ultrasound-guided brachial plexus block: a systematic review and meta-analysis

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Background and aims: In a busy operating theatre, rapid procedure time and high success rates are critical to efficient care. This meta-analysis aimed to evaluate the optimal number of injections for ultrasound-guided brachial plexus block to ensure both efficient procedure time and high success rates.

Methods: This meta-analysis was performed according to the PRISMA statement guidelines. The primary outcome was block success rate, analysed according to the technique of injection (single versus multiple injections). Secondary outcomes included procedure time, onset time of action, rate of paraesthesia during the procedure and persistent neurological deficit (>24h).

Results: Nine controlled trials, including 859 patients were identified. The overall success rate of brachial plexus block was 92%. A single injection technique is equivalent to a multiple injection technique (p = 0.77), in all subgroups except the supravacularvular subgroup (p = 0.03) (fig. 1). However, when a random effects model was applied to the supravacularvular subgroup, where P value was 56%, no statistically significant difference was observed (p = 0.21). Procedure time was shorter in the single-injection group (mean difference: −2 min; 95%CI: −3, −1; p < 0.00001) with equivalent onset time of action (mean difference: 2 min; 95%CI: −1, 5; p = 0.14). The lower number of needle passes (mean difference: −2; 95%CI: −4.1, p = 0.0001) was associated with fewer episodes of paraesthesia (risk ratio: 0.6; 95%CI: 0.4, 1.0; p = 0.04), but without difference in persistent neurological deficit (risk ratio: 0.7; 95%CI: 0.2, 2.3; p = 0.39).

Conclusions: During ultrasound-guided brachial plexus block, a single-injection technique provides an equivalent success rate to a multiple-injection technique, but with reduced procedure times and fewer paraesthesias.
Continuous femoral nerve block does not worsen functional outcomes after anterior cruciate ligament reconstruction: a randomized, controlled, simple-blind trial

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Background and aims: Continuous femoral nerve block (CFNB) after anterior cruciate ligament reconstruction (ACLR) may result in femoral nerve injury, in turn worsening functional outcomes. This RCT compared electrophysiological and functional outcomes after ACLR where analgesia was provided with CFNB or intravenous patient-controlled analgesia (IVPCA) of morphine.

Methods: After ethics committee approval, 54 patients scheduled for ACLR were randomized to receive either a CFNB placed prior to surgery, followed by an infusion of ropivacaine for 2 days with oxycodone or IVPCA of morphine. The primary outcome was compound muscle action potential (CMAP) area from the quadriceps muscle measured at 6 weeks postoperatively. Secondary outcomes were range of active flexion, quadriceps muscle power, and distance walked. Other outcomes included total equivalent intravenous morphine consumption, pain scores, and rate of PONV at 24 and 48 h postoperatively.

Table 1 Functional outcomes. Data are presented as mean and 95% confidence interval.

<table>
<thead>
<tr>
<th>Group CFNB</th>
<th>Group IVPCA</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active flexion (°)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>67.2 (59.7;74.8)</td>
<td>57.2 (49.2;65.1)</td>
</tr>
<tr>
<td>POD 2</td>
<td>75.1 (69.6;80.7)</td>
<td>72.1 (65.0;79.3)</td>
</tr>
<tr>
<td>POD 3</td>
<td>76.2 (67.7;84.7)</td>
<td>78.8 (68.2;89.3)</td>
</tr>
<tr>
<td>Quadriceps muscle strength (subjective scale 1–5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>2.1 (1.8;2.4)</td>
<td>2.5 (2.3;2.7)</td>
</tr>
<tr>
<td>POD 2</td>
<td>2.5 (2.3;2.8)</td>
<td>2.8 (2.5;3.0)</td>
</tr>
<tr>
<td>POD 3</td>
<td>2.7 (2.4;3.1)</td>
<td>3.0 (3.0;3.5)</td>
</tr>
<tr>
<td>Distance walked (m)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>46.6 (34.5;58.7)</td>
<td>55.3 (36.4;74.2)</td>
</tr>
<tr>
<td>POD 2</td>
<td>86.0 (68.9;103.1)</td>
<td>88.0 (62.6;113.4)</td>
</tr>
<tr>
<td>POD 3</td>
<td>124.0 (91.0;157.0)</td>
<td>124.5 (85.7;163.4)</td>
</tr>
</tbody>
</table>

Table 2 Pain related outcomes. Data are presented as mean and 95% confidence interval.

<table>
<thead>
<tr>
<th>Group CFNB</th>
<th>Group IVPCA</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative IV morphine equivalent (mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–24 hours</td>
<td>18.6 (13.5;23.7)</td>
<td>35.9 (25.8;46.0)</td>
</tr>
<tr>
<td>24–48 hours</td>
<td>5.2 (1.2;9.2)</td>
<td>11.8 (5.8;17.8)</td>
</tr>
<tr>
<td>Pain (VRS, 0-10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>1.3 (0.6;2.0)</td>
<td>1.6 (0.8;2.3)</td>
</tr>
<tr>
<td>POD 2</td>
<td>0.8 (0.3;1.2)</td>
<td>0.7 (0.2;1.3)</td>
</tr>
<tr>
<td>POD 3</td>
<td>0.7 (0.1;1.2)</td>
<td>0.5 (0.4;1.4)</td>
</tr>
<tr>
<td>Incidence of PONV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>POD 2</td>
<td>4%</td>
<td>17%</td>
</tr>
<tr>
<td>POD 3</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Results: CMAP area at 6 weeks was equivalent in both groups (group CFNB: 47±4 mV·ms; group PCA: 51±6 mV·ms; p = 0.50). While no statistically significant differences were detected between groups in functional (table 1) or pain outcomes, morphine consumption at 24h was reduced by CFNB (table 2).

Conclusions: Despite prior contrary findings, CFNB in this study did not result in femoral nerve injury or worsen functional outcomes after ACLR. Analgesia was not improved beyond 24 postoperative hours although this secondary outcome should be interpreted with caution.

The analgesic efficacy of sciatic nerve block in addition to femoral nerve block in patients undergoing total knee arthroplasty: A systematic review and meta-analysis

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Table 1

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials</th>
<th>SNB+FNB</th>
<th>FNB</th>
<th>RR (95% CI)</th>
<th>Mean difference (95% CI)</th>
<th>P (%)</th>
<th>Test for heterogeneity (p)</th>
<th>Test for overall effect (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV morphine consumption (mg)</td>
<td>24h postop</td>
<td>5</td>
<td>167</td>
<td>106</td>
<td>-6 (-5, -7)</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IV morphine consumption (mg)</td>
<td>48h postop</td>
<td>3</td>
<td>98</td>
<td>106</td>
<td>2 (3, 0)</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pain scores (VAS, VRS or NRS,</td>
<td>0–100) at rest 12h postop</td>
<td>8</td>
<td>229</td>
<td>223</td>
<td>-6 (-4, -7)</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pain scores (VAS, VRS or NRS,</td>
<td>0–100) on movement 12h postop</td>
<td>3</td>
<td>75</td>
<td>76</td>
<td>-6 (-2, -8)</td>
<td>0.16</td>
<td>0.0003*</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Pain scores (VAS, VRS or NRS,</td>
<td>0–100) at rest 24h postop</td>
<td>9</td>
<td>255</td>
<td>259</td>
<td>2 (4, 1)</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pain scores (VAS, VRS or NRS,</td>
<td>0–100) on movement 24h postop</td>
<td>6</td>
<td>173</td>
<td>182</td>
<td>3 (5, 0.1)</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Background: A previous review on the analgesic contribution of sciatic nerve block (SNB) in patients undergoing total knee arthroplasty (TKA) with femoral nerve block (FNB) remained inconclusive, but was not based on formal statistical evaluation [1]. We undertook a meta-analysis to assess the postoperative analgesic efficacy of SNB in addition to FNB after TKA.

Method: The primary outcome of this meta-analysis was cumulative IV morphine consumption at 12h postoperatively, analysed according to the type of block: FNB+SNB (single-shot injection or continuous SNB) vs FNB only. Secondary outcomes were IV morphine consumption at 24h and 48h postoperatively, pain scores at rest and on movement at 12, 24 and 24h postoperatively and rate of PONV at 24h postoperatively.

Figure 1
Cumulative IV morphine consumption at 12h postop (mg).

Table 1
Secondary endpoints. * denotes significant results
Results: 11 controlled trials were identified including 514 patients. When added to FNB, SNB significantly reduced cumulative iv morphine consumption at 12h postoperatively, with a mean difference of 7 mg (95%CI: –10; –4; p <0.0001; fig. 1). All secondary outcomes were also significantly reduced (table 1).

Conclusion: SNB confers additional postoperative analgesia in patients undergoing TKA with FNB.

Reference

Table 1
Secondary outcomes.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials</th>
<th>Lidocaine</th>
<th>Placebo</th>
<th>Mean difference</th>
<th>I² (%)</th>
<th>Test for overall effect (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first analgesic request (hours)</td>
<td>9</td>
<td>224</td>
<td>227</td>
<td>12.1 [0.3, 23.9]</td>
<td>96</td>
<td>0.04</td>
</tr>
<tr>
<td>IV morphine consumption at 2h postoperatively (mg)</td>
<td>22</td>
<td>569</td>
<td>564</td>
<td>–3.4 [–5.5, –1.3]</td>
<td>97</td>
<td>0.002</td>
</tr>
<tr>
<td>IV morphine consumption at 12h postoperatively (mg)</td>
<td>5</td>
<td>156</td>
<td>212</td>
<td>–3.6 [–5.0, –2.2]</td>
<td>0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Early pain scores at rest (VAS, VRS or NRS, 0–100)</td>
<td>24</td>
<td>681</td>
<td>673</td>
<td>–6.9 [–9.5, –4.4]</td>
<td>75</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Intermediate pain scores at rest (VAS, VRS or NRS, 0–100)</td>
<td>22</td>
<td>601</td>
<td>599</td>
<td>–5.7 [–7.6, –3.7]</td>
<td>66</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Late pain scores at rest (VAS, VRS or NRS, 0–100)</td>
<td>31</td>
<td>849</td>
<td>843</td>
<td>–2.72 [–4.9, –0.6]</td>
<td>82</td>
<td>0.01</td>
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<td>Rate of PONV</td>
<td>28</td>
<td>773</td>
<td>827</td>
<td>0.8 [0.7, 0.9]</td>
<td>0</td>
<td>0.003</td>
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<td>Hospital length of stay (day)</td>
<td>21</td>
<td>604</td>
<td>600</td>
<td>–0.3 [–0.8, 0.1]</td>
<td>81</td>
<td>&lt;0.00001</td>
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Methods: This meta-analysis was performed according to the PRISMA statement guidelines. The primary outcome was cumulative IV morphine consumption at 24h postoperatively, analysed according to the type of surgery (bowel surgery, urologic surgery, gynaecologic surgery, orthopaedic surgery, miscellaneous). Secondary outcomes included IV morphine consumption at 2h and 12h postoperatively, pain scores at rest at 2h, 12h and 24h postoperatively, rate of postoperative nausea and vomiting, hospital length of stay, and lidocaine-related side-effects (drowsiness, sedation, arrhythmias).

Results: Forty controlled trials, including 2,205 patients were identified. Administration of IV lidocaine reduced cumulative IV morphine consumption at 24h postoperatively by 5 mg (95%CI: –8, –2.0 mg; p = 0.0005) (fig. 1). Subgroup analysis revealed statistically significant reductions in all subgroups except orthopaedic surgery and miscellaneous. All secondary outcomes were similarly improved in the lidocaine group (table 1). No differences were observed in the rates of the lidocaine related side-effects (table 2).

Conclusions: Intravenous lidocaine improves postoperative pain in bowel, urologic, and gynaecologic surgery, without side-effects. The reduction in hospital length of stay observed should be confirmed by prospective trials as it was a secondary outcome of this investigation.
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