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FM 1

Hip fracture accelerated surgical treatment and care track (HIP ATTACK) trial-feasibility pilot

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Objective: Hip fractures lead to hypercoagulability, stress, and immobility that result in postoperative complications. The 30-day mortality is 6–9%. Researchers hypothesized that early surgery improves outcomes by reducing the exposure to these harmful states. Observational data (1) suggest a mortality reduction after early surgery. Medical clearance and limited operation room (OR) access are considered the main factors for delay. We designed the HIP ATTACK pilot to assess the feasibility of a randomized controlled trial (RCT) comparing surgery within 6 hours of diagnosis versus standard care.
Methods: We randomized patients with a hip fracture requiring surgery during working hours. We excluded patients with open hip fractures, and with intake of non-reversible anticoagulants. Patients were randomized to accelerated care or standard care. Accelerated care consisted in accelerated medical clearance by a dedicated medical team and accelerated operation room access (i.e. the accelerated patients gained priority over elective orthopedic cases). The primary endpoint of the pilot was feasibility of accelerated surgery, i.e. within 6 hours of diagnosis. Further, we collected data on the incidence of a composite of all-cause mortality, nonfatal myocardial infarction, stroke, pneumonia, pulmonary embolism, and major bleeding at 30 days after randomization.
Results: We recruited 60 patients (63% women) in 3 sites. The mean age was 81 years (standard deviation 9). Fifty-five percent (n = 33) of the patients underwent open reduction and internal fixation. Neuroaxial anesthesia was performed in 82% (n = 49). The median time between diagnosis and surgery was 6.0 hours (Q1-Q3 4.2–9.4) in the accelerated and 24.2 hours (Q1–Q3 11.1–29.5) in the standard care group, respectively (p <0.0001). Five (8.3%) patients died within 30 days. The composite endpoint occurred in 13.3% (n = 4) of the accelerated and 30% (n = 9) in the standard patients (hazard ratio 0.6, 95% confidence interval 0.26-1.39).
Discussion: The target time of 6 hours between hip fracture diagnosis and OR arrival was feasible. The30-day incidence of major complications and mortality was very high, with promising results in the accelerated care group. We are planning a large-size RCT to test the hypothesis that accelerated surgery repair improves outcomes.

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FM 2

Anesthetic Conditioning in Liver Transplantation: A multicenter randomized controlled trial

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Background: Due to organ scarcity and increasing use of older organ grafts for liver transplantation, organ-protective strategies are gaining importance. Pharmacologic conditioning with volatile anesthetics attenuates ischemia-reperfusion injury during liver resection [1, 2]. Whether it improves outcome in the setting of liver transplantation is unknown. The aim of this study was to assess the effect of pharmacological conditioning with sevoflurane on liver graft function and clinical outcome of patients undergoing cadaveric orthotopic liver transplantation.
Methods: Liver recipients were randomized from 03/2009 to 08/2012 at three University Centers (Zurich, Sao Paulo, Ghent). After ethic committee approval eligible patients were randomly assigned to receive anesthesia with either propofol (control group) or sevoflurane (sevoflurane group) during organ implantation. Postoperative peak of the aspartate transaminase (AST) was defined as primary endpoint. Secondary endpoints included postoperative peak alanine transaminase (ALT), in-hospital complications (grade I–V) and length of hospital- and ICU stay. Data are presented as median (interquartile range) and odds ratio (95% confidence interval). P <0.05 was considered statistically significant.
Results: Ninety-eight patients were included in the study, 50 receiving sevoflurane and 48 propofol for anesthesia. Biochemical endpoints did not differ significantly between groups: Median peak values of AST were 925 (IQR: 512–3274) U/l and 1097 (IQR: 540–2633) U/l in control and sevoflurane group. Similar results were found for ALT. Regarding clinical endpoints overall complication rate did not differ between groups. However, a trend towards less severe complications was found in patients receiving sevoflurane: Median complication score was grade IIIa (II–IVb) compared to grade II (0-IIIb) in control and sevoflurane group (OR = 0.51 (0.24 to 1.09), p = 0.08). Delayed graft function was seen in 11 patients (23%) receiving propofol compared to 7 patients (14%) receiving sevoflurane (OR = 0.64 (0.20 to 2.02), p = 0.45).
Conclusion: This first multicenter trial evaluating protective effects of volatile anesthetic sevoflurane compared to intravenous propofol in liver transplantation failed to show significant benefits of sevoflurane. However, sevoflurane application showed a trend towards less severe postoperative complications.

1 Beck-Schimmer B, et al. Ann Surg. 2008;248:909–18.
2 Beck-Schimmer B, et al. Ann Surg. 2012;256:837–45.

FM 3

A restrictive fluid regimen combined with norepinephrine during open radical cystectomy decreases the postoperative complication rate and accelerates recovery

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Introduction: Anesthesics and neuraxial anesthesia commonly result in vasodilation/hypotension. Norepinephrine could counteract this effect and thus allow for decreased intraoperative hydration. We investigated whether this approach may reduce postoperative complication rate in patients undergoing radical cystectomy with urinary diversion.
Materials & Methods: In this single-centre, double-blind, randomized trial, 166 patients undergoing radical cystectomy and urinary diversion were equally allocated to receive 1 $ml \cdot kg^{-1} \cdot h^{-1}$ of balanced Ringer's solution until the end of cystectomy and then 3 $ml \cdot kg^{-1} \cdot h^{-1}$ until the end of surgery combined with preemptive norepinephrine infusion at an initial rate of 2 $\mu g \cdot kg^{-1} \cdot h^{-1}$ (low-volume group; n = 83) or 6 $ml \cdot kg^{-1} \cdot h^{-1}$ of balanced Ringer's solution throughout surgery (control group; n = 83). Primary endpoint was the in-hospital complication rate according tot he modified Clavien-Dindo classification for cystectomy. Secondary endpoints were the need for intraoperative/postoperative blood transfusion, and length of hospital stay.
Results: Baseline characteristics were equally balanced between the groups. Forty-four patients developed complications during hospitalization in the low-volume group (52%) versus 63 patients (73%) in the control group ($P = 0.003$). Gastrointestinal complications were lower in the restrictive fluid group (5 [6%] vs. 31 [37%], $P < 0.001$). There were significantly lower incidences of ileus (0 [0%] vs. 8 [10%]; $P = 0.007$) in the low-volume group. The total number of cardiac events was also lower in the low-volume group (17 [20%] vs. 39 [48%], $P < 0.001$). The number of renal, infectious, pulmonary and thromboembolic complications did not differ between the two groups. Median blood loss was 800ml (range: 300–1800 ml) in the low-volume group versus 1200 ml (range: 400–3000 ml) in the control group ($P < 0.001$). Fewer patients in the low-volume group (7 [8%]) needed intraoperative blood transfusion than in the control group (26 [31%]) ($P < 0.001$). Twenty-three patients (28%) in the low-volume group needed postoperative blood transfusion versus 40 patients (48%) in the control group ($P = 0.01$).
The length of stay was shorter in the low-volume group than in the control group; median 15 days [range 11-27] vs.17 [11-95] ($P = 0.02$).
Conclusion: In patients undergoing radical cystectomy with urinary diversion, a restrictive deferred intraoperative crystalloid hydration reduces the incidence of in-hospital complications and accelerates recovery.

FM 4

Effect of different deployment techniques in transapical aortic valve implantation on transcranial Doppler microembolic signals

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Objective: Transapical aortic valve implantation (TA-AVI) is associated with high intensity transient signals (HITS) on transcranial Doppler (TCD) indicative of cerebral microembolism. Since the peak HITS frequency has been observed during prosthesis deployment, improved implantation techniques would be desirable. The Symetis Acurate™ (SA), a new self-expanding system for TA-AVI, is characterized by a two-step deployment mechanism facilitating correct valve positioning. Whether this novel system reduces intraprocedural HITS has not been clarified. The aim of this study was to quantify differences in HITS frequency and pattern during TA-AVI, comparing SA with Edwards Sapien™ (ES).

Methods: TCD recordings of twenty-six patients (median logistic EuroScore 23%) undergoing TA-AVI (SA and ES, n = 13 each) were analyzed for HITS during the following procedural intervals: instrumentation (IN) prior to valvuloplasty, balloon valvuloplasty, prosthesis deployment (DP) and postimplantation (PI) including any maneuvers until transapical access closure.
Results: No differences were detected in interval-related or total bihemispheric procedural HITS load (SA: 303 [200; 594], ES: 499 [285; 941], p = 0.16). With both devices, peak HITS count occurred during DP (almost half of total HITS load). DP released significantly more HITS than IN (SA: p = 0.002; ES: <0.001) or PI (SA: p = 0.007; ES: <0.001). One patient (group ES) suffered new stroke. Total 30-day mortality was 3/26 (SA, n = 1; ES, n = 2; n.s.).
Conclusions: Compared to ES, the novel deployment technique of the SA device was not associated with a reduction of intraprocedural HITS load. Similarity of HITS frequency and pattern with the two TA-AVI devices indicates a common pathomechanism for cerebral microembolism.

FM 5

Selective antegrade cerebral perfusion: effect of increasing flow rate on cerebral oxygen saturation and transcranial Doppler flow velocity

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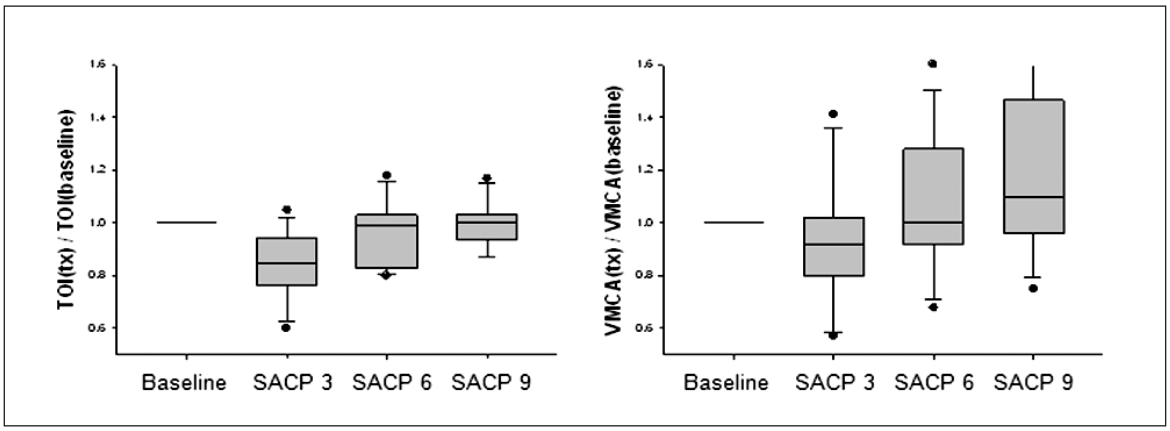
Introduction: Minimal safe selective antegrade cerebral perfusion (SACP) flow is close to 6 ml kg^{-1} min^{-1} in large animals [1], whereas it is uncertain in humans. We assessed the effect of 3 SACP flow rates on cerebral tissue oxygenation index (TOI) and middle cerebral artery flow velocity (VMCA) in patients undergoing hemi-arch replacement in hypothermic circulatory arrest (HCA).
Method: With IRB approval, TOI and VMCA were measured (near-infrared spectroscopy and transcranial Doppler sonography) immediately prior to HCA (baseline), and during stable SACP at 3, 6, and 9 ml kg^{-1} min^{-1}, respectively. Data are mean ± SD; TOI and VMCA are expressed as a fraction of baseline. Statistics used were Friedman test for SACP flow rates, and post-hoc analysis with Wilcoxon's signed-rank test with Bonferroni correction; alpha = 0.05.

Results: In 8 patients (age 67 ± 7 yr; HCA 19 ± 10 min; SACP 17 ± 16 min at 23.1 ± 0.6°C), complete NIRS/TCD data sets were analysed (figure). There was a significant difference in TOI (P <0.001) and VMCA (P = 0.003) during different SACP flow rates. TOI at SACP 3 differed significantly from all other time points (P against baseline, SACP 6 and 9: 0.003, 0.001, and 0.002, respectively). VMCA differed significant between SACP 3 vs. 6, 3 vs. 9, and 6 vs. 9 (P 0.013, 0.002, and 0.015, respectively).

Conclusions: SACP flow augmentation is reflected by increasing TOI and VMCA. At SACP ≥6 ml kg^{-1} min^{-1}, TOI recovers to pre-HCA baseline. Our preliminary human data support animal findings of a lower SACP limit of 6 ml kg^{-1} min^{-1} [1].

Reference:
1 Jonsson O, Morrel A, Zemgulis V, et al. Minimal safe arterial blood flow during selective antegrade cerebral perfusion at 20° centigrade. Ann Thorac Surg. 2011;91:1198–205.



FM 6

The pediatric supraglottic airway devices AirQ™ and Ambu Aura-i™ – blind intubation cannot be recommended

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Background: The pediatric intubating supraglottic airway devices (SAD) AirQ™ and Ambu Aura-i™ have been successfully used for fiberoptic-guided intubation [1]. Blind intubation through adult SADs is a standard procedure with a high success rate. We performed this prospective randomized controlled trial to evaluate blind intubation through the two pediatric SADs. Based on data of the fiberoptic view of the vocal cords [2, 3], we hypothesized that the success rate of the Ambu Aura-i would be at least 50% higher than that of the AirQ.

Methods: With IRB approval and written informed consent, we included 42 children, ASA class I-III with a weight of 5–50 kg. After induction and effective ventilation through the randomized device, the tip of a fiberscope was placed inside the tracheal tube to simulate blind tracheal intubation [2]. Advancement of the tube could be visualized, while there was no fiberoptic guidance. Primary outcome was success rate of simulated blind intubation.
Results: Demographic data did not differ between groups (p >0.05). Particularly, weight and distribution of mask sizes were equal. SAD insertion was successful at first attempt in all but one AirQ, and in all cases at second attempt (p = 1.00). Insertion times (27 ± 5 vs. 23 ± 10 sec, p = 0.14) and leak pressures (16 ± 4 vs. 16 ± 4 cmH_2O, p = 0.88) did not differ between the AirQ and Ambu Aura-i group. Likewise, epiglottic downfolding (15% vs. 5%, p = 0.34) and number of patients showing a full fiberoptic view of the vocal cords (25% vs. 5%, p = 0.09)

were similar. Success of simulated blind tracheal intubation was higher in the AirQ group (20% vs. 0% with the Ambu Aura-i, p = 0.048). In one case, the tube dislodged during removal of the AirQ. In most unsuccessful blind intubation attempts, the ETT was deviating towards the esophagus. There were no major complications.
Discussion: Both SADs are efficient for ventilation. In contrast to our hypothesis, blind intubation success rate was higher for the AirQ, but still unacceptably low (20%). Blind intubation through either AirQ or Ambu Aura-i cannot be recommended. For anesthesia providers who anesthetize children and need a back-up system for emergency airway cases, a suitable fiberscope is mandatory to perform fast and safe fiberoptic-guided intubation through these pediatric intubating SADs.

References
1 Jagannathan. Pediatr Anest. 2012;22(12):1197–204.
2 Theiler Br J. Anaesth. 2011;107(2):243–50.
3 Jagannathan. Anesth Analg. 2011;112(1):176–82.

FM 7

Automated assessment of difficult ventilation with facial recognition techniques

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Introduction: Failure/difficulty in mask ventilation for patients undergoing general anesthesia represent a significant cause of morbidity and mortality. Upper airway collapse or anatomical features play a role and a close relationship between difficult ventilation and intubation exists. No simple test can effectively predict difficulty and no scale has been unanimously recognized to grade difficulty. We propose a method using computer vision and machine learning to grade and predict difficult ventilation.
Methods: Patients necessitating general anesthesia were enrolled at the anesthetic consultation. Besides demographics, video recordings and depth maps of the head and neck were collected with two webcams and a Kinect®. Computer vision models computed morphological features (MF) known as relevant to difficult ventilation or intubation in static, dynamic, frontal and lateral mode. A classifier was trained to assign the patient a 4 grade mask ventilation difficulty scale against the anesthetist assessment while in the operating room (1 = ventilated by mask 2 1+oral airway 3 = 2+necessitating two providers 4 = impossible to ventilate). ANOVA, t-test and Fischer's exact test were applied as appropriate.
Results: In the first 12 months of the study, ventilation difficulty was assessed for 665 patients (Grade 1 = 469, Grade 2 = 136, Grade 3 = 60). No patients were described as impossible to ventilate. Among grade 3 patients, statistically significant factors were male gender (n = 50, 83.3%), patients with denture, especially if upper complete dentures (n = 7, 11.7%) and BMI >26 kg/m^2 (n = 45, 75.0%) and Mallampati (MP) III classes (n = 11, 18.3%) while MP IV as a single predictor was not significant. Correlation between difficult ventilation and difficult intubation (n = 10, 16.7%) was also found.
Training a classifier with unbalanced classes allows risk of over fitting. Therefore, the machine analysis was restricted to 180 patients.
The classifier underlined relevance of relationship between mouth opening surface and that of the tongue, the morphology of the tongue (convex, concave or horizontal) and jaw mobility. Analysis of the 2000 next patients is underway and will add precision to identification of morphological features as well as further increase the specification of the classifier.
Conclusions: This study presents encouraging results for a fully automatic computer vision based system while identifying new MF to assess the difficulty of ventilation.

FM 8

Performance of the pediatric Laryngeal Mask Airway Supreme™ compared with the pediatric Ambu Aura Once™

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Background: A growing number of pediatric supraglottic airway devices (SAD) are released. The LMA Supreme (LMA-S) has been successfully tested in adults and offers the advantage of gastric access, but pediatric data are limited. We performed this prospective observational study to evaluate the performance of the LMA-S, and compared it to our published data from the pediatric Ambu Aura Once in 73 children [1]. The primary hypothesis was that the mean leak pressure of the LMA-S would not differ >10% from the 18 cmH_2O of the Aura Once.
Methods: With IRB approval and a waiver for written informed consent, we included children with a weight of 5–30 kg, scheduled for elective surgery under general anesthesia with a SAD. Primary outcome parameter was airway leak pressure.
Results: We included 80 children. Weight in the LMA-S group and in the Aura Once group was 19.8 ± 5.9 vs. 18.4 ± 5.7 kg, respectively (p = 0.15). Data about performance are given in table 1. The 95% confidence interval of the difference in airway leak pressure was –0.82 to 1.42 cmH_2O. Therefore, the difference was <10%, confirming our primary hypothesis. There was no difference in success rates. The Aura Once showed a better alignment with laryngeal structures as reflected by a lower incidence of epiglottic downfolding and a better fiberoptic view on the glottis through the opening of the SAD. Participants judged the LMA-S as easier to insert (p = 0.02). There were no major side effects in either group.
Discussion: With high success rates >95%, both the LMA Supreme and the Ambu Aura Once seem suitable for ventilation of anesthetized children. Both devices show equal airway leak pressures, insertion times, and success rates. The LMA-S was deemed easier to insert, but it showed a less favorable alignment with the laryngeal structures.

Reference
1 Theiler et al. Anesthesiology. 2011;115:102–10.

Table 1: Supraglottic airway device performance. Data are n (%) or mean ± SD.

	LMA Supreme (n = 80)	Aura Once (n = 73)	p-value
Airway leak pressure (cmH_2O)	17.9 ± 3.5	18.2 ± 3.5	0.60
Success at first attempt	77 (96)	67 (92)	0.41
Overall success	79 (99)	71 (97)	0.94
Difficulty of insertion on a scale from 1-5	77/ 2 / 0/ 0/ 0 (96/ 4/ 0/ 0/ 0)	57/ 10/ 2/ 1/ 0 (81/ 14/ 3/ 1/ 0)	0.02
Time until successful ventilation (sec)	23.9 ± 5.8	24.8 ± 8.2	0.43
Epiglottic downfolding	11 (16)	3 (4)	0.04
Fiberoptic view grade 1/2 /3 /4*	27/ 29/ 10/ 2 (34/ 36/ 13/ 3	61/ 8/ 0/ 0 (86/ 11/ 0/ 0)	<0.01

* 1 = full view of glottis, 2 = partial view, 3 = only epiglottis, 4 = no glottic structures

FM 9

Evaluation of 6 video-laryngoscopes in a difficult airway scenario. A multicenter trial involving 720 anesthetized patients

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Background: Video-laryngoscopes (VLS) are increasingly used and are aggressively marketed, but independent evaluation of efficacy and success in managing difficult airways is scarce. This multicenter, prospective randomized controlled trial evaluates six different VLS in a difficult airway scenario using a stiff extrication collar in a planned total of 720 elective surgical patients.
Methods: After IRB approval and written informed consent, 720 patients without predictors for a difficult airway, scheduled for elective surgery at the University Hospitals in Bern, Lausanne and Geneva are included. After induction of anesthesia, an extrication collar was adjusted to the patient's neck, limiting mouth opening and neck movement. Operators were attending anesthesiologists who had experience with all VLS studied. We evaluated the clinical performance of 6 VLS with and without a guiding channel for intubation (see table). Primary outcome was intubation success at first attempt within 180 seconds.
Results: So far, 179 patients have been enrolled. Allocation of the VLS see table below. Sixty-eight (38%) were females, age was 50 ± 18 yrs, height 175 ± 11cm, weight 77 ± 15 kg, BMI 26 ± 4 kg*m^{-2}, mouth opening after neck collar placement was decreased by 21 ± 6 mm to 24 ± 4 mm (p <0.001). We found no demographic differences between the groups. All outcome data are presented in the table below. There were no serious adverse events and no periods of hypoxia during intubation.
Discussion: Not all VLS evaluated reached the desirable intubation success rate of >90%. Most devices required two attempts to reach this success rate. The integrated tracheal tube guidance does not seem to offer any advantages over unguided laryngoscopes in the hands of experienced anesthesiologists.

Table
Data presented as mean ± SD or number (%). Statistical significance level p <0.05.

	Devices without a guiding channel for tracheal intubation			Devices with a guiding channel for tracheal intubation			
Outcome	C-MAC™ n = 33	GlideScope™ n = 28	McGrath™ n = 27	Airtraq™ n = 24	A. P. Advance™ n = 31	King Vision™ n = 36	p-value
Success at 1st attempt	31 (94)	24 (86)	26 (96)	18 (75)	16 (52)*	29 (81)	<0.001
Overall success rate	32 (97)	28 (100)	26 (96)	23 (96)	26 (84)	36 (100)	0.02
Time necessary for the successful attempt	76 ± 45	85 ± 46	80 ± 38	57 ± 36	108 ± 52**	87 ± 42	0.01
Percentage of glottic opening visible	88 ± 16	90 ± 21	82 ± 21	93 ± 9	61 ± 33***	87 ± 16	<0.001

* statistically different to C-MAC, GlideScope and McGrath
** statistically different to Airtraq
*** statistically different to all other five devices
Bonferroni correction factor applied

FM 10

Volatile anaesthetics and positive pressure ventilation impair left atrial performance – A transthoracic echocardiographic study in young healthy adults

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Background: Animal and *in vitro* studies suggest that volatile anaesthetics affect left atrial (LA) function [1, 2]. We hypothesized that human LA function and dimensions are altered by volatile anaesthetics *in vivo*.
Methods: We studied 59 healthy adults (aged 18–48 years; 20 female) undergoing minor surgery under general anaesthesia. The unpremedicated patients were randomly assigned to general anesthesia with sevoflurane, isoflurane or desflurane. Examinations by transthoracic echocardiography (TTE) were performed at baseline and after induction of anaesthesia and placement of a laryngeal mask during spontaneous breathing (SB). After changing to intermittent positive pressure ventilation (IPPV), an additional TTE was performed. TTE examinations were focused on velocity-time integral of late peak transmitral inflow velocity (A_{VTI}) and maximal LA volume. In addition, late diastolic velocity (a') of the mitral annulus, and calculated LA ejection fraction and force were evaluated by an investigator blinded to the type of volatile anaesthetic.
Results: The three volatile anaesthetics similarly reduced A_{VTI}, a', LA ejection fraction, LA ejection forces. Addition of IPPV markedly added to these effects and decreased maximal LA volume.
Conclusions: Volatile anaesthetics in vivo negatively affected human LA conctractile function. Addition of IPPV decreased LA maximal volume and further impaired LA function. The clinical implications of these findings need to be assessed in further studies.

References:
1 Gare et al. Anesthesiology 2001.
2 Hanouz et al. Anesthesiology 2000.

All patients (n = 59)	Baseline	SB	PPV	P
Maximal volume (cm^3)	44.2 ± 18.9†	42.2 ± 16.9#	33.3 ± 16.1†#	0.002
Minimal volume (cm^3)	15.5 ± 8.2	16.1 ± 8.6	15.5 ± 9.0	0.895
A_{VTI} (cm)	4.1 ± 1.2*†	3.2 ± 1.1*	2.8 ± 1.0†	<0.001
a' (cm s^{-1})	7.6 ± 1.5*†	6.1 ± 1.7*#	4.6 ± 1.6†#	<0.001
LA Ejection fraction (%)	66 ± 10†	61 ± 12#	55 ± 12†#	<0.001
Ejection force (kdynes)	12.9 ± 5.8*†	8.9 ± 4.1*	7.4 ± 4.1†	<0.001

*baseline *vs* SB <0.025; † baseline *vs* IPPV <0.025; # SB *vs* IPPV <0.025 by ANOVA and Bonferroni adjustment.

FM 11

The maximum effective needle-to-nerve distance for ultrasound-guided interscalene block

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Introduction: Direct needle trauma and intraneural injection are important mechanisms of nerve injury associated with regional anesthesia. Despite ultrasound (US) guidance, unintentional intraneural needle tip placement is common, especially during interscalene block (ISB) [1]. While needle-to-nerve proximity is the fundamental requisite for a successful block [2], the maximum effective distance between the needle tip and the target nerve is unknown. This study aimed to determine the maximum distance the needle tip can be placed from the roots of the interscalene brachial plexus while still achieving a successful block for shoulder surgery.
Material and methods: Twenty adult patients scheduled for ambulatory arthroscopic or open shoulder surgery received an US-guided ISB using 20 mL of bupivacaine 0.5% with epinephrine. The first block was performed with the needle tip positioned outside but in contact with the brachial plexus sheath, at a location equidistant between C5-C6. For subsequent blocks, the Dixon up-and-down method was followed: the distance from needle tip to sheath was increased or decreased by 2 mm for each consecutive patient according to the block success or failure respectively, in the previous patient. The primary outcome was the maximum effective distance required to achieve a successful block in 50% (MED_{50}) of patients.
Results: The MED_{50} and MED_{95} were 8.3 mm (95%CI: 6.3–11.0 mm) and 1.6 mm (95%CI: 0.0–7.0 mm), respectively. Among the 11 patients with a successful ISB, the median intraoperative and postoperative fentanyl consumption was 150 μg (Interquartile Range [IQR] 150–175 μg) and 75 μg (IQR 25–75 μg), respectively. The median NRS pain score in Phase I recovery was 2 (IQR 0–3). Median durations of motor and sensory blockade were 19.8 hours (h) (IQR 15.0–22.3 h) and 10.1 h (IQR 8.5–12.2 h), respectively. The time to first dose of oral opioid analgesic at home was 9.6 h (IQR 9.3–12.1 h). No complications were reported.
Discussion: A successful ISB can be achieved with a distance of 8 mm between the needle tip and the brachial plexus sheath in 50% of patients. Our results suggest that it may not be necessary to position the needle tip as close as possible to the nerve roots during US-guided ISB. Future studies are required to explore the concept of maximum effective needle-to-nerve distance for other types of peripheral nerve blocks with a view towards enhancing safety.

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FM 12

Ultrasound-guided transversus abdominis plane (tap) block for laparoscopic gastric-bypass surgery: a prospective randomized controlled double-blinded trial

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Introduction: Despite the laparoscopic approach, patients can suffer moderate to severe pain following bariatric surgery [1]. The transversus abdominis plane (TAP) block has been demonstrated to improve pain-related outcomes after both laparoscopic [2] and open [3] abdominal procedures. This randomized controlled double-blinded trial investigated the analgesic efficacy of ultrasound-guided TAP blocks for laparoscopic gastric-bypass surgery (LGBS).
Materials and Methods: Seventy patients undergoing LGBS were randomized to receive either bilateral ultrasound-guided subcostal TAP block injections after induction of general anesthesia or none. All patients received trochar insertion site local anesthetic infiltration and systemic analgesia. The primary outcome was cumulative opioid consumption (IV morphine equivalent) during the first 24 hours postoperatively. Interval opioid consumption, pain severity scores, rates of nausea or vomiting, and rates of pruritus were measured during Phase I recovery, and at 24 and 48 hours postoperatively.
Results: There was no difference in cumulative opioid consumption during the first 24 hours postoperatively between the TAP (32.2 mg [95%CI: 27.6–36.7]) and control (35.6 mg [95%CI: 28.6–42.5]; P = 0.41) groups. Postoperative opioid consumptions during Phase I recovery and the 24–48 hour interval were similar between groups, as were pain scores at rest and with movement during all measured intervals. The rates of nausea or vomiting and pruritus were equivalent. There were no complications related to any of the block procedures.
Discussion: Bilateral TAP blocks do not provide additional analgesic benefit when added to trochar insertion site local anesthetic infiltration and systemic analgesia for laparoscopic gastric-bypass surgery.

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FM 13

Quality and Outcome after Bariatric Surgery: European Benchmarking with PAIN-OUT

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Background: Subjects presenting for bariatric surgery are a patient cohort at risk for perioperative complications due to morbid obesity as well as metabolic, cardio-vascular and pulmonary co-morbidity. As several patients had suffered from severe adverse events, e.g. respiratory depression, in the past a prospective analysis of outcome data was performed using the international Acute Pain Registry PAIN OUT (FP7/EC). The aim of this registry is to develop an effective, evidence-based approach to improve the care of patients. Tools for data collection, feedback, benchmarking and decision support are provided via an internet-based register (www.pain-out.eu).
Methods: After approval of the ethics committee and written informed consent patients provided outcome data by filling in the validated *International Pain Outcome* questionnaire on the first day after surgery. Anesthesia and surgery related perioperative variables were documented. Descriptive statistics: mean ± SD or median ($1^{st}/3^{rd}$ quartile).
Results: Complete data of 123 patients (laparoscopic gastric bypass 87, laparoscopic gastric sleeve 20, others 16) could be analyzed. Although the patients received high doses of opioids (recovery room morphine 33.4 ± 28.2 mg, fentanyl 198.3 ± 225.5 μg) and 75% of the patients had a PCA-device for subsequent pain management, pain was not sufficiently treated in the recovery room (mean duration of stay 12.9 ± 6.9 hours) and on the ward. The worst pain experienced after surgery was described with a pain score (NRS = numeric rating scale 0–10) of 7(5/9). Pain related interference with sleep, deep breathing and coughing, activities in and out of bed (mobilization) were mentioned by most of the patients (28–93%).
Although 85.3% had received a prophylactic antiemetic treatment before emergence from anesthesia, 63.5% of the patients suffered from nausea, 19.8% vomited. The PAIN OUT benchmarking tool enabled a comparison to three other hospitals enrolling bariatric patients. Worst pain, time interval suffering from severe pain of NRS >7 and nausea were the variables showing an unfavorable outcome. Further symptoms reported were dizziness (78%) and pruritus (34.6%)
Conclusions: Despite high opioid doses patients experienced significant pain, interfering with coughing, sleep and activities out of bed as well as PONV. Current practice has to be improved and a standardized analgesic regimen using less WHO III opioids and scheduled non-opioid analgesics has to be implemented.

FM 14

Accuracy and procedural time of ultrasound-guided cervical facet joint nerve blocks

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Background: Ultrasound (US)-guidance to block the cervical facet joint nerves has been described in both healthy volunteers and pain patients. Still most practitioners prefer fluoroscopy because of concerns related to accuracy and procedural times with US. We determined the accuracy of US-guided cervical facet joint nerve blocks in chronic neck pain patients and compared the procedural time with the classic fluoroscopic technique.
Methods: 61 patients were randomized to an US-group (n = 47) or control-group with fluoroscopy (n = 14). The joints to be tested were selected depending on the areas of pain. In the US-group, the needle was guided to the target with US-imaging and 0.2 ml of contrast-dye was injected. Fluoroscopic imaging was then performed to evaluate the accuracy of needle placement. The procedural time for the first nerve block of each US-procedure was recorded and compared with the procedural time of the control-group.
Results: A total of 98 needles were placed in the 47 patients of the ultrasound group. Successful block rate (contrast dye at bony target) varied from 86% (95% CI 76–96%) for a C3 and C7 medial branch block to 100% for C5 and C6. The mean procedural time was 86 seconds (SD: 25) in the US-group and 71 seconds (SD: 21) in the control group (p = 0.14).
Conclusions: Ultrasound-imaging is an accurate technique to perform cervical facet joint nerve blocks. Although the procedural time was slightly longer in the US-group than in the control-group, this can be considered as clinically irrelevant.

FM 15

Assessment of labour pain using hand grip force

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The most effective treatment for labor pain is epidural analgesia, but in case of contraindications or maternal preference patient-controlled analgesia (PCA) with intravenous remifentanil may be an alternative. A practical problem during the use of remifentanil PCA is timing of the bolus application. A bolus at the beginning of a contraction is too late for optimum maternal comfort, since the delay of onset of remifentanil action is about 30 sec, and there is a further delay to peak action. A method to predict future contractions would be useful to improve timing of remifentanil bolus. The tocographic signal is too unreliable to be used as a predictor. An alternative may be a signal generated by voluntary action of the parturient. Here, we tested the possibility to use hand grip force measured by dynamometer to signal the pain experienced during the contractions and create a time series for prediction of further contractions. The aim of the study was to evaluate A) if the dynamometer signal is sufficiently reliable to predict further contractions and B) if a correlation between hand grip force and pain intensity evaluated on a numeric rating scale can be obtained.
Methods: 42 parturients were included in an observational study. A dynamometer was calibrated for individual hand muscle strength corresponding to pain intensities of 5 and 10 on a 0–10 numeric rating scale (NRS). Pain was recorded during early and late labor for 10–20 min using dynamometer and NRS. Primary endpoint was the correlation coefficient (Pearson) between NRS ratings and the intensity of the peaks recorded by the dynamometer.
Results: All contractions recorded by the external tocogram were also registered by the dynamometer. Hand grip force in early labor was only moderately correlated with the subjective pain level expressed on the NRS ($r^2 = 0.36$).
Discussion: The signal of a hand dynamometer appears to be reliable enough to be used to calculate a time series to predict a future contraction and thus guide remifentanil bolus administration. The correlation between hand grip force and pain intensity, however, is too weak to be used to adjust bolus dose. The future application of the dynamometer to improve remifentanil PCA use during labor will depend on the performance of a mathematical model to predict the occurrence of the next contraction. Longer time series data are needed to develop such a model.

FM 16

Effect of Rufinamide and Oxcarbazepine on peripheral nerve excitability

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Systemic sodium channel blockers are successfully used in the treatment of neuropathic pain. However, their impact on the peripheral nervous system remains unclear. The aim of this study was to evaluate the effect of rufinamide and oxcarbacepine on axonal excitability of peripheral sensory nerves.
Methods: After obtaining institutional ethics committee approval (KEK-ZH-Nr. 2010-0068) and written informed consent, we included 24 healthy volunteers in a randomized, double-blinded, placebo-controlled, crossover study. Over a 10-day period the drugs were gradually increased up to a therapeutic level. We measured nerve excitability parameters of sensory afferents on the median nerve (strength-duration time constant, the recovery cycle after a supramaximal stimulus and threshold electrotonus) using computerized threshold tracking technique (QTRAC®).
Results: Rufinamde affected significantly superexcitability, depolarizing threshold parameters and refractoriness of both, sensory and motor nerve fibers. Oxcarbazepine showed similar changes on motor fibers. However, oxcarbazepine changed significantly peak response, subexcitability and refractoriness in sensory fibers.
Conclusion: Threshold tracking techniques are a suitable tool to measure effects of systemic sodium channel blockers on peripheral nerve excitability. Oxcarbazepine showed a differential effect on sensory peripheral nerve.

FM 17

Long-term exposure to sevoflurane or desflurane attenuates pulmonary inflammatory response *in-vitro*

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Background: Acute lung injury (ALI) and ventilator associated pneumonia (VAP) are still contributing to high morbidity and mortality in intensive care units (ICU) patients [1, 2]. Long-term sedation using volatile anesthetics may attenuate ALI and possibly prevent VAP.
Material & Methods: Rat alveolar epithelial cells type II (L2-AEC; CC-149) were grown until 80% confluence and stimulated with lipopolysaccharide (LPS) to simulate acute pulmonary inflammation in target cells. Cells were incubated in air-tight chambers with 5% CO_2, adding 0.5 MAC sevoflurane (1.1 Vol%), 0.5 MAC desflurane (3.0 Vol%) or air (control) for 24, 48 and 72 hours. To demonstrate validity of the results and the impact on cell death cytotoxicity was measured determining lactate dehydrogenase assay (LDH). Viability was assessed using MTT assay. Interleukin-6 (IL-6) and cytokine-induced neutrophil chemoattractant-1 (CINC-1) as two key inflammatory mediators were measured in the supernatants with the help of ELISA technique. Results were analyzed using linear regression.
Results: Stimulation with LPS provoked a time-dependent increase of IL-6 (+8190 pg/mL, p <0.001) and CINC-1 protein levels (+7580 pg/mL, p <0.001) in the supernatants. This increase in inflammatory mediators was attenuated when cells were exposed to sevoflurane (IL-6: -3727 pg/mL, p = 0.006; CINC-1: –1870 pg/mL, p <0.001), but in an even more pronounced way, when incubated with desflurane (IL-6: –3970 pg/mL, p = 0.002; CINC-1: –2030 pg/mL, p <0.001). In the presence of volatile anesthetics LPS-stimulated cells had slightly higher MTT values in relation to controls (+9%, p = 0.008). LDH levels were not influenced by LPS, sevoflurane, or desflurane.
Conclusion: In this *in-vitro* study we demonstrate for the first time, that the inflammatory response in AEC is attenuated in the long-term presence of volatile anesthetics, without affecting cell viablility. These findings suggest that this *in-vitro* model should be further validated *in-vivo*. Volatile anesthetics could be a future option in ICU patients to treat ALI and to decrease the number of VAP.

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FM 18

Involvement of Inflammatory Cytokines in Nociceptin Receptor Expression in Human Blood Cell Cultures

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Introduction: The nociceptin receptor (NOP) is a G protein-coupled receptor which has high homology with other opioid receptors. It is widely expressed throughout the human immune system and plays a role in immune response and pain. NOP is expressed in human peripheral blood [1, 2] and detected in all leukocyte subsets [3]. However, modulation of NOP in peripheral blood cells is still not clear to date. The aim of this study was to investigate regulation of NOP in human peripheral white blood cells under inflammatory conditions and explore possible mechanisms contributing to the modulation.
Methods: After approval of the ethics committee and written informed consent, 30 healthy volunteers were enrolled in this observational ex vivo study. Peripheral blood was cultured for 0, 3, 6 and 24 hrs with or without lipopolysaccharide (LPS), tumour necrosis factor (TNF)-α, interleukin (IL)-1β, IL-10 or interferon (IFN)-γ. NOP mRNA in white blood cells was detected by quantitative RT-PCR. Cytokine concentrations in supernatants of cultures were measured using ELISA. An additional intervention experiment using anti-cytokine antibodies was conducted to evaluate possible mechanisms involved in the modulation of NOP by LPS.
Results: NOP was constitutively expressed in human peripheral white blood cells (median normalized ratio (1st/3rd quartile): 1.1 (0.8/1.3)). LPS dose-dependently down-regulated NOP mRNA expression at a concentration range between 0.5–10^4 pg/ml with an EC_{50} of 15 pg/ml. LPS 10 ng/ml significantly suppressed NOP when compared to baseline measures (median area under the mRNA-expression-time curve (1st/3rd quartile): 5.4 (4.6/6.6) vs 22.7 (17.1/25.3) normalized ratio · hr, p <0.001). TNF-α 3 ng/ml, IL-1β 3 ng/ml, IL-10 50 ng/ml and IFN-γ 10 ng/ml decreased NOP mRNA levels to varying extents (p <0.05 for all). Anti-TNF-α, anti-IL-1β and the combination of these two antibodies increased NOP mRNA expression 1.6 (95% CI: 1.2–2.0), 1.4 (1.0-1.6) and 1.8 (1.4–2.1)-fold compared to the control (LPS + isotype Ab) (p <0.001 for all). Anti-IL-10 and anti-INF-γ had no effect.
Conclusions: Inflammatory mediators influence NOP mRNA expression in human whole blood cultures. Pro-inflammatory cytokines TNF-α, IL-1β are involved in the LPS induced down-regulation of NOP mRNA.

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FM 19

CD62L (L-Selectin) shedding for assessment of perioperative immune sensitivity in patients undergoing cardiac surgery with cardiopulmonary bypass

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Objective: To investigate the suitability of blood granulocyte and monocyte sensitivity, as measured by the quantity of different agonists required to induce CD62L shedding, for assessment of perioperative immune changes in patients undergoing cardiac surgery with cardiopulmonary bypass.
Methods: Patients scheduled for aortocoronary bypass grafting or for valve surgery were included in this prospective observational study. Blood samples were drawn before anesthesia induction, directly after surgery and 48 hours after anesthesia induction. We determined the concentration of two different inflammatory stimuli – lipoteichoic acid (LTA) and tumor necrosis factor alpha (TNF) – required to induce shedding of 50% of surface CD62L from blood granulocytes and monocytes. In parallel monocyte surface human leukocyte antigen (HLA)-DR, and plasma interleukin (IL)-8, soluble (s)CD62L, soluble (s) Toll-like receptor (TLR)-2 and ADAM17 quantification were used to illustrate perioperative immunomodulation.
Results: 25 patients were enrolled. Blood granulocytes and monocytes showed decreased sensitivity to the TLR 2/6 agonist Staphylococcus aureus LTA immediately after surgery (p = 0.001 and p = 0.004 respectively). In contrast, granulocytes (p = 0.01), but not monocytes (p = 0.057) displayed a decreased postoperative sensitivity to TNF. We confirmed the presence of a systemic inflammatory response and a decreased immune sensitivity in the post-surgical period by measuring significant increases in the perioperative plasma concentration of IL-8 (p#0.001) and sTLR (p = 0.004), and decreases in monocyte HLA-DR (p,0.001), plasma sCD62L (p#0.001). In contrast, ADAM17 plasma levels did not show significant differences over the observation period (p = 0.401).
Conclusions: Monitoring granulocyte and monocyte sensitivity using the "CD62L shedding assay" in the perioperative period in cardiac surgical patients treated with the use of cardiopulmonary bypass reveals common changes in sensitivity to TLR2/6 ligands and to TNF stimulus. Further long-term follow-up studies will address the predictive value of these observations for clinical purposes.

FM 20

Expanding the genetic and electrophysiological spectrum of Paroxysmal extreme pain disorder (PEPD) – A novel L1612P Nav1.7 mutation study

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Background and aims: Paroxysmal extreme pain disorder (PEPD) is a chronic disease characterized by episodes of excruciating pain which is produced by mutations in the SCN9A gene encoding for the alpha-subunit of the Nav1.7 sodium channel. Disease-causing mutations impair the inactivation of the channel. We here describe the genetic, clinical and electrophysiological aspects of a previously unknown PEPD causing mutation (L1612P) and its response to amitriptyline (AMI), a first line drug for neuropathic pain and strong sodium channel blocker.
Methods: We analyzed for SCN9A mutations and/or evaluated clinically the family over 4 generations. We performed whole-cell patch clamp recordings from HEK293 cells transfected with wild-type (WT) or mutant Nav1.7 plasmid. We tested the effect of AMI on the mutation in vitro as well as clinically.
Results: Sequencing of the SCN9A gene identified a novel p.L1216P mutation in all 4 available affected individuals, but not in the 3 at-risk unaffected family members (co-segregation with disease). The mutation induced a huge 30.9 mV depolarizing shift of the steady-state fast inactivation (SSI) curve (V1/2 from –61.8 ± 4.5 (WT) to –30.9 ± 2.2 mV (L1612P)) with a depolarizing shift of the activation curve (V1/2 from –9.0 ± 7.2 (WT) to 0.0 ± 1.9 mV (L1612P)). The theoretical increase in the window current was corroborated by a significant difference in ramp current (1.8 ± 1.4% (WT) and 3.4 ± 0.7% (L1612P)). The L1612P channel also demonstrated a slower current decay, the absence of persistent current and a shorter repriming. AMI was not efficient in treating the index patient. AMI only partially corrected the SSI curve of the mutant channel (–8.51mV) to more hyperpolarized values. Carbamazepine, the usual treatment for PEPD, was not efficient in the 2 patients treated. The mechanism of carbamazepine in PEPD is thought to be the reduction of persistent current, which is absent in our mutation.
Conclusions: 1) The combination of electrophysiological, genetic and clinical evaluation over 4 generations convinces for pathogenicity of this newly described PEPD-causing mutation of SCN9A 2) The lack of efficacy of AMI and carbamazepine are in line with the electrophysiological data 3) There is a potential to implement drug screening in vitro before the administration to patients suffering from PEPD 4) AMI could be helpful in PEPD patients associated with mutation causing a lesser shift in SSI.

P 1

Standart of care in Transfusion Management: The same if Patients participates in a clinical trial or not?

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Introduction: We previously investigated the impact of point-of-care (POC) coagulation monitoring of prothrombin time on intraoperative transfusion management and outcome in a randomized controlled trial (RCT). Here, we analyze if patients who were randomized to "standart of care" in the RCT were treated different than patients not included in a study. Our hypothesis was that inclusion in a RCT about transfusion management decreases transfusion compared to patients not participating in a study.
Methods: Data from patients undergoing elective surgery with an estimated blood loss exceeding 20% of the estimated total blood volume (70 ml/kg) were analyzed. In a retrospective way, we compared two groups: 1.Patients who were randomized to the standart of care group in the RCT and 2.Patients who underwent major orthopedic surgery during the same time period but did not participate in the RCT for organizational, language or other reasons. Outcome parameters were FFP, PRBC and platelets concentrate transfusions, transfusions from a cell salvage device, PACU stay, ICU stay and days in hospital.
Results: Demographic characteristics were comparable in both groups. Of 423 patients not enrolled in the RCT, 139 bled more than 20% of their total blood volume and therfore met the inclusion criteria. In the RCT standart care group 46 (54%) received any allogenic blood products versus 69 (50%) in the daily clinical practice group (p = 0.52). In the RCT 27 (32%) received FFP versus 37 (27%) in daily clinical practice (p = 0.41). 42 (40%) received PRBC in the RCT vs. 66 (47%) in daily clinical practice (p = 0.78). Numbers of patients transferred to the PACU (p = 0.58) or ICU (p = 0.19) and duration of hospitalization (p = 0.53) showed no difference between both patient groups.
Discussion: This retrospective analysis did not detect a difference in transfusion management or outcome parameters between patients included into an RCT and patients in daily clinical practice.
Summary: We compared transfusion management and postoperative outcome of patients with major intraoperative bleeding in patients enrolled in a RCT with a retrospective control cohort not enrolled in a study. Results showed no difference, indicating that participating in a study per se does not influence transfusion management and outcome.

P 2

Model-based cost-consequence analysis of postoperative Troponin T screening in patients undergoing noncardiac surgery – 1-year

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Introduction: Myocardial ischemia after noncardiac surgery (NCS) is associated with 30-day mortality [1]. The majority of these events are asymptomatic [1].
Methods: We conducted a model-based cost-consequence analysis from the perspective of the Canadian public health care. We compared a postoperative Troponin T screening vs. standard care, i.e. Troponin T measurements triggered by ischemic symptoms. We measured the health consequences as the number of prevented death at 1-year and life-years saved over a horizon of 5 years after NCS. Detected myocardial injury after NCS (MINS) during the screening period was defined by a Troponin T ≥0.03 ug/L after NCS without alternative explanation. The model was structured as a decision tree and it assumed the same treatment effect in MINS as in nonoperative myocardial infarctions by aspirin, B-Blockers, ACE-inhibitors and statins. Cost estimates (2011 Canadian dollars [CAD$]) included intervention costs and cost related to subsequent events. Model inputs based on Canadian and international patients enrolled in the Vascular events In Non-cardiac Surgery patIents cOhort evaluatioN (VISION) Study, a large international cohort study that enrolls patients aged ≥45 years undergoing NCS with overnight hospitalisation. We run probabilistic sensitivity analyses with 10,000 iterations and conducted extensive sensitivity analyses.
Results: The screening results were based on 6,021Canadian patients (47.9% men) aged a mean of 65 years (standard deviation 12), the events' incidence on 13,913 patients. The cost to prevent a death at 1 year amounted to CAD$ 22,229. The number needed to screen (NNS) to prevent a 1-year death was 224. The incremental cost per life-year was CAD$ 3,886, the corresponding NNS to prevent a death at 5 years was 149.
Discussion: Based on the estimated incremental cost per health gain, the implementation of a postoperative Troponin T screening after noncardiac surgery seems appealing, in particular in patients at high risk for MINS.

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P 3

Model-based cost-consequence analysis of postoperative Troponin T screening in patients undergoing noncardiac surgery – case dection

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Introduction: Myocardial ischemia after noncardiac surgery (NCS) is associated with 30-day mortality (1). The majority of these events are asymptomatic [1].
Methods: We conducted a model-based cost-consequence analysis from the perspective of the Canadian public health care. We compared a postoperative Troponin T screening vs. standard care, i.e. Troponin T measurements triggered by ischemic symptoms. We measured the health consequences as the number of detected myocardial injury after NCS (MINS) during the screening period. MINS was defined by a Troponin T ≥0.03 ug/L after NCS without alternative explanation. We expressed cost as 2011 Canadian dollars (CAD$). The model was structured as a decision tree and it included the following health states at the end of the screening period: "true positive" (detected MINS), "true negative" (no MINS), "false negative" (missed MINS), and "false positive" (nonischemic Troponin elevations for the screening and noncardiac chest pain, dyspnea or pulmonary edema for the standard care alternative, respectively). Model inputs based on Canadian patients enrolled in the Vascular events In Non-cardiac Surgery patIents cOhort evaluatioN (VISION) Study, a large international cohort study that enrolls patients aged ≥45 years undergoing NCS with overnight hospitalisation. We run probability sensitivity analyses with 10,000 iterations (Microsoft Excel spreadsheets). We conducted extensive sensitivity analyses.
Results: The data were based on 6,021 patients (47.9% men) aged a mean of 65 years (standard deviation 12). The cost to avoid missing an event amounted to CAD$ 1,567 for MINS. The cost-effectiveness of the postoperative Troponin screening was higher in patients' subgroups at higher risk for MINS, e.g. patients undergoing urgent surgery ($ 1,119) or with coronary artery disease ($ 1,025). In the worst and best case scenarios in terms of resource utilisation, the cost to avoid missing a MINS were $ 2,045 and $ 1,097. The 30-day mortality of MINS was 9.6% (95% confidence interval 8.0–11.4%).
Discussion: Based on the estimated incremental cost per health gain, the implementation of a postoperative Troponin T screening after noncardiac surgery seems appealing, in particular in patients at high risk for MINS.

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P 4

Anaesthesia in patients undergoing cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy: A single center experience

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Background: Over the last two decades, cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has become an established therapy for selected patients. The procedure is long and complex with relevant pathophysiological alterations. Regarding anaesthesia management, experience is very limited. Our aim was to analyse the perioperative management and clinical course of patients undergoing CRS and HIPEC.
Methods: After ethic committee approval, anaesthesia and surgical data were gathered retrospectively from electronic patient records (KISIM™). We reviewed all charts of patients undergoing CRS with HIPEC at the University Hospital Zurich from January first, 2009 to December 31, 2011. Furthermore, the post-operative course and specific complications were recorded. Analysis was intervention based. Results are presented as median (range). P <0.05 was regarded as statistically significant.
Results: Fifty-four patients underwent 57 interventions. Median anaesthesia time took 715 (370–1135) minutes. HIPEC induced hyperthermia with median overall peak temperature of 38.1 (35.7–40.2) °C and haemodynamic alterations. Median documented blood loss was 0.8 (0-6) l. Sixteen interventions (28%) were associated with blood transfusions, in 21 operations (40%) coagulation factors were

given. Major surgical complications occurred after 13 interventions (23%) leading to death in 2 patients (4%). Anaesthesia and operation time, bleeding, need for blood tansfusion and coagulation factors were associated with a significantly higher risk for major complications. Odds ratio for major complications was 6.6 (95% confidence interval: 1.3–33.3) if operation time was exceeding the initially scheduled time. Postoperative ventilation was needed after 33 interventions (58%). We found increasing operation time, blood loss and amount of opiods given to increase the risk of postoperative ventilation. Kidney injury occurred after three interventions. In patients younger than 60 years the administration of hydroxyethyl-starch was associated with a higher risk of impaired post-operative kidney function.
Conclusion: CRS with HIPEC is a high risk surgical procedure, requiring coordinated patient-centered management. Besides primary disease and complexity of surgery, the type and amount of fluids administered, blood loss, transfusions and anaesthesia management might have an impact on the patient's outcome.

P 5

Beta-defensin gene copy number variations in sepsis patients

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Background: Sepsis is a systemic inflammatory response after infection, trauma or large operation. 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 effect to modulate immune system. Beta-defensin genes (DEFB) were found to be variable in copy number (2 to 12 per diploid genome). Gene copy number (CN) of *DEFB4* was reported to be proportional to mRNA expression in lymphoblastoid cell lines. Significant association between higher DEFB CN and risk of psoriasis were reported. Based on the functions in immune system and genomic variation for beta-defensins, it is reasonable to investigate the association between DEFB CN and the predisposition to and the clinical course of sepsis.
Method: 721 sepsis patients with complete clinical data and 283 healthy controls were enrolled in this study. Genomic DNA was isolated from peripheral whole blood. DEFB CN was determined by Multiplex Ligation-dependent Probe Amplification (MLPA).
Result: The medians of DEFB CN in both sepsis patients and healthy controls were 4 (P = 0.91), and the distributions of DEFB CN in two cohorts were not significantly different (three categories including CN ≤3, = 4 and ≥5, P = 0.72). In male patients, the median of DEFB CN in non-survivals (5) was significantly higher than that in survivals (4) (P = 0.028). Moreover, a linear trend between DEFB CN and mortality was found (P = 0.024). Logistic regression analysis also showed DEFB CN was an independent factor to determine the outcome. Finally a linear regression model was established between DEFB CN and mortality (r^2 = 0.86, P = 0.0075), and the equation suggests that each increase by 1 copy from 2 copies adds 6.8% (95% confidence interval: 3.04–10.62%) to the mortality. In female patients, the medians of DEFB CN in both survivals and non-survivals were 4 (*P* = 0.97), and the distributions of DEFB CN in survivals and non-survivals were comparable (three categories including CN ≤3, = 4 and ≥5, *P* = 0.40). Logistic regression analysis excluded DEFB CN as an independent factor to determine the outcome.
Conclusion: DEFB CN is not associated with the predisposition to sepsis. Besides, DEFB CN is not associated with outcome of sepsis in female patients. However, increased DEFB CN is associated with bad outcome of sepsis in male patients.

P 6

Validation of Multiple Inert Gas Elimination Technique by Micropore Membrane Inlet Mass Spectrometry in an In-Vitro Lung Model of Lung Compartments With Low-to-Normal Ventilation-Perfusion Ratios

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Background: MMIMS-MIGET has been designed as rapid and direct method to assess the full range of V*A*/Q distributions [1, 2]. In an in-vitro lung model (IVLM), MMIMS-MIGET shunt has been shown to correlate well with preset model shunt [3]. In this study we aimed to compare low (0.005 <V/Q <0.1) to normal (0.1 <V/Q <10) [4] V/Q compartments determined by MMIMS-MIGET (MM-VQ) with reference low -to-normal V*A*/Q compartments as preset in the IVLM (IVLM-VQ).
Method: One single oxygenator (QUADROX-iD Pediatric; MAQUET): was used: (I) sweep gas (air) flows were set at random to 0.05, 0.1, 0.2, 0.4, 0.6, 0.8 and 1 L min^{-1} (V) and (II) saline flow rate was fixed to 2.5 L min^{-1} (Q) using a micro-diagonal pump (DeltaStreamDP-II, Medos), resulting in defined IVLM V/Q ratios. Inert gas solution1 (6 solubilities) was infused at a rate of 1.5 ml min^{-1}.
Perfusate duplicate samples were taken at each preset IVLM-VQ (0.02, 0.04, 0.08, 0.16, 0.24, 0.32, 0.4) simultaneously from up- and downstream mixing chambers of the gas exchange assembly (representing arterial and venous vascular beds), and were analyzed by MMIMS-MIGET to determine MM-VQ from retention data [5]. V/Q ratios (geometric means of V and Q peaks representing MM-VQ) were taken from MM-V/Q distributions for comparison with preset IVLM-VQ.
Results: The IVLM performed well, allowing stable control of compartmental saline and gas flows, as well as reproducible inert gas transfer. Fourteen pairs of preset IVLM-VQ (range 0.02 to 0.4) and MM-VQ (range 0.0355 to 0.652) were feasible for analysis. Overall coefficient of variation for MM-VQ was 10.3%.
Linear regression: logMM-VQ = 0.92*logIVLM-VQ + 0.15 (P <0.0001, r^2 = 0.98).
Bland-Altman analysis: Mean bias (± 2 SD) = –0.105 (± 0.154). Overall Coefficient of Variation for MM-VQ was 10.3%.
Conclusions: Low-to normal V/Q ratios generated in an IVLM are detected by MMIMS-MIGET with good accuracy and precision. This IVLM appears as convenient system to validate and test MIGET systems and underlying assumptions by generating known V/Q relationships.

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P 7

Near-Real Time Pulmonary Shunt and Deadspace Measurement With Multiple Inert Gas Elimination Technique (MIGET) by Micropore Membrane Inlet Mass Spectrometry

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Background: MIGET using gas chromatography (GC) is a well established but time consuming method to determine ventilation/perfusion (V_A/Q) distributions. A MIGET variant (Micropore Membrane Inlet Mass Spectrometry, MMIMS) fitted with a single-pore probe already reduced analytic complexity substantially compared to GC [1, 2], with shunt data correlating well with the Riley model [2, 3]. Recently a multi-pore probe was introduced, enhancing MMIMS sensitivity 400-fold. This reduces inert gas solution load to a third of the single-pore MMIMS system. This study evaluated MIGET by multi-pore MMIMS and aimed to compare fractional (I) MMIMS-MIGET shunt (MMS) with Riley shunt (RS) and (II) MMIMS-MIGET deadspace (MMV_D) with deadspace based on volumetric capnography (VCV_D) [4].
Method: With animal care committee approval, anaesthetized pigs (24 ± 1 kg; lavage injury, n = 15; autologous clot pulmonary embolism; n = 10) were studied. A dissolved inert gas (IG) mixture [2] was infused at a rate of 8 $mlkg^{-1}h^{-1}$. Arterial, mixed venous and mixed expired samples were collected at baseline and after lung injury induction in 15 minutes intervals. Samples were analyzed for IG partial pressures using a multipore MMIMS system (Oscillogy LLC, Folsom PA). Resultant retention and excretion data were transformed to V_A/Q distributions [5]. As compartments of interest, fractional MMS and MMV_D were determined as shunt ≡ V_A/Q <0.005, deadspace ≡ V_A/Q >100. RS and VCV_D fractions were calculated as previously reported [2, 3].
Results: Analysis was based on n = 349 data pairs, comparing MMS to RS and MMV_D to VCV_D. As indicator of experimental error, the MMIMS dataset had a residual sum of squares (RSS) <5.3 in 27.8%, RSS <10.6 in 51.3% and RSS <16.8 in 63%.

	Range	Linear regression	r^2	P	bias	2 SD
MMS	0 – 0.36	MMS = 0.82RS – 0.04	0.58	< 0.0001	- 0.06	0.10
RS	0.04 – 0.58					
MMVD	0.23 – 0.58	MMS = 0.96RS – 0.06	0.48	< 0.0001	- 0.09	0.14
VCVD	0.47 – 0.89					

Conclusions: MMS and MMV_D correlate well with conventionally determined RS and VCV_D. Whether systematic negative offsets reflect superior resolution by MIGET at the extremes of V_A/Q distribution, requires further study. MMIMS-MIGET emerges as a near real-time technique for true V_A/Q distributional analysis.

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P 8

Epidural Catheter: sutured or glued?

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Background: Despite different devices are available, the fixation of epidural catheters still seems to be an unsolved problem, since the possibility of dislodgment of the catheter can be reduced, but not excluded. Studies in literature show that, according to various fixation devices, epidural catheters dislocate at a rate between 5 and 30% [1, 2].
Methods: 90 patients ASA physical status I-III scheduled for surgery requiring general anesthesia combined with epidural analgesia were prospectively enrolled in the period between 1/12/11 and 1/12/12. The patients were randomized into two groups: in the Mastisol Groupe the fixation of the epidural catheter was performed with synthetic glue (Mastisol®, Ferndale Laboratories, Inc., Ferndale, MI 48220, USA); in the Suture Groupe the catheter was sutured to the skin with non-absorbable polyamide (Ethilon II * 2-0, Johnson & Johnsons, USA).
Results: The two groups did not present significant differences with regard to sex, age, weight, height, BMI, ASA risk class, duration of surgery and surgical specialties.
During the follow-up, 2 patients were transferred to another hospital before the end of the epidural analgesia and in 6 patients some variables were not collected. Therefore we analyzed 42 patients in the Mastisol group and 40 in the Suture group.
In 33/42 patients of Mastisol group and in 33/40 patients of Suture group, the analgesic therapy lasted until the end of the indication.
At the level of its insertion to the skin, the displacement of the epidural catheter was detected in 8/42 patients belonging to the Mastisol group and in 5/40 patients inside the Suture group: there was not a significant difference between the 2 groups.
Discussion: Synthetic glue appears to be a viable alternative for the establishment of epidural catheters since, according to our study protocol, its dislocation rate did not differ significantly with respect to the suture.
Currently we believe that the use of synthetic glue offers advantages over the suture, as well as being less invasive, and simpler to apply (unlike the suture, it doesn't require an initial training).
Conclusions: Both suture and synthetic glue appear to be two good alternatives for the fixation of epidural catheters.

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P 9

Activity Monitoring as Outcome Measure for Neuromodulatory Therapy Using Smartphones – A Feasibility Study

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Background and aims: Monitoring physical activity has been shown to be an important outcome measure in the clinical management of chronic pain.
Methods: We performed a feasibility study in two patients with neuropathic pain before and after neuromodulative therapy using a smartphone system providing physical activity measurements from acceleration, barometer and location GPS data.
We measured the following smartphone parameters: daily recording time, number of location clusters visited, number of transitions in between different location clusters, number of steps, number of instances climbing stairs and the time the patient walked at a certain speed. The clinical evaluation included: pain intensity, physical functioning and patients ratings of overall improvement. We also evaluated the health related quality of life.
Results: Our results suggest that the changes in smartphone parameters before and after neuromodulative therapy were considerable. Improvement of activity was achieved particularly in the home environment reflected by an increase in walking, a gain in fast cadence activities and a decrease in rest cadence. Activity questionnaires, however, did not correlate with these measurements. There was a significant increase in the three clinical core outcome domains and in the quality of life.
Conclusions: We conclude that smartphone based activity monitoring has the potential to provide objective intervention outcomes to clinicians with a minimal interference in the patient's daily life.

P 10

Prediction of acute postoperative pain following breast cancer surgery using the pain sensitivity questionnaire

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Introduction: Postoperative pain treatment may be improved by identifying patients at risk for severe postoperative pain before surgery. Previous studies have indicated that preoperative pain sensitivity correlates with postoperative pain intensity. However, testing of pain sensitivity is time-consuming and painful. In volunteers it has been shown that pain sensitivity can also be assessed by self-rating, and a "pain sensitivity questionnaire (PSQ)" has been developed. To investigate whether the PSQ can also be used to predict acute postoperative pain we tested individual pain sensitivity in patients scheduled for breast cancer surgery both objectively and subjectively using the PSQ.
Methods: Following ethics committee approval and written informed consent, 90 patients scheduled for breast cancer surgery were included. Pain sensitivity was objectively assessed using electrical stimuli applied to the sural nerve and a hot water bath. Patients self-rated their pain sensitivity on the PSQ and were told to imagine the postoperative pain intensity on a 0-10 NRS scale (imagined pain score). Patients also completed questionnaires to assess anxiety (STAI) and depressivity (BDI).
Postoperative outcome criteria were: maximum and average pain during the first 24h, and average pain during the first 6 postoperative days. Pearson correlation coefficients were calculated using SPSS vs21.
Results:
Significant correlations (Pearson) are presented in the following table:

	PSQ score	Imagined Pain Score	STAI-state score
Maximum pain during the first 24h	.28	.44	.27
Average pain during the first 24h	.18	.46	.26
Average pain during the first 6 days	.29	.38	.34

None of the objective criteria of pain sensitivity had a significant correlation with any outcome parameter. The PSQ score was correlated with neither the objectively measured parameters of pain sensitivity nor the imagined pain score. It was, however, weakly correlated with the BDI depression score and the STAI state anxiety score.
Discussion: In the context of breast cancer surgery, the PSQ score, but not objective measures of pain sensitivity, are correlated with postoperative pain intensity.
Interestingly, the simple question "how intense do you imagine the pain after your surgery" was even stronger correlated with postoperative pain intensity. Potentially factors such as anxiety and catastrophizing are more important determinants of postoperative pain in this context than pain sensitivity itself.

P 11

The analgesic efficacy of ultrasound guided transversus abdominis plane block (TAP BLOCK): a meta-analysis

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Background and aims: Meta-analyses on the TAP block have reported to improve postoperative pain [1, 2], but they included enthusiastic trials using anatomical landmarks. Thereafter, prospective studies based on ultrasound-guided techniques described conflicting results. This meta-analysis aimed to evaluate the postoperative analgesic efficacy of ultrasound-guided TAP block.
Methods: The authors searched the electronic databases MEDLINE and EMBASE among others. The primary endpoint was IV morphine consumption at 6h postoperatively, analysed according to the type of surgery. Secondary endpoints were IV morphine consumption at 24h postoperatively, pain scores at rest and on movement at 6 and 24h postoperatively, rates of PONV and pruritus at 24h postoperatively, and complications. Meta-analyses were performed with "Review Manager" software (RevMan_version_5.1.6).
Results: Twenty trials were identified. Ultrasound-guided TAP block reduced cumulative IV morphine consumption at 6h postoperatively by 43% (mean difference: –4.5 mg, 95%CI: –6.5, –2.6 mg; p <0.00001). Other endpoints are summarized in table 1. No complications were reported.

Conclusions: Ultrasound-guided TAP block reduces morphine consumption and pain scores at 6h postoperatively.

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Keywords
Analgesia, Analgesic adjunct, Perioperative medicine, Postoperative pain, TAP block, Ultrasound

Table 1 Secondary endpoints. Significant results are highlighted with an asterisk.

Outcome	References	Total number of patients or number of patients with outcome/total number of patients %		Mean difference (95% IC) or RR (95% CI)°	Test for overall effect (p)
		TAP group	Placebo group		
IV morphine consumption (mg) at 24 h postoperatively	Baaj 2010, Belavy 2009, Costello 2009, El-Dawlatly 2009, Kane 2012, Niraj 2009, Siriramka 2012	257	238	-11.7 (-20.2,-3.1)	0.008*
Pain scores (VAS, VRS or NRS 0-100) at rest at 6 h postoperatively	Atim 2011, Baaj 2010, Bollag 2012, Costello 2009, Griffiths 2010, Melinikov 2012, Kane 2012, Khan 2012, Kim 2012, Ra 2010, Shin 2011, Tsuchiya 2012	294	305	-12.2 (-19.6,-4.77)	0.001*
Pain scores (VAS, VRS or NRS, 0-100) on movement at 6 h postoperatively	Atim 2011, Bollag 2012, Costello 2009, Griffiths 2010, Kim 2012, Melinikov 2012, Shin 2011	179	188	-12.4 (-19.4, -5.4)	0.0005)*
Pain scores (VAS, VRS or NRS 0-100) at rest at 24 h postoperatively	Atim 2011, Baaj 2010, Belavy 2009, Bollag 2012, Costello 2009, Griffiths 2010, Hosgood 2012, Melinikov 2012, Kane 2012, Kim 2012, Ra 2010, Shin 2011	292	300	-4.5 (-12.4, 3.49)	0.27
Pain scores (VAS, VRS or NRS 0-100) on movement at 24 h postoperatively	Atim 2011, Baaj 2010, Belavy 2009, Bollag 2012, Costello 2009, Griffiths 2010, Melinikov 2012, Kim 2012, Shin 2011	222	232	-8.3 (-20.7, 4.03)	0.19
PONV at 24 h postoperatively	Baaj 2010, Belavy 2009, Bollag 2012, Hosgood 2012	11/92 (12%)	11/96 (11%)	0.97 (0.46, 2.01)°	0.93
Pruritus at 24 h postoperatively	Belavy 2009, Bollag 2012	16/48 (33%)	17/54 (31%)	1.0 (0.61,1.63)°	0.30

P 12

PIEB – a new addition to the epidural labour analgesia family

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Neuraxial analgesia is the most effective labour analgesia. While the influence on the unborn baby is minimal, neuraxial labour analgesia can influence labour per se and there seem to be more instrumental vaginal deliveries (i.e. forceps and vacuum) in patients receiving epidural labour analgesia. Ambulation per se does not affect the mode of delivery, but motor block seems to have an important impact. In addition parturients with no or minimal motor block have a higher satisfaction with labour analgesia.
Modern neuraxial labour analgesia is delivered as a patient-controlled epidural analgesia (PCEA). The addition of a background continuos epidural infusion (CEI) reduces clinical interventions and increases patient satisfaction. The downside of CEI is accumulation of local anaesthetics over time and development of motor block. Recent research has aimed at improving local anaesthetic distribution by delivering the local anaesthetic as a timed bolus rather than a CEI.
A couple of months ago the first commercially available pumps with programmed intermittent epidural bolus (PIEB) became available.
Methods: In a pilot study we wanted to acquire experience with this novel model of labour analgesia. Bupivacaine 1 mg/ml (n = 7) or 0.625 mg/ml (n = 3) with fentanyl 2 ug/ml was used. The loading dose was 15–20 ml. The pump was set to deliver a PIEB of 5 ml every hour. PCEA settings were 5 ml bolus with a lockout time of 20 minutes. Motor block was recorded every 60–90 minutes.
Results: Ten women were included in this pilot study. All women were mobilised at least once after inititation of epidural analgesia. Two women developed motor block some degree of motor block, while two did not want to ambulate.
Discussion: PIEB is a promising new mode to administer epidural labour analgesia. Further studies need to investigate the development of motor block over time and the mode of delivery.

P 13

Time course of conditioned pain modulation in patients with acute and chronic low back pain

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Background and aims: The endogenous pain modulatory system can be evaluated in humans by conditioned pain modulation (CPM). CPM occurs when pain with a test stimulus is inhibited by an additional conditioning painful stimulus, reflecting efficient endogenous pain modulation. Disturbed endogenous pain modulation is likely one of the mechanisms underlying central hypersensitivity and might be a contributing factor for the development and maintenance of chronic pain. We tested whether CPM is altered in patients with acute and chronic low back pain, as compared to pain free controls.
Methods: We studied 40 patients with acute low back, 34 patients with chronic low back, and 30 healthy controls. Test-stimulus was pain tolerance threshold to pressure at the 2nd toe (PPTT). Cold pressor test was the conditioning stimulus (hand immersed into ice water). PPTT was measured before, immediately after, 3, 5 and 10 minutes after cold pressor test. CPM was calculated as the difference between PPTT after and PPTT before ice water test. The data were analyzed by linear regression models.
Results: CPM was equally functioning in all the groups immediately after cold pressor test. However, CPM declined significantly faster in the two patient groups, compared with the control group. This was evident already three minutes after cold pressor test ($p = 0.009$ and 0.03 in acute and chronic low back pain, respectively).
Conclusions: The rapid decline in the inhibitory effect of the conditioning stimulus indicates that the endogenous pain modulatory system of patients with acute and chronic low back pain is malfunctioning. This may contribute to the magnitude of pain and disability.
Key words: conditioned pain modulation, acute low back pain, chronic low back pain.

P 14

Concentration-dependent isoflurane effects on withdrawal reflexes in pigs and the role of the stimulation paradigm

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Suppression of complex purposeful movement in response to noxious stimulation is a common end-point of MAC determination studies. How inhaled anaesthetics affect reflex movements in different species is less investigated and might provide interesting information about anaesthetic immobility mechanisms.
Our study aimed at evaluating the role of the stimulation paradigm on the depressant effects of isoflurane on a limb withdrawal reflex in pigs. The hypothesis was that depression of both reflex and purposeful movements would occur at MAC.
In this prospective experimental trial, 10 pigs were anaesthetized twice with isoflurane only. First the individual MAC was determined, and then the effects of increasing end-tidal isoflurane concentrations, from 1.6 to 2.8% on withdrawal reflexes were assessed. Single, 10 and 60 repeated electrical stimulations were used to evoke withdrawal reflexes recorded and quantified by electromyography. Recruitment curves for reflex amplitude for increasing stimulation intensities and isoflurane concentrations were built.
Mean isoflurane MAC was 1.9 ± 0.3%. Reflexes evoked by repeated stimulation were suppressed at isoflurane concentration significantly higher than those able to suppress complex movements during MAC determination ($P = 0.014$ and $P = 0.006$ for 10 and 60 repeated stimuli respectively). Isoflurane up to 2.8% was still not able to abolish reflex activity evoked by repeated stimulations in all pigs. Single stimulation reflexes were suppressed at significantly lower concentrations than repeated stimulation reflexes ($P = 0.008$ for 10 stimuli and $P = 0.004$ for 60 stimuli). Reflex amplitude was significantly correlated with isoflurane concentration ($P < 0.001$, $r = -0.85$) independently from the individual MAC.
These findings suggest that 1) the level at which isoflurane suppresses withdrawal reflexes is dependent on the stimulation paradigm (single vs. repeated electrical stimulation), and there is limited value in expressing reflex withdrawal suppression in terms of MAC as purposeful and reflex movements are independently affected by isoflurane in individual animals 2) in pigs undergoing invasive experimental surgeries and anaesthetized at isoflurane concentrations well above MAC supplemental analgesics should be provided to prevent temporal summation and thus central sensitization.

P 15

Effects of magnesium and calcium on peripheral nerve excitability

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Background and aims: An important limitation of clinical nerve excitability studies is the difficulty of interpreting pathological changes in excitability properties and attribute changes to defined cellular or extracellular abnormalities. The current study aimed at investigating the impact of extracellular $MgSO_4$ and Calcium on nerve excitability parameters.
Methods: We used a computerized threshold-tracking program (QTRAC, ©Institute of Neurology, London, UK) in a skin-nerve in-vitro preparation of the rat saphenous nerve. QTRAC adjusts the stimulus intensity of a constant current stimulation to a 40% target response of the maximal Aβ action potential and tracked the stimulus current required to elicit this target amplitude applying different concentrations of MgSO4 and Calcium.
Results: Low concentrations of $MgSO_4$ and Calcium led to increased excitability whereas higher concentration had less effects. Both, low and high concentrations resulted in longer strength-duration time constants (τSD). After a train of preconditioning stimuli, threshold increased with low calcium but decreased with low $MgSO_4$. Relative refractoriness was longer with low concentrations of calcium whereas the different concentrations of $MgSO_4$ did not change the relative refractory period. Low concentrated $MgSO_4$ induced a significant increase of excitability at the end of the 100 ms-lasting subthreshold depolarisation. After a long hyperpolarising conditioning current low concentrated calcium but not $MgSO_4$ significantly inhibits inwardly rectifying currents (Ih).
Conclusion: The results presented in this study have shown that application of extracellular divalent ions $MgSO_4$ and calcium have different effects on sensory A compound action potentials; Persistant sodium channels, slow potassium channels and inwardly rectifying channel (Ih) are all modulated by $MgSO_4$ and calcium.

The numbers refer to the pages of this supplement.