

Established in 1871

SMW

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

Supplementum 184

ad Swiss Med Wkly
2010;140
October 16, 2010

The European Journal of Medical Sciences

Annual meeting of the Swiss Society of Anaesthesiology and Resuscitation

Lausanne (Switzerland), November 4–6, 2010

Suppl. 184
ad Swiss Med Wkly
2010;140
October 16, 2010

Free communications I – Basic science (FM1–FM6)	2 S
Free communications II – Pain (FM7–FM12)	3 S
Free communications III – Paediatric Anaesthesia / Regional Anaesthesia (FM13–FM18)	6 S
Free communications IV – General Anaesthesia (FM20–FM24)	8 S
Posters (P1–P29)	9 S

Index of first authors

The numbers refer to the pages of this supplement.

Ablinger P 20 S	Gosselin R-D 10 S	Neziri AY 4 S, 10 S	Theiler L 14 S
Aguirre JA 2 S, 3 S	Herrmann IK 3 S	Perruchoud C 11 S, 15 S	Thierrin L 5 S
Bandschapp O 8 S	Immer-Bansi A 5 S	Romano R 12 S	Trachsel S 19 S
Basciani RM 18 S	Jordi Ritz E-M 20 S	Rossi A 8 S	Uehlin J 12 S
Bolliger D 8 S	Kleine-Brueggemey M 13 S	Schild JC 2 S	Urner M 17 S
Burkhart CS 8 S	Laedermann C 3 S	Schlicker A 12 S, 17 S	Vastani N 10 S
Cachemaille M 9 S	Luyet C 7 S, 15 S	Schmitz A 6 S, 15 S	Vogt A 17 S
Dave MH 14 S	Mauch J 2 S, 4 S, 6 S	Seiler S 6 S	Walther D 11 S
Despond O 16 S	Maurer K 10 S	Siegenthaler A 13 S	Wipfli M 15 S
Erdoes G 19 S	Mlekusch S 13 S	Spielmann N 19 S	Wuethrich PY 9 S, 13 S, 18 S
Frick R 17 S	Müller-Edenborn B 2 S	Straessle R 16 S	
		Suter MR 9 S	

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EMH Swiss Medical Publishers Ltd.
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ISSN printed version: 1424-7860
ISSN online version: 1424-3997
Regular subscription price for 2010:
CHF 150.– (shipping not included)
12 issues per year

FM 1

Does self-inflation mechanism with minimal cuff pressure reduce tracheal mucosal damage? A scanning electron microscopy study in piglets

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Background: Modern high volume – low pressure tube cuffs allow sufficient air sealing at cuff pressures much lower than peak inspiratory pressures [1]. This is because of self-sealing mechanism [2]. The aim of this study was to determine if cuff self-inflation at minimal cuff pressure reduces tracheal mucosal damage compared to constant pressure cuff inflation.

Materials and methods: The tracheas of 18 piglets (4.6 kg – 5.4 kg, median 5.2 kg) were intubated with an ID 4.0 mm high volume – low pressure cuffed tracheal tube (Microcuff PET, Kimberly Clark, Atlanta, USA). Animals were randomly allocated to two groups: minimal cuff pressure group ($n = 9$) and constant cuff pressure (20 cmH₂O) group ($n = 9$). The pigs were artificially ventilated with a pressure controlled ventilator (Pmax 20 mbar, PEEP 5 mbar) and respiratory rate was set to achieve an end-tidal carbon dioxide of 4.7 kPa \pm 0.3 kPa. Cuffs were inflated with air to either minimal pressure to seal the trachea (Group M) or to constant pressure of 20 cmH₂O (Group C). Cuff pressure was monitored using a cuff manometer during the following 4-hour study period. Afterwards, the pigs were euthanized. The cuff position in the trachea was marked *in situ*, the whole trachea was then resected and prepared for scanning electron microscopy (SEM) examination. Pictures from SEM were histologically graded [3] and percentage of intact mucosal area assessed by a blinded observer. Histological grades were compared with the chi square test and percentage of intact mucosal area was compared using student's t-test.

Results and discussion: Minimal cuff pressure to seal the cuff in group M ranged from 12 to 18 cmH₂O (median: 14 cmH₂O). A total of 492 (group M) and 508 (group C) pictures were analysed. In the minimal cuff pressure group histological grades were significantly higher ($p < 0.05$) and a lower percentage of normal appearance was seen ($7 \pm 20\%$) (mean \pm SD) than in the constant cuff pressure group ($18 \pm 30\%$) ($p < 0.05$).

Conclusion: Self inflation mechanism with minimal cuff pressure does not reduce damage to the tracheal mucosa compared to constant cuff pressure in this short-term bench-top animal trial. Probably cyclical cuff pressure increase causes traumatic tracheal mucosal injury, as this is reported by cyclic airway pressure during IPPV itself [4].

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FM 2

Immunomodulating effect of desflurane in endotoxin-injured alveolar epithelial cells

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Background and goal of study: Recent studies have shown that sevoflurane is able to ameliorate lung damage caused by inflammation *in vivo* and *in vitro*. This lead to the question whether this might be a general effect of volatile anaesthetics. Desflurane is a widely used volatile anaesthetic in daily practice, but only limited data regarding lung protection is available at the moment. In this study we investigated for the first time possible immunomodulatory effects of desflurane in an *in vitro* model of acute lung injury with sevoflurane as reference gas.

Material and methods: Monolayers of a cell line of alveolar epithelial cells (AEC, L2 cells) were stimulated for 2 hours with 20 µg/ml lipopolysaccharide (LPS), followed by a 2 h or 4 h co-exposure to a CO₂/air-mixture with or without 1 of MAC desflurane or sevoflurane, respectively. mRNA levels of monocyte chemoattractant protein-1 (MCP-1) and cytokine induced neutrophil chemoattractant protein-1 (CINC-1) were assessed at 4h via qRT-PCR. Chemotactic activity of supernatants regarding neutrophil recruitment was assessed. Student's t-test was performed. For all analyses, we considered $p < 0.05$ to be statistically significant.

Results and discussion: When treated with volatiles, mRNA-expression for MCP-1 was reduced by $33.1\% \pm 22.1$ in the desflurane/LPS group and by $53.3\% \pm 13.8$ in the sevoflurane/LPS group compared to untreated inflamed cells. The level of CINC-1 mRNA was also significantly lower in the desflurane/LPS ($-46.9\% \pm 22.2$) and sevoflurane/LPS group ($-47.2\% \pm 23.2$) compared to air/LPS.

Chemotactic response was attenuated in the desflurane/LPS group as compared to LPS.

Conclusions: Desflurane seems to have a similar anti-inflammatory potential as previously shown with sevoflurane. Both volatile anaesthetics influence the inflammatory cascade by interfering with the same molecular pathway. This is a crucial step in acute lung injury for subsequent upregulation of inflammatory mediators. These data underline the hypothesis that the anti-inflammatory action of volatile agents is due to a group effect.

FM 3

Volatile Anesthetics Attenuate Neutrophil Response to CXCL8 in a Time-Dependent Manner, Potentially by Downregulation of CXCR1

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Introduction: CXCL8-concentrations are elevated in the bronchoalveolar lavage fluid in various pulmonary diseases including bronchopulmonary dysplasia, acute respiratory distress syndrome and ventilator-associated lung injury. Persistent pulmonary neutrophilia is a key feature in these diseases [1, 2]. We aimed to investigate the potential benefit of volatile anaesthetics (VA) on the neutrophil response to CXCL8 in an *in vitro* model.

Methods: Human neutrophils were isolated, stimulated with 10 nM CXCL8, and incubated for 0.5 h, 1 h or 2 h in the presence of 1 MAC of sevoflurane, desflurane or air, respectively. Expression of the β_2 -Integrin CD11b/MAC-1 and CXCL8-receptors CXCR1/CD181 and CXCR2/CD182 was measured by flow cytometry. Adherent potential of neutrophils was quantified with fluorescent-labeled fibrinogen. Intergroup analysis were carried out with One-way ANOVA. The Spearman rank correlation coefficient was used for correlations between receptors.

Results: CD11b-expression was decreased in stimulated neutrophils when exposed to sevoflurane ($p < 0.05$) and desflurane ($p < 0.01$) as compared to air at 1h and 2h. Fibrinogen-adherence at 2h was decreased in the desflurane group only ($p < 0.01$). The attenuated expression of CD11b correlated with decreased expression of CXCR1 in the sevoflurane and desflurane group at 1 h and 2 h ($p < 0.01$). No differences in CD11b- or CXCR1-expression between groups were observed at 0.5 h. CXCR2 was internalized in all groups to $>90\%$ at all timepoints ($p < 0.01$).

Discussion: Signaling through CXCR1 and CXCR2 plays an important role in neutrophil function such as adhesion. CXCR1 and CXCR2 are known to undergo CXCL8-induced receptor internalization and subsequently are recycled back to the surface. We observed an attenuated response to CXCL8 in the presence of VA, accompanied by a decreased surface expression of CXCR1 when incubated for 1h or longer. It might be that VA interfere with the internalization- or recycling-process of CXCR1, resulting in an attenuated neutrophil response to CXCL8.

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FM 4

Ropivacaine Protects Against Ventilator-Induced Pulmonary Capillary Leak

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Background: Mechanical ventilation, particularly at high tidal volumes, can contribute to increases in vascular permeability, a main feature of ventilator-induced lung injury (VILI). Our previous study demonstrated that caveolin-1 phosphorylation functions as a critical mechanism mediating oxidant-induced pulmonary vascular hyperpermeability. A recent study also showed that a ropivacaine intervention substantially attenuated the inflammatory response in acute lung injury. In this study, we examine the effect of ropivacaine on caveolin-1 phosphorylation and subsequent VILI-induced vascular permeability in the mouse model.

Methods: Saline or ropivacaine (1 µM) was administered intratracheally for 1 h and then the mice were subjected to normal (7 ml/kg) or high (28 ml/kg) tidal volume ventilation for another 2 h. At the end of the experiment, the lungs were either homogenized or lavaged. Src kinase activation and caveolin-1 expression and its phosphorylation were determined by Western blot analysis. The integrity of the alveolar-capillary barrier and pulmonary microvascular

permeability were assessed by measuring the concentration of total protein in bronchoalveolar lavage fluid. Statistical analysis was performed using an analysis of variance and the Student-Newman-Keuls test.

Results: Compared to normal tidal volume ventilation, high tidal volume ventilation causes a remarkable increase in Src kinase activation, caveolin-1 phosphorylation and vascular permeability. Ropivacaine inhibited these effects (fig. 1).

Conclusion: We demonstrated the important role of Src-mediated caveolin-1 phosphorylation in the regulation of VILI. Importantly, ropivacaine attenuated VILI-induced vascular hyperpermeability via suppression of Src kinase activation and caveolin-1 phosphorylation. These findings suggest that intratracheal instillation of local anesthetic ropivacaine may be a new direction for its potential therapeutic application in VILI.

Figure 1

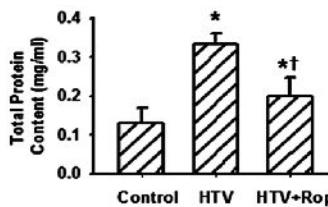


Figure 1. Effects of high tidal volume ventilation (HTV) and ropivacaine on pulmonary microvascular permeability. * $P<0.05$ vs. control. † $P<0.05$ vs. HTV.

Treatment of osteoblasts with diclofenac in group 1 resulted in a significant decrease of live cells after low concentrations with similar effects in the group 2, with increasing concentrations of diclofenac as in group 1. Ketorolac showed a clearly less toxic reaction at low concentrations in fibroblasts and osteoblasts and a lower toxic reaction at high concentrations also in both cell groups.

Conclusions: Our study shows a concentration-, time-, group- and cell-dependent cytotoxic effect of diclofenac and ketorolac on fibroblasts and mainly osteoblasts *in vitro*. Fibroblasts after a short incubation time (but not after permanent incubation at lower or higher doses) with diclofenac and ketorolac seem to undergo regeneration at lower concentrations. Osteoblasts do not show any regeneration characteristics. Apoptosis seems to be an important mechanism NSAIDs-induced cell death.

FM 6

Therapeutic blood purification using functionalized core/shell nanomagnets

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The direct removal of disease causing factors from blood would be most attractive in a number of clinical situations (e.g., intoxications, severe inflammatory response syndrome and sepsis). At present, such direct removal is routinely performed for small molecules (urea, potassium) by (hemo-) dialysis, filtration and adsorption. These processes depend on diffusion through membrane barriers where the pore size and structure currently limit hemodialysis to low-molecular compounds (filter cut off at ~50 kDa). The majority of harmful substances, e.g. endo-/exotoxins in sepsis, antibodies and immune-complexes in immunologic disorders are large biomolecules and therefore poorly accessible to dialysis. As a result, patients require whole plasma exchange (full loss of plasma, risk of transfusion reactions) or purification through an adsorbent (e.g. charcoal). In this work, the direct injection of stable nanomagnets into whole blood for the efficient, magnetic extraction-based extracorporeal removal of low and high molecular compounds is investigated. We demonstrate the successful extraction of metal ions (Pb^{2+}), steroid drugs (digoxin) and proteins (Interleukin-6, inflammatory mediator) whilst monitoring blood integrity using a series of clinically important parameters. Carbon coated metal nanomagnets equipped with heavy metal complexants, digoxin antibody fragments and human interleukin-6-antibodies were added to fresh human whole blood. During gentle swinging, the nanomagnets scanned the liquid driven by Brownian motion and captured the target compounds. After removal of the toxin-loaded nanomagnets by magnetic separation, the blood was analyzed for remaining toxin or inflammation markers, iron metabolism and blood integrity. Lead, digoxin and interleukin 6 levels were significantly decreased after the blood purification procedure.

Treatment with nanomagnets did not affect the integrity of blood and all levels remained in the clinical norm range. Caspase-3 assays

showed a reduced anti-apoptotic effect after interleukin-6 removal underlining the biological relevance of the achieved removal efficiency in a functional test.

Combined with existing therapies, these results may have major implications for the treatment of severe intoxications, sepsis (specific filtering of cytokines or toxins), metabolic disorders (thyrotoxicosis,

hyperfibrinogenemia and hyperlipoproteinemia) and auto-immune diseases (removal of pathogenic auto-antibodies or immune-complexes).

FM 5

In vitro exposure of human fibroblasts and human osteoblasts to the NSAIDs diclofenac and ketorolac is cytotoxic

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Background: Diclofenac and Ketorolac are routinely used to control postoperative pain using infusion techniques. However, sparse data exist focusing on the possible interaction of these NSAIDs with fibroblasts and osteoblasts.

Methods: Monolayers of human fibroblasts and osteoblasts were exposed to different concentrations of diclofenac (low concentrations: 6.25 µg/ml to 50 µg/ml and high concentrations: 0.156 µg/ml to 1.25 µg/ml) and different concentrations of ketorolac (low concentrations: 0.938 µg/ml to 7.5 µg/ml and high concentrations: 1.25 µg/ml to 10 µg/ml) for 2 days, followed by an incubation with normal medium for another 1 day or 4 days (group 1). Alternatively, cells were incubated with diclofenac or ketorolac for 3 days and 6 days (group 2). At each time point, live cells were counted using the DNA quantitative test, cell viability was assessed with the tetrazolium bromide (MTT) assay, proliferation tests were performed with the help of the colorimetric bromodeoxyuridine (BrdU) assay. At the lower concentrations cells were stimulated with lipopolysaccharide (LPS) to simulate an inflammation. Caspase-3 activity was determined to assess apoptosis as possible mechanism of cell death.

Results: Treatment of fibroblasts with diclofenac in group 1 at low concentrations did not result in a decrease of live cells whereas in group 2 the decrease was significant with increasing concentrations.

FM 7

Regulation of the voltage-gated sodium channel Nav1.7 by ubiquitin ligase Nedd4-2

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Background and aim: Neuropathic pain (NP) is a frequent and disabling disorder occurring as a consequence of a direct lesion of the nervous system and recurrently associated with a positive shift toward

nervous system excitability. Peripheral nerve activity is mainly carried by voltage-gated sodium channels (VGSC), with Nav1.7 isoform being an important candidate since loss of function mutations of its gene is associated with congenital inability to experience pain. Interestingly, ubiquitin ligases from the Nedd4 family are well known proteins that regulate the turnover of many membrane proteins such as VGSC and we showed Nedd4-2 is downregulated in experimental models of chronic pain. The aim of this study was to investigate the importance of Nedd4-2 in the modulation of Nav1.7 at the membrane.

Methods: *In vitro:* whole cell patch clamp on HEK293 cell line stably expressing Nav1.7 was used to record sodium currents (INa), where the peak current of INa reflects the quantity of functional Nav1.7 expressed at the membrane. The possibility that Nedd4-2 modulates the currents was assessed by investigating the effect of its co-transfection on INa. Biotinylation of cell surface was used to isolate

Free communications II – Pain

membrane-targeted Nav1.7. Furthermore, as the interaction between Nedd4-2 and Nav isoforms was previously reported to rely on an xPPxYx sequence (PY-motif), we mutated this latter to study its impact in the specific interaction between Nav1.7 and Nedd4-2. GST-fusion proteins composed of the Nav1.7 c terminal 66 amino acids (wild-type or PY mutated) and GST were used to pull-down Nedd4-2 from lysates.

Results: Co-transfection of Nav1.7 with Nedd4-2 reduced the Nav1.7 current amplitude by ~80% (n = 36, p < 0.001), without modifying the biophysical properties of INa. In addition, we show that the quantity of Nav1.7 at the membrane was decreased when Nedd4-2 was present. This effect was dependent on the PY-motif since mutations in this sequence abolished the down-regulatory effect of Nedd4-2. The importance of this motif was further confirmed by pull down experiments since the PY mutant completely eliminate the interaction with Nedd4-2.

Perspectives: Altogether, these results point to the importance of Nedd4-2 as a Nav1.7 regulator through cell surface modulation of this sodium channel. Further experiments in freshly dissociated neurons from wild type and *Scn1b^{lox/lox}*/Nedd4-2^{Cre} mice are needed to confirm *in vivo* these preliminary data.

FM 8

Reference Values for Central Hyper- and Hyposensitivity of Mechanical and Thermal Pain Tests in a Pain-Free Population

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Background: Quantitative sensory tests are widely used in human research to evaluate the effect of analgesics and explore altered pain mechanisms, such as central hypersensitivity and hyperalgesia. In order to apply these tests in clinical practice, knowledge of reference values is essential. This study was designed to determine the reference values of pain thresholds for mechanical and thermal stimuli in a pain-free population.

Methods: 300 healthy subjects (152 males and 148 females, 18–80 years old) were tested. Pain detection and pain tolerance thresholds to pressure, heat and cold were determined at three body sites: 1) 2nd toe (for pressure) or the lateral aspect of the leg (for heat and cold tests), 2) low back (LBa), and 3) suprascapular region (SRe). The influences of gender, age, height, weight, body mass index, body side of testing, depression, anxiety, catastrophizing and parameters of Short-Form 36 were analyzed by multiple regressions.

Results: Quantile regressions were performed to define the 5th, 10th and 25th percentiles as reference values for pain hypersensitivity and the 75th, 90th and 95th percentiles as reference values for pain hyposensitivity. Gender, age and/or the interaction of age with gender were the only variables that consistently affected the pain measures. Therefore, reference values were stratified by gender and age. Here we present a selection of the data, i.e. the 10th percentiles of pain detection thresholds (determination of central hypersensitivity) for pressure and heat stimulation. The 10th percentile of pressure pain detection threshold for 2nd toe, LBa and SRe for age group 20–49 years were: for females 122, 143 and 123 kPa, respectively; for males 125, 227 and 168, respectively. Concerning heat pain detection thresholds, the 10th percentiles for leg, LBa and SRe were: for females of the age group 20–49 39.6, 38.1 and 38.5 °C; for males 40.0, 38.3 and 39.0 °C, respectively.

Conclusions: Reference values of parameters related to pressure and thermal pain stimuli were defined. These reference values can be clinically applied for detecting abnormal pain reactions in individual patients. They may be utilized as a diagnostic tool for central hypersensitivity and hyperalgesia, as a prognostic tool to predict the course of the disease or screen patients for studies on mechanism-based treatment strategies.

Key words: Reference values; pain thresholds; pressure; heat; central hypersensitivity; hyperalgesia.

FM 9

The Importance of Multi-Modal Pain Assessment: Factor Analysis of Responses to Thermal, Electrical, and Mechanical Painful Stimuli

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Background: During the last decade, a multi-modal approach has been established in human experimental pain research for assessing pain thresholds/responses to various experimental pain modalities. Studies have concluded that differences in responses to pain stimuli are mainly related to variation between individuals rather than variation in response to different stimulus modalities.

Methods: In a factor analysis of 300 consecutive volunteers (152 males, 148 females) who underwent tests with different experimental pain modalities, it was determined whether responses to different pain modalities represent distinct individual uncorrelated dimensions of pain perception. Volunteers underwent single painful electrical stimulation, repeated painful electrical stimulation (temporal summation), test for reflex receptive field, pressure pain stimulation, heat pain stimulation, cold pain stimulation and a cold pressor test (ice water test).

Results: Five distinct factors were found representing responses to five distinct experimental pain modalities: pressure, heat, cold, electrical stimulation and reflex receptive fields. Each of the factors explained approximately 12 to 23% of the observed variance, and the five factors cumulatively explained 89% of the variance. The correlation between the five factors was near null (median rho 0.00, range -0.04 to 0.05), with 95% confidence intervals for pair-wise correlations between two factors excluding any relevant correlation. Results were almost similar for analyses stratified according to gender and age.

Conclusions: Responses to different experimental pain modalities represent different pathways and should be assessed separately in future clinical and pharmacological studies. This will further increase our understanding of the complexity of mechanisms leading to chronic or acute pain and its modification in experimental settings and clinical practice.

Acknowledgments: This work was funded by the Swiss Science National Foundation, the Danish Research Council for Technology and Production and the Scientific Funds of the University Department of Anesthesiology and Pain Therapy of the University of Bern.

CTU Bern is supported by the Swiss National Science Foundation.

Key words: Factor analysis; Pain Threshold; Pain assessment; Experimental pain models.

FM 10

Impact of local anaesthetic injection speed on serum levels of bupivacaine and therapeutic safety in piglets

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Objectives: Systemic local anaesthetic (LA) toxicity due to inadvertent intravascular injection of LA is a rare but potentially catastrophic complication of regional anaesthesia. Strategies such as early recognition of intravascular injection and approaches to increase therapeutic safety are therefore required. This study aimed to investigate the impact of intravascular injection speed of bupivacaine on LA induced cardio-vascular morbidity and mortality in piglets.

Materials and methods: In 55 neonatal pigs, anaesthetised with sevoflurane, endotracheally intubated, and artificially ventilated, blood was drawn for the assessment of acid base state and plasma protein concentration. Then, bupivacaine was continuously infused through a central venous catheter at a rate of 1 mg/kg/min (group A) or 4 mg/kg/min (group B) and 16 mg/kg/min (group C) until mean arterial pressure (MAP, invasively measured) was 50% of initial value. Thereafter bupivacaine infusion was stopped and spontaneous course of haemodynamic observed. Time start-stop of bupivacaine infusion, amount of bupivacaine infused, bupivacaine plasma level at infusion stop, number of spontaneous survivors and time from bupivacaine stop to circulatory arrest was recorded. Data are compared using Kruskal-Wallis and Mann-Whitney tests ($\alpha = 0.05$). Data are in median (range).

Results: There were no differences in weight, protein plasma level and pH among the three groups. Time to MAP 50% was shortest in group C (63 s), longer in group B (119 s) and most delayed in group A (297 s) ($p < 0.001$). Total amount of bupivacaine infused until MAP decreased to 50% of initial value was 4.95 (3.06–24.36) mg/kg in group A, 7.82 (5.45–12.91) mg/kg in group B and 17 (12–20) mg/kg in group C ($p < 0.001$). Bupivacaine plasma levels at MAP 50% were 53.8 (40.6–101.9) µg/L in group A, 155.9 (83.1–686.1) µg/L in group B and 438.9 (245–693) µg/L in group C ($p < 0.001$). Five of 15 piglets in group

A spontaneously recovered, while in group B and C all animals died from pulseless electric activity or asystole within 120 and 20.5 s respectively ($p < 0.001$).

Conclusion: Higher infusion rates of bupivacaine coincide with much higher plasma bupivacaine levels when compared to absolute amount infused. This is most likely caused by reduced distribution time. Slow administration of LA increases therapeutic safety of local anaesthetics if inadvertently intravascular injection occurs and is therefore mandatory, whenever LA are administered in patients.

FM 11

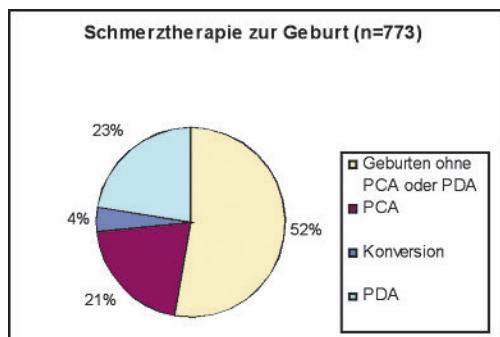
The launch of Patient-Controlled Analgesia with Remifentanil during Labour in a Private Hospital in Switzerland

A. Immer-Bansi, A. Melber, D. Reinhardt
Salem-Spital, Hirslanden Bern

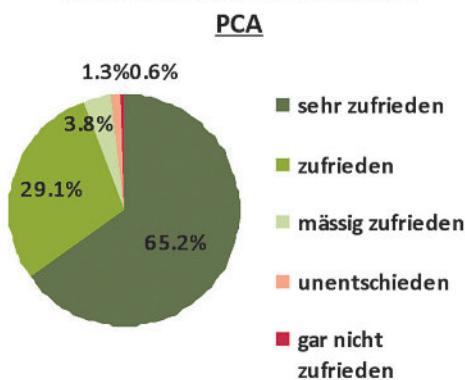
Introduction: Due to its profile of action the strong opioid remifentanil serves as an ideal analgesic drug during labour. Applied as PCA (patient controlled analgesia) this method offers optimal safety and comfort for the parturient and the child. Although frequently used in other countries in Europe, its routine use has not yet been established in Switzerland.

Methods: Initiated from Salem Spital in Bern, a website was created to phase this method in Switzerland. This website contains a concise direction for the professionals and a questionnaire, collecting a database for each application. This database comprises the course, the complications for mother and child as well as the satisfaction of all parties.

Results: After a pilot project with 40 parturients this method was implemented for routine use in labour. Up to now more than 200 women (25% of all births) delivered with the support of a Remifentanil PCA. Pain Score, side effects of mother and child and satisfaction of mother and midwife were analysed. 95% of parturients and midwives would choose this method again or recommend it for childbirth.



Zufriedenheit der Mutter mit



Discussion: Despite overwhelming results large numbers are often needed to detect rare complications or side effects. If all applications from any participating hospitals, even with small numbers, are registered via this website (www.soscisurvey.de/ultiva) a large datapool can be collected in a short time. This allows constant adjustment of the procedure as well a quick feedback in case adverse affects should appear.

Conclusion: The routine use of Remifentanil PCA in labour is a safe method with excellent acceptance of parturients, midwives, obstetricians and anaesthetists. Furthermore it reduces costs, because less invasive analgesic methods are needed.

The webbased data collection offers a quick nationwide launch together with excellent quality management.

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FM 12

Patients's satisfaction concerning postoperative analgesia after caesarean section: a comparison of 4 alternative analgesic regimen

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Introduction: Different routes of postoperative analgesia may be used after cesarean section: systemic, spinal or epidural [1]. Although the efficacy of these alternative analgesic regimen has already been studied [2, 3], very few studies have compared patients' satisfaction between them.

Methodology: After ethical committee acceptance, 100 ASA 1 patients scheduled for an elective cesarean section were randomized in 4 groups. After a standardized spinal anesthesia (hyperbaric bupivacaine 10 mg and fentanyl 20 µg), each group had a different postoperative analgesic regimen:

- Group 1:** oral paracetamol 4x1 g/24 h, oral ibuprofene 3x600 mg/24 h and subcutaneous morphine on need (0.1 mg/kg 6x/24 h)
- Group 2:** intrathecal morphine (100 µg) and then same as Group 1
- Group 3:** oral paracetamol 4x1 g/24 h, oral ibuprofene 3x600 mg/24 h and PCEA with fentanyl 5 µg/ml epidural solution
- Group 4:** oral paracetamol 4x1g/24 h, oral ibuprofene 3x600 mg/24 h and PCEA with bupivacaine 0.1% and fentanyl 2 µg/ml epidural solution

After 48 hours, a specific satisfaction questionnaire was given to all patients which permitted to obtain 2 different scores concerning postoperative analgesia: a global satisfaction score (0–10) and a detailed satisfaction score (5 questions scored 0–10 with a summative score of 0–50). Both scores, expressed as mean \pm SD, were compared between the 4 groups with a Kruskall-Wallis test and between each group with a Mann-Whitney test. A P-value <0.05 was considered significant.

Results:

Satisfaction scores	Gr. 1 (n = 25)	Gr. 2 (n = 25)	Gr. 3 (n = 25)	Gr. 4 (n = 25)	P-value
global (0–10)	8.2 \pm 1.2	9.0 \pm 1.0	7.8 \pm 2.1	6.5 \pm 2.5	0.0006
detailed (0–50)	40 \pm 6	43 \pm 5	38 \pm 6	34 \pm 8	0.0002

Conclusion: Satisfaction scores were significantly better in patients who received a systemic postoperative analgesia only (Groups 1 and 2) compared to patients who received systemic and epidural postoperative analgesia (Groups 3 and 4). The best scores were achieved with the combination of intrathecal morphine and multimodal systemic analgesia (Group 2) which allowed early ambulation without significant pain. Patients treated with postoperative epidural analgesia with combined local anesthetics and opioids (Group 4) obtained the worse scores (more restrictive nursing with less mobility, frequent asymmetrical block with insufficient analgesia on one side and motor block on the other).

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FM 13

ECG alterations in children during intravenous application of three different test solutions for regional anaesthesia

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Background: Animal studies have shown that ECG alterations caused by intravenous injection of a local anaesthetic test dose are caused by epinephrine [1]. The aim of this study was to elucidate whether these ECG findings in small pigs provoked by a test dose of epinephrine, bupivacaine and their combination are reproducible in paediatric patients.

Methods: With Hospital Ethics Committee approval and written parental/patient consent, paediatric patients from birth up to 16 years of age undergoing general anaesthesia were randomized into three groups. After induction of general anaesthesia using sevoflurane, muscle paralysis and tracheal intubation 0.2 ml/kg of the corresponding test solution was rapidly intravenously administered: group 1 received bupivacaine 0.125%, group 2 bupivacaine 0.125% plus epinephrine 1:200000, and group 3 plain epinephrine 1:200000. The ECG was recorded and analysed later on by a blinded assessor for alterations in heart rate and T-wave elevation. An increase of heart rate of ≥ 10 bpm and an increase in T-wave of $\geq 25\%$ respectively above baseline value were considered as a positive result [2].

Results: So far 26 paediatric patients aged 0.2–14.8 yrs (median 5.5 yrs) weighing 4.1–58 kg (19 kg) were studied. After intravenous injection of 0.2 ml/kg test solution, an increase in heart rate of ≥ 10 bpm was found in 0 (0%) patient of group 1 (n = 7), in 7 (78%) of group 2 (n = 9) and in 7 (78%) of group 3 (n = 9). T-elevation was found in 0 patient of group 1 and in all patients of group 2 (n = 9) and 3 (n = 10).

Discussion and conclusion: The preliminary findings of this study demonstrate that in children ECG alterations caused by intravascular injection of a local anaesthetic (LA) test dose are caused by epinephrine. The manifestation of elevated T-wave seems to be more sensitive than increase in heart rate to detect intravascular injection of a LA test dose with epinephrine. The intravascular injection of plain bupivacaine alone cannot be detected by ECG. Based on our study results, an epinephrine containing LA solution and ECG control must be used for the reliable detection of inadvertent LA injection in children.

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FM 14

The performance of the pediatric-sized i-gel™ compared with the Ambu Aura Once™ Laryngeal Mask in anesthetized and ventilated children

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Goal of study: The pediatric i-gel (Intersurgical Ltd, Wokingham, Berkshire, UK) is a downsized adult i-gel which features a gastric channel (except size 1). The aim of this prospective RCT was to compare the performance of the widely used Ambu Aura Once mask (Ambu A/S, Ballerup, Denmark) with the i-gel in children, assuming equal success and airway seal pressure.

Materials and methods: With IRB approval and informed consent we included 201 children of both genders, aged 0–17 years, 5–50 kg, ASA physical status I–II, scheduled at the University Hospital of Bern for elective surgery under general anaesthesia. Block randomization according to children's weight was performed after induction of anaesthesia. Primary outcome variables were insertion success and airway leak pressure; secondary outcomes included time to sufficient ventilation, fiberoptic glottic view, success of gastric catheter insertion with the i-gel, and adverse events.

Results and discussion: Demographic data of the 201 children did not differ between groups (age 6.2 ± 3.8 years, $p = 0.844$; weight 24.5 ± 11.2 kg, $p = 0.904$; ASA physical status, $p = 0.920$). Male:female ratio was 147:54 and equal between the groups ($p = 0.192$); more boys were included due to the high number of circumcisions. The Ambu was inserted in 99 and the i-gel in 102 children. In 44 of the 95 successfully inserted i-gels (46%), the device had the tendency to slide out and needed to be taped down to maintain sufficient airway leak pressure while this was not necessary in the 97 successful Ambu masks ($p < 0.001$). There were no major side effects with both devices.

Table 1
 Supraglottic mask performance in 201 children.

	Ambu Aura Once (n = 99)	i-gel (n = 102)	p-value
Success n (%)	97 (98)	95/102 (93)	0.187
Airway Leak Pressure (cm H ₂ O)	19 \pm 4	21 \pm 5	0.001
Insertion time (sec)	23 \pm 8	27 \pm 11	0.045
Fiberoptic view grade 1/ 2/ 3/ 4/ missing * n (%)	85/8/1/0/3 (88/8/1/0/3)	84/9/2/0/0 (88/9/2/0/0)	0.737
Gastric tube insertion successful n (%)	Not possible	92/95 (97)	n.a.

* 1 = full view of glottis, 2 = partial view, 3 = only epiglottis visible, 4 = no glottic structures visible; grade 3 and 4 matched for statistical analysis. n.a. = not applicable.

Conclusion: The pediatric-sized i-gel is suitable for ventilation of anaesthetized children and offers the additional advantage of gastric access. Compared to the Ambu Aura Once, it shows higher airway leak pressures, but longer insertion times. However, especially in small children, the i-gel has the tendency to slide out and often needs to be taped down.

FM 15

Evaluation of Gastric Fluid Volume after Intake of Clear Fluids with Magnetic Resonance Imaging in Healthy Children – Preliminary Data

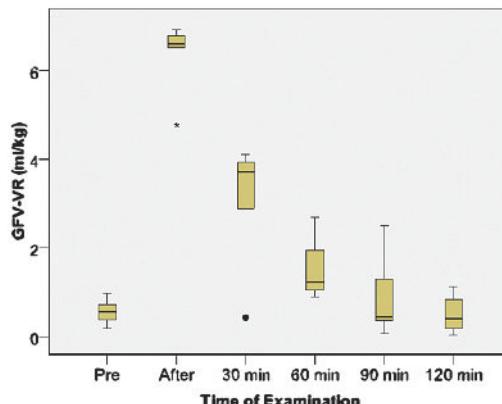
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Background: Modern guidelines prescribe preoperative fasting of 2 hours for clear fluids [1, 2]. This is often exceeded because of organisational delay. Existing data do not cover fluid intake within less than 2 hours before induction, and rely on aspiration of gastric contents [3].

Methods: Healthy volunteers aged from 6 to 12 years were asked to drink 7 ml/kg of diluted raspberry syrup after overnight fasting. Axial images covering the entire stomach were obtained by magnetic resonance imaging (MRI) before ("Pre") and 0 to 5 ("After"), 30, 60, 90 and 120 min after ingestion of syrup. Gastric fluid volume was determined in a blinded manner and related to body weight (GFV-WR). Data are presented as range (median).

Results: 33 MRI examinations in 16 healthy children aged from 6.4 to 12.8 (9.2) years, weighing 21.6 to 40.7 (31.8) kg, have been evaluated so far (n = 7, 5, 5, 3, 8 and 5 for "Pre", "After", 30, 60, 90 and 120 min, respectively). GFV-WR ranged from 0.05 to 6.9 (0.8) ml/kg.



Conclusion: GFV declines rapidly after intake of clear fluid, but pre-ingestion volumes are reached only after 90 min, with more scattering than volumes after overnight fasting. To decide whether free intake of clear fluid until premedication or 2 hours fasting time for clear fluid is safer, acidity of gastric contents has to be considered.

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FM 16

Thoracic paravertebral puncture and placement of catheters in human cadavers: where do catheters go?

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Introduction: Paravertebral regional anesthesia is used to treat pain after thoracic, cardiac, breast and upper abdominal surgery, avoids epidural space puncture and may therefore reduce possible injury of the thoracic spinal cord. The aim of this anatomical study was: 1. To develop an ultrasound-guided approach to the paravertebral space; 2. To investigate a possible discrepancy between needle tip and final catheter tip position.

Methods: 6 cadavers were studied with Institutional approval for the procedure. A total of 36 paravertebral punctures using an 18 G Tuohy needle were performed (three punctures on each side of the thoracic vertebral column). The needle tips were advanced under real-time ultrasound guidance slightly lateral and deeper to the lateral border of the inferior articular process of a vertebra (which is easily visualized using ultrasound) in an out-of-plane approach. The position of the needle tip was controlled by performing the first CT-scan. After placement of the catheters through the needles – the catheter insertion depth was randomly varied between 1 and 3 cm – the position of the catheter tips were again assessed by a second CT-scan and image reconstructions.

Results: The first CT-scan showed that all needle tips were correctly positioned into the paravertebral space, close to the intervertebral foramen by using ultrasound guidance. One catheter could not be advanced beyond the needle tip despite turning the axis of the needle and further injections of saline to dilate the space. All 35 other catheters could be advanced through the needles. The second CT-scan showed a discrepancy between needle tip position and final catheter tip position. 25 catheter tips were found subpleurally at the level of the vertebral body or prevertebrally; 5 catheters remained close to the intervertebral foramen; 3 catheters were placed laterally in the subpleural space at the intercostal level; 2 catheters were completely misplaced into the pleural space.

Conclusion: We developed a novel ultrasound approach to precisely place the tip of the needle into the paravertebral space close to the emerging intercostal nerve. The introduced catheters through the correctly positioned needles were found misplaced in most cases which might explain parts of the current conflicting reports about the use of paravertebral catheters.

FM 17

Novel Catheters For Regional Anesthesia – The Paravertebral Pigtail Catheter

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Introduction: Placing catheters into the paravertebral space for continuous infusion of local anesthetics has the advantage of providing long lasting analgesia. However, there are conflicting results regarding the use of catheter-based techniques because of a variable and often limited extend of local anesthetic spread within the paravertebral space. One problem could be a discrepancy between needle tip position and final catheter position (Luyet et al. unpublished, Cowie et al. A&A 2010). A possible explanation for this discrepancy is the catheter material; catheters in current use are stiff and designed to avoid kinking. We developed a pigtail catheter which coils as soon as it is advanced beyond the needle tip. This allows the catheter tip to remain close to the initial needle tip position. The aim of this anatomical study was to test the new pigtail catheter in human cadavers.

Methods: 10 cadavers in legal custody of the Institute of Anatomy of Bern, have been studied with institutional approval. First, Tuohy needles were placed into the thoracic paravertebral space close to the emerging intercostal nerves under real-time ultrasound guidance. Next, the pigtail catheters were blindly introduced through the needles and the needles were left in place. 60 needles and catheters were placed, three on each side of the thoracic vertebral column. To detect the needle tip and the exact catheter location a CT-scan of the entire thorax was performed.

Results: Catheter placement was accomplished without difficulty in 58 cases. In 2 instances, the catheters could only be introduced after a new puncture. CT-evaluation revealed that only 3 catheters failed to form a coil after placement. 52 catheter tips were found to lie in the paravertebral space, either close to the intervertebral foramen, slightly lateral but subpleurally, or slightly anterior to the intervertebral foramen but also subpleurally. 8 catheters were in the paravertebral space but anteriorly, at the level of the sympathetic trunk. No catheter was misplaced into the epidural, pleural or the prevertebral spaces. The mean distance of the catheter tips to the needle tips was 0.8 cm (SD 0.5).

Conclusion: The combination of an ultrasound guided approach together with a novel pigtail catheter might be the solution to provide an exact catheter placement into the paravertebral space. This is mandatory for an effective and long lasting postoperative analgesia during continuous infusion of local anesthetics.

FM 18

Novel Catheters For Regional Anesthesia – Pigtail Catheter for Continuous Sciatic Nerve Block

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Introduction: The use of continuous peripheral nerve blocks for pain therapy after orthopedic surgery provides sustained analgesia, while potentially minimizing the need for opioids. A major concern with the use of continuous peripheral nerve block is the difficulty to place the catheter tips close enough to the nerves to accomplish effective analgesia. The final position of the catheter tip is not predictable and can be inadequate in 10–50% of cases (Capdevila X, Anesth Analg 2002). The use of ultrasound guidance to precisely place needles adjacent to nerves is undisputed. However, ultrasound is less effective regarding catheter positioning. The explanation for this unsatisfactory performance during placement may lie in the catheter construction material; currently used catheters are stiff and designed to avoid kinking and are often leaving the initial place of insertion. Therefore, we developed a soft pigtail catheter which coils as it is advanced beyond the needle tip, thus allowing the catheter tip to remain close to the initial needle tip position.

Methods: 10 cadavers conserved according to the method of Walther Thiel, have been studied. 40 needles (17 G Tuohy) were placed anterior to the sciatic nerves using ultrasound guidance (needle-in-plane/nerve in short-axis approach). Next, the pigtail catheters were blindly introduced through the needles and the needles withdrawn. A total of 40 catheters were placed, two per sciatic nerve on both legs of all cadavers. To detect the exact catheter location, a CT-scan of the legs was performed. Thereafter, 5 mL of contrast dye was injected through the catheters and the spread of contrast in relation to the neurovascular bundle was assessed by magnetic resonance imaging and image reconstruction.

Results: CT-evaluation revealed that there was a direct contact of the coil with the nerve in 37/40 cases. In the 3 cases without direct nerve contact, the shortest distance from the coils to the nerves was 5, 6 and 7 mm. In all cases the contrast dye was noted directly in contact with the neurovascular bundle, with only one exception. In this single case, a layer of fatty tissue lied between the nerve and the contrast dye. The mean circumferential covering of the nerve by contrast dye was 50% (SD 19.5).

Conclusion: Following ultrasound-guided introducer needle placement, the use of a novel pigtail catheter minimizes misplacements of catheter tips away from the initial needle tip position.

FM 20

Tropisetron blocks analgesic action of acetaminophen – a human pain model study

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Background: The mechanism underlying the analgesic action of acetaminophen is still unclear. Therefore we investigated a possible interaction of acetaminophen with central serotonergic pathways. The effects of acetaminophen, tropisetron, the combination of both drugs, and saline on pain perception and central sensitization in healthy volunteers were compared.

Methods: Sixteen healthy volunteers were included in this randomized, double-blind, placebo-controlled, cross-over study. Intracutaneous electrical stimulation (46.1 ± 19.1 mA) induced acute pain (numeric rating scale, 6 of 10) and stable areas of hyperalgesia and allodynia. Pain intensities and areas of hyperalgesia and allodynia were regularly assessed before, during, and after a 15 min infusion of acetaminophen, tropisetron, the combination of both drugs, and saline. Acetaminophen concentration measurements were performed to rule out any pharmacokinetic interaction.

Results: Both acetaminophen and tropisetron led to decreased pain ratings as compared to saline. However, when acetaminophen and tropisetron were administered simultaneously, the pain ratings were not affected. There was no significant difference in the evolution of the hyperalgesic and allodynic areas during the study period between the study groups. Acetaminophen serum levels were not significantly different when associated with tropisetron, although we observed a trend to lower acetaminophen concentrations when both drugs were concurrently administered.

Conclusions: While the combination of acetaminophen and tropisetron showed no analgesic action, either drug on its own led to decreased pain ratings as compared to saline.

Interpretation: In this small group of patients, high IL-6 values postoperatively were associated with POCD supporting a role for systemic inflammation in the development of POCD. In patients with POCD, duration of anaesthesia was significantly longer, and intraoperative blood losses were larger. These risk factors will need to be confirmed in a larger group of patients. The difference in length of stay may be indicative of postoperative complications, which have been linked to POCD earlier.

Supported by SNF Grant 32003B-121956

FM 22

Serum anticholinergic activity and postoperative cognitive dysfunction in elderly patients

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Background: Cerebral cholinergic transmission plays a key role in cognitive function and anticholinergic drugs are associated with impaired cognitive functions [1]. In the perioperative phase many substances with anticholinergic effects are administered and disturbed cholinergic transmission is a hypothetical cause of postoperative cognitive dysfunction (POCD). Serum anticholinergic activity (SAA; pmol/ml) may be measured as a summary marker of anticholinergic activity in an individual patient's blood. We hypothesised that an increase in SAA from preoperatively to one week postoperatively is associated with POCD in elderly patients.

Methods: Thirty-two patients aged >65 yrs undergoing elective major surgery under standardized general anaesthesia (thiopental, sevoflurane, fentanyl) were investigated. Cognitive functions were measured preoperatively and 7 days postoperatively using the extended version of the Consortium to Establish a Registry for Alzheimer's Disease – Neuropsychological Assessment Battery. POCD was defined as a postoperative decline >1 z-score in at least 2 cognitive domains. SAA was measured preoperatively and 7 days postoperatively at the time of cognitive testing.

Results: 50% of the investigated patients developed POCD. There were no statistically significant differences between patients with and without POCD regarding age, education, baseline cognitive function, duration of anaesthesia, SAA preoperatively (median (range) 1.0 (0.3 to 5.0) vs 1.5 (0.4 to 5.0), SAA 7 days postoperatively (median (range) 1.3 (0.1 to 7.0) vs 1.4 (0.6 to 5.5) or changes in SAA (median (range) 0.1 (-1.6 to 2.2) vs 0.2 (-1.4 to 2.8). The variability of SAA in individual patients was considerable and marked changes in SAA between the two examinations were observed in some patients. However, there was no significant relationship between changes in SAA and changes in cognitive function.

Conclusion: In this preliminary analysis of a small group of patients, changes in SAA in the perioperative phase were highly variable. SAA was not associated with POCD suggesting that POCD is not simply caused by anticholinergic medications administered in the perioperative phase. A further analysis of a larger group of patients is in progress.

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Supported by SNF Grant 32003B-121956

FM 23

Effects of von Willebrand syndrome type IIA on postoperative bleeding in patients undergoing aortic valve replacement

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Introduction: Acquired von Willebrand syndrome type IIA describes the loss of the largest von Willebrand factor multimers and is frequently found in patients with severe aortic stenosis [1]. We hypothesized that patients undergoing aortic valve replacement with von Willebrand syndrome type IIA will have increased postoperative bleeding due to impaired primary haemostasis.

Methods: With written informed consent we included 30 consecutive patients with severe aortic stenosis defined as valve orifice area <1.0 cm² in this preliminary analysis. We performed von Willebrand factor multimer analysis and measured plasma von Willebrand factor antigen and collagen binding activity by ELISA immediately before and on the first day after surgery. In all patients, postsurgical blood loss from mediastinal drainages was documented after 3, 6, 12 and 24 hours.

Table 1	POCD (n = 14)	No POCD (n = 17)	p value
CRP (mg/dl) preop.	4.0 [1.0–245]	4.2 [0.3–36.2]	0.6
2 days postop.	223 [20–318]	98 [4.5–384]	0.07
7 days postop.	58 [15–147]	44 [11–148]	0.2
IL-6 (U/ml) preop.	2 [2–28.1]	2 [2–7.3]	0.8
2 days postop.	56 [17–315]	20 [2–123]	0.009
7 days postop.	9 [2–77]	4 [2–16]	0.03

Results: Mean age in the enrolled patients (15 male and 15 female) was 74 ± 9 years (range, 58–88 years). Based on the preoperative multimer analysis, von Willebrand syndrome type IIA was diagnosed in 25 (81%) patients. In the preoperative analysis, collagen binding and von Willebrand factor antigen activity were reduced in 15 patients (50%) and 3 (10%) patients, respectively. On the first day after surgery, multimer analysis, von Willebrand factor antigen activity, and collagen-binding activity were already normalized in all patients. Cumulative postsurgical blood loss was 120 ± 150 ml (mean \pm SD) after 3 hours, 210 ± 215 ml after 6 hours, 300 ± 285 ml after 12 hours, and 425 ± 315 ml after 24 hours. Blood loss of more than 1000 ml after the first 24 hours was found in two patients (6%), both of them had a loss of the largest von Willebrand factor multimers. No patient required re-exploration for massive bleeding.

Conclusion: Von Willebrand syndrome type IIA was common in patients with aortic stenosis but normalized within 24 hours of aortic valve replacement, and it did not cause increased postoperative bleeding due to impaired primary haemostasis. Despite these findings in our small patient population, von Willebrand syndrome type IIA has to be taken into consideration when massive postoperative bleeding occurs in patients with aortic stenosis in whom other reasons for impaired haemostasis have been excluded.

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FM 24

Do Patients with Postoperative Thoracic Epidural Analgesia Need an Indwelling Transurethral Catheter after Thoracic Surgery?

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Background: In contrast to our expectations, we found in a previous study that thoracic epidural analgesia (TEA) within the segments T4-T11 for postoperative pain management after open renal surgery significantly impaired bladder function with decreased detrusor

contractility and increased postvoid residuals under urodynamic assessment. These findings suggest that postvoid residual urine volumes should be monitored under TEA or a transurethral catheter left in place. Here we evaluated the effect of TEA on bladder emptying pre- and postoperatively using ultrasound in patients with TEA between the segments T4-T8 in patients undergoing thoracotomy. Increased knowledge on bladder function under TEA could result in a more restrictive use of perioperative transurethral catheters.

Methods: In a prospective, open, observational, follow-up study, 13 male and 13 female patients with no pre-existing lower urinary tract symptoms (International Prostate Symptom Score ≤ 7) and with a postvoid residual <100 ml underwent sonographic assessment of the postvoid residual the day before thoracotomy without TEA and 2 days postoperatively under TEA. The epidural catheter was inserted at level T4/5 or 5/6. Continuous epidural analgesia was maintained with a mixture of bupivacaine 1 mg/ml, epinephrine 2 μ g/ml and fentanyl 2 μ g/ml postoperatively. Primary outcome was the difference in postvoid residual before vs during TEA.

Results: The median postvoid residual did not change significantly pre- and postoperatively (0 ml (0–95) vs 0 ml (0–430), $P = 0.09$). However, a significant decrease in bladder capacity at strong desire to void and voided volumes was observed ($P < 0.01$). Of the 3 male patients with an initial IPSS >3 and ≤ 7 , all developed a postvoid residual >100 ml (140, 310 and 430 ml), which required an indwelling catheter.

Conclusions: As observed in our previous study, we found a decrease in the voided volume. However, the majority of patients under TEA after thoracotomy had normal postvoid residuals and did not need a transurethral catheter. Our findings further suggest that patients with an IPSS >3 should be closely monitored postoperatively as they may be at risk of developing a significant postvoid residual under TEA.

Posters

P 1

Nedd4-2 ubiquitin ligase: a contributor to experimental neuropathic pain?

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Background: Neuropathic pain is associated with altered expression of voltage-gated sodium channels (VGSCs) leading to peripheral nerve hyperexcitability. Interestingly, in cell expression systems, the ubiquitin ligase Nedd4-2 regulates the cell membrane density of the most abundant peripheral and pain-related VGSC, namely Nav1.7, and decreases its sodium current. Yet nothing is known about the involvement of Nedd4-2 in nociception and chronic pain. Therefore, the goal of this study is (i) to characterize Nedd4-2 and Nav1.7 expression in an experimental model of neuropathic pain (ii) to design by viral vector-mediated gene therapy an approach to depict the implication of Nedd4-2 in chronic pain.

Methods: Western Blot and immunohistochemistry experiments detecting Nav1.7 and Nedd4-2 were performed in rodent DRGs 7 days after spared nerve injury (SNI). For the viral vector-mediated gene therapy, a recombinant Adeno-Associated Virus (rAAV2/6) was generated expressing the Nedd4-2 gene. Intrathecal injection of rAAV2/6 was followed 2 weeks after by the SNI surgery. Data are expressed in mean \pm SEM, $n = 4$ in each condition.

Results: Immunofluorescence on DRGs neurons reveals a decreased number of positive Nedd4-2 cells in the SNI model ($27.0 \pm 1.2\%$) versus sham group ($43.4 \pm 3.5\%$; $p < 0.005$), as well as an increase in positive Nav1.7 cells in SNI ($50.1 \pm 2.9\%$) versus Sham ($41.6 \pm 1.8\%$; $p < 0.05$). The change of Nedd4-2 expression was confirmed by western-blot analysis. In addition, we show that Nedd4-2 and Nav1.7 are largely expressed in overlapping cell populations, chiefly colocalizing with markers of small nociceptive neurons. Furthermore, we report that intrathecal injection of rAAV is able to counteract the reduction of Nedd4-2 expression in SNI animals.

Conclusion: Our results indicate that Nedd4-2 is mainly expressed in nociceptors and downregulated after nerve injury. Moreover, our data suggest that the reduction of Nedd4-2, after nerve injury, may modulate Nav1.7 activity and contribute to hyperexcitability in neuropathic pain. A normal level of Nedd4-2 can be restored using a viral vector and we will further assess its functional effect on pain sensitivity.

P 2

Effect of rufinamide on gating properties of voltage-gated sodium channel Na_v1.7

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Background: Voltage-gated sodium channels (Nav1.x) are important players in chronic pain. A particular interest has grown in Nav1.7, expressed in nociceptors, since mutations in its gene are associated to two inherited pain syndromes or insensitivity to pain. Rufinamide, a drug used to treat refractory epilepsy such as the Lennox-Gastaut syndrome, has been shown to reduce the number of action potentials in cortical neurons without completely blocking Na channels.

Aim: The goal of this study was to investigate the effect of rufinamide on Nav1.7 current.

Methods and results: Whole-cell patch clamp experiments were performed using HEK293 cells stably expressing Nav1.7. Rufinamide significantly decreased peak sodium current by 28.3, 21.2 and 12.5% at concentrations of 500, 100 and 50 μ M respectively (precise EC50 could not be calculated since higher rufinamide concentrations could not be achieved in physiological buffer solution). No significant difference on the V1/2 of voltage-dependence of activation was seen; however a shift in the steady-state inactivation curve was observed

(-82.6 mV to -88.8 mV and -81.8 to -87.6 mV for 50 and 100 μ M rufinamide respectively, $p < 0.005$). Frequency-dependent inhibition of Nav1.7 was also influenced by the drug. One hundred μ M rufinamide reduced the peak sodium current (in % of the peak current taken at the first sweep of a train of 50) from 90.8 to 80.8% (5Hz), 88.7 to 71.8% (10 Hz), 69.1 to 49.2% (25 Hz) and 22.3 to 9.8% (50 Hz) (all $p < 0.05$). Onset of fast inactivation was not influenced by the drug since no difference in the time constant of current decay was observed.

Conclusion: In the concentration range of plasma level in human treated for epilepsy, 15 μ M, rufinamide only minimally blocks Nav1.7. However, it stabilizes the inactivated state and exerts frequency-dependent inhibition of Nav1.7. These pharmacological properties may be of use in reducing ectopic discharges as a causal and symptom-related contributor of neuropathic pain syndrome.

P 3

Small depolarizing ramp currents can be used to block nerve conduction in the presence of low concentrations of local anesthetics

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Aims: Voltage gated sodium (Na^+) channels are essential for the initiation and propagation of action potentials in primary sensory afferents. DC depolarization can cause sufficient sodium channel inactivation to increase excitability thresholds of C fibers. Recent investigations suggest that a slow membrane depolarization is a specific stimulus for the activation of Nav1.7. This subtype of sodium channels has been shown to be essential for signalling pain. We investigated the effects of different sodium channel blockers on unmyelinated C fibres stimulated with and without a pre-conditioning slow depolarization.

Methods: C fibre compound action potentials (C-CAP) were recorded extracellularly in vitro using a skin nerve preparation from adult rats. A computerized threshold tracking program (Qtrac[®]) was used to determine the membrane threshold, peak amplitude and latency. Parameters were tracked continuously over time. Nerve fibres were stimulated with a supramaximal 1 ms current pulse either alone or after a small, slow 300 ms conditioning polarizing ramp current, in the presence and absence of various sodium channel blockers (TTX, Lidocaine, Rufinamide). Different depolarizing and hyperpolarizing ramps (between -10 and +100% of the original threshold current) were investigated.

Results: The membrane threshold at the end of the 20% depolarizing ramp is strongly raised in the presence of both 60 nM TTX (108 \pm 4%) and 80 μ M lidocaine (147 \pm 15%; $n = 10$), in comparison to control threshold. The effect is significantly larger using a 20 % conditioning ramp, compared to 10%. In separate experiments the same effect is shown to be concentration dependent with lidocaine (80 μ M: 157 \pm 13%, $n = 10$). A weaker effect is seen with rufinamide.

Conclusions: The level of preconditioning ramp stimuli determines the inactivation of sodium current. In the presence of sodium channel blockers the same ramp stimuli cause an increase in threshold which is much larger than expected by the sodium channel blocker alone. Therefore, we conclude that small depolarizing ramp currents can be used to block nerve conduction in the presence of low concentrations of local anesthetics. The threshold tracking technique in C fibres is a useful tool in revealing the possible mechanisms by which different sodium channel blockers may be exerting their effect on sodium channel subtypes.

P 4

Peripheral Nerve Neuropathy is Associated with a Glial Reaction in the Gracile Nucleus Associated with a regulation of the GABA transporter GAT-1

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Allodynia (pain in response to normally non painful stimulation) and paresthesia (erroneous sensory experience) are two debilitating symptoms of neuropathic pain. These stem, at least partly, from profound changes in the non-nociceptive sensory pathway that comprises large myelinated neuronal afferents terminating in the gracile and cuneate nuclei. Further than neuronal changes, well admitted evidence indicates that glial cells (especially in the spinal cord) are key actors in neuropathic pain, in particular the possible alteration in astrocytic capacity to reuptake neurotransmitters (glutamate and GABA). Yet, the possibility of such a changed astrocytic scavenging capacity remains unexplored in the dorsal column pathway. The present study was therefore undertaken to assess whether peripheral nerve injury (spared nerve injury model, SNI) could trigger a glial reaction, and especially changes in glutamate and GABA transporters, in the gracile nucleus. SNI surgery was performed on male Sprague-Dawley rats. Seven days after surgery,

rats were used for immunofluorescence (fixation and brain slicing), western-blot (fresh brain freezing and protein extraction) or GABA reuptake on synaptosomes. We found that SNI results in a profound glial reaction in the ipsilateral gracile nucleus. This reaction was characterized by an enhanced immunolabelling for microglial marker Iba1 as well as astrocytic protein GFAP (further confirmed by western-blot, $p < 0.05$, $n = 7$). These changes were not observed in sham animals. Immunofluorescence and western-blot analysis shows that the GABA transporter GAT-1 is upregulated in the ipsilateral gracile nucleus ($p < 0.001$; $n = 7$), with no detectable change in GAT-3 or glutamate transporters EAAT-1 and EAAT-2. Double immunofluorescence shows that GAT-1 and GFAP colocalize within the same cells. Furthermore, the upregulation of GFAP and GAT-1 were shown to occur all along the rostrocaudal axis of the gracile nucleus. Finally, synaptosomes from ipsilateral gracile nucleus show an increased capacity to reuptake GABA. Together, the data presented herein show that glial cells in the gracile nucleus react to neuropathic lesion, in particular through an upregulation of the GABA transporter GAT-1. Hence, this study points to role of an increased GABA transport in the dorsal column nuclei in neuropathic pain, calling attention to GAT-1 as a putative future pharmacological target to treat allodynia and paresthesia.

P 5

Induction of general anesthesia with propofol and sevoflurane change axonal excitability of primary sensory afferents

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Aim: To evaluate the effect of propofol (di-iso-propyl-phenol) and sevoflurane on axonal excitability of peripheral sensory nerves after induction of anesthesia.

Methods: After obtaining institutional ethics committee approval (University Hospital Zurich, Stv. 5-2008) and written informed consent, we randomized 40 patients who underwent surgery under general anesthesia into a propofol or sevoflurane group. Before induction of anesthesia 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[®]). No opioids, benzodiazepins or muscle relaxants were used during the measurement period. 15 minutes after the induction the same electrophysiological parameters were measured. Values are presented as mean \pm SEM. For normally distributed data we used a paired t-test to compare changes within the two groups and an unpaired t-test to compare changes between the two groups. A p -value < 0.01 was considered significant.

Results: Both, propofol and sevoflurane induced a significant increase in skin temperature (propofol: $+1.2 \pm 0.5^\circ\text{C}$; sevo: $+1.7 \pm 0.5^\circ\text{C}$) and a significant decrease in mean arterial pressure (propofol: -20.4 ± 2.5 mm Hg; sevo: -23.1 ± 3.5 mm Hg). Certain electrophysiological parameters significantly change: peak response decreased (propofol: -0.10 ± 0.02 mV, sevo: -0.16 ± 0.03 mV), relative refractory period shortened (propofol: -0.58 ± 0.16 ms, sevo: -0.54 ± 0.11 ms) and overshoot after a hyperpolarizing conditioning stimulus decreased (propofol: $3.5 \pm 0.8\%$ mV, sevo: $4.1 \pm 1.0\%$). We found no difference in the extent of those changes between the propofol and the sevoflurane group.

Conclusion: Propofol and sevoflurane evoked similar changes in nerve excitability of sensory afferents during anesthesia induction. An increase of the skin temperature at the recording site caused a faster kinetic of voltage-gated ion channels and therefore accounts partially for the observed changes (e.g., relative refractory period). At the same time, propofol and sevoflurane caused a partial block of the same ion channels (e.g. peak response). Our results demonstrate that both, propofol and sevoflurane, modulate excitability of primary sensory afferents in concentrations used in clinical practice.

P 6

Evidence for Expansion of Spinal Reflex Receptive Fields in Chronic Pain Patients with Endometriosis

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Background: Widespread central hypersensitivity is present in many chronic pain conditions and contributes to pain and disability. Expansion of receptive fields of spinal cord nociceptive neurons may

be one of the mechanisms underlying central hypersensitivity, but so far no method to assess receptive fields in humans has been available. Using a novel method to quantify nociceptive receptive fields by means of spinal withdrawal reflexes, we tested the hypothesis that patients with chronic endometriosis pelvic pain display an expansion of receptive fields, compared with pain-free subjects. Secondary endpoints were the subjective pain thresholds and the thresholds to evoke a nociceptive reflex after single and repeated (temporal summation) electrical sural nerve stimulation.

Methods: 20 patients and 25 pain-free female subjects were tested. Electrical stimuli were applied to 10 sites on the foot sole to evoke reflexes in the tibialis anterior muscle. The reflex receptive field (RRF) was defined as the area of the foot (expressed as fraction of the foot sole) from which a nociceptive reflex could be evoked by the electrical stimulus. For the secondary endpoints, the electrical stimuli were applied at the cutaneous innervation area of the sural nerve. Pain and reflex thresholds after single and repeated stimulation (5 stimuli at 2 Hz) were recorded.

Results: Endometriosis patients displayed a larger RRF area compared with pain-free subjects. Median (25–75 percentiles) of the two groups were 0.48 (0.38–0.54) and 0.33 (0.27–0.39), respectively ($p = 0.008$). Pain and reflex thresholds after sural nerve stimulation (secondary endpoints) were significantly lower in patients than in controls ($p < 0.001$ for all measurements).

Conclusions: This study provides for the first time evidence for widespread expansion of receptive fields in chronic pain patients. It thereby identifies a mechanism that may underlie central hypersensitivity in human chronic pain conditions. This phenomenon may become target for the development of future therapeutic interventions.

Acknowledgments: This work was funded by the Swiss Science National Foundation, the Danish Research Council for Technology and Production and the Scientific Funds of the University Department of Anesthesiology and Pain Therapy of the University of Bern.

Key words: Receptive fields, Central Sensitization, Nociceptive Reflex, Endometriosis, Pelvic pain.

Intrathecal administration of Ziconotide: does single-shot injection predict efficacy?

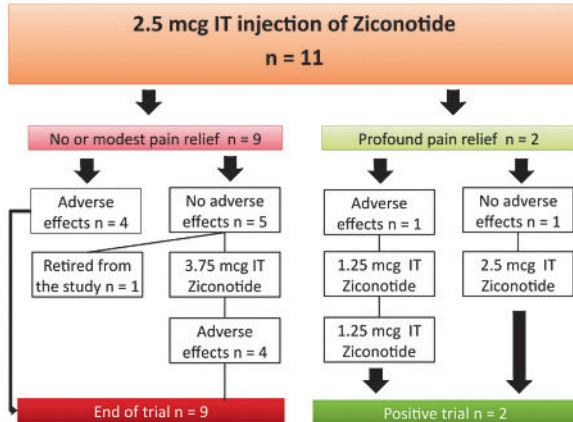
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Introduction: Though a trial of intrathecal (IT) therapy should always be performed before implantation of a definitive intrathecal pump, there is no agreement as to how this test should be performed. Ziconotide is trialed in most of cases with continuous IT administration using implanted catheters. Unlike other intrathecal drugs, there is little experience with single bolus IT injections of ziconotide. The aim of the study is to assess the feasibility of single-shot IT trialing with ziconotide.

Patients and methods: Eleven consecutive patients with chronic neuropathic intractable pain were trialed with a single IT bolus of 2.5 mcg of ziconotide. Pain and side effects are monitored for at least 72 hours after the injection. Depending on the response, a second injection is given a week later, with either the same dose (if VAS decreased $\geq 50\%$ without side effects), a higher dose of 3.75 mcg (if VAS decreased $< 50\%$ without side effects) or a lower dose of 1.25 mcg (if VAS decreased $\geq 50\%$ but with side effects). If VAS decreased less than 50% and side effects occurred, no further injection was performed. When VAS decreased $> 50\%$ without side effects after the first or the second dose, the result is confirmed by one more injection of the same dose one week later. The trial is considered positive if two successive injections provide a VAS decreased more than 50% without side effects.

Results: Eleven patients (6 females and 5 males) were included. Nine patients experienced modest or no pain relief. Four of these had significant side effects (dizziness, nausea, vomiting or abdominal pain) and had no further injection. In the others 5, one patient retired from study and four received a second injection of 3.75 mcg. The trial was negative in all 5 cases because of side effects (dizziness, drowsiness, weakness, muscle cramps), the pain decreased in only 2 patients. Two patients experienced profound pain relief with an IT injection of 2.5 mcg. One patient had no side effects and the other had dizziness and drowsiness that disappeared with an injection of 1.25 mcg. Pain relief without adverse effects was confirmed with the second injection. The trial was considered positive for those two patients.



Discussion and conclusion: The response rate of 18% (2/11) is consistent with the success rate of a continuous infusion trialing with an implanted catheter. Single-shot injection of ziconotide may therefore predict efficacy.

Evaluation of pain caused by locoregional anesthesia procedures

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Introduction: Locoregional anesthesia can be a painful procedure and may therefore decrease patient's acceptance. The purpose of the present study was to evaluate the pain caused by different locoregional anesthesia techniques in comparison to pain induced by peripheral intravenous (IV) cannulation.

Methods: This prospective observational study used a visual analogue scale (VAS), consisting of a 100 mm line, in order to quantify the levels of pain perceived during single-shot peripheral nerve blocks, continuous peripheral nerve blocks, spinal anesthesia and peripheral IV cannulation. Peripheral nerve blocks were performed with both neurostimulation and ultrasound guidance.

Results: Seventy-six locoregional interventions were assessed. Mean locoregional anesthesia VAS scores (17 mm; 95% CI 13–21 mm) were significantly different from mean VAS scores for peripheral IV cannulation (11 mm; 95% CI, 8–14 mm) ($P = 0.0226$). A direct correlation was found between these two pain experiences ($r = 0.561$, $P < 0.001$). For anesthesia procedures, pain experienced was independent of puncture site, whether interscalene (16 mm; 95% CI, 8–24 mm), femoral (24 mm; 95% CI, 11–36 mm), popliteal, (14 mm; 95% CI, 8–21 mm) or lumbar (for spinal anesthesia) (17 mm; 95% CI, 10–24 mm) ($P = 0.5195$). In peripheral nerve blocks, pain experienced did not depend on the insertion (18 mm; 95% CI, 11–25 mm) or not (16 mm; 95% CI, 10–23 mm) of a catheter ($P = 0.9189$). No difference was found in pain perception for locoregional anesthesia between men (19 mm; 95% CI, 13–24 mm) and women (15 mm; 95% CI, 10–20 mm) ($P = 0.3238$).

Conclusions: The mean VAS score for locoregional anesthesia was slightly higher than that for peripheral IV cannulation. These results allow for a founded dialogue with patients, on what pain to expect during locoregional anesthesia, using peripheral IV cannulation as a reference point.

P 10

Obstetric analgesia and anesthesia in Switzerland in 2007

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Introduction: The last twenty years has witnessed important changes in the field of obstetric analgesia and anesthesia. In 2007, we conducted a survey to obtain information regarding the clinical practice of obstetric anesthesia in our country. The main objective was to ascertain whether recent developments in obstetric anesthesia had been adequately implemented into current clinical practice.

Methodology: A confidential questionnaire was sent to 391 identified Swiss obstetric anesthetists. The questionnaire included 58 questions on 5 main topics: activity and organization of the obstetric unit, practice of labor analgesia, practice of anesthesia for cesarean section, prevention of aspiration syndrome, and pain treatment after cesarean section.

Results: The response rate was 80% (311/391). 66% of the surveyed anesthetists worked in intermediate size obstetric units (500–1500 deliveries per year). An anesthetist was on site 24/24 hours in only 53% of the obstetric units. Epidural labor analgesia with low dose local anesthetics combined with opioids was used by 87% but only 30% used patient controlled epidural analgesia (PCEA). Spinal anesthesia was the first choice for elective and urgent cesarean section for 95% of the responders. Adequate prevention of aspiration syndrome was prescribed by 78%. After cesarean section, a multimodal analgesic regimen was prescribed by 74%.

Conclusion: When comparing these results with those of the two previous Swiss surveys [1, 2], it clearly appears that Swiss obstetric anesthetists have progressively adapted their practice to current clinical recommendations. But this survey also revealed some insufficiencies:

1. Of the public health system:
 - a. Insufficient number of obstetric anesthetists on site 24 hours/24.
 - b. Lack of budget in some hospitals to purchase PCEA pumps.
2. Of individual medical practice:
 - a. Frequent excessive dosage of hyperbaric bupivacaine during spinal anesthesia for cesarean section.
 - b. Frequent use of crystalloid preload before spinal anesthesia for cesarean section.
 - c. Frequent systematic use of opioids when inducing general anesthesia for cesarean section.
 - d. Fentanyl as the first choice opioid during induction of general anesthesia for severe preeclampsia.

In the future, wider and more systematic information campaigns by the mean of the Swiss Association of Obstetric Anesthesia (SAOA) should be able to correct these points.

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P 11

A specific expertise for acute pain management is essential for the patient's safety

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Background and aims: The Riaz Hospital is an acute care hospital providing 94 beds, 50 of which are dedicated to surgery and 6 to multidisciplinary continuous adult care. In 2009, 72% of 7913 anaesthesiologist's acts have concerned the acute pain treatment. The locoregional anaesthesia represents 57% of the analgesic techniques, whose follow-up was made by the nurses initiated to analgesia and the anaesthesiologist. Despite this monitoring, several

near-accidents were documented in the post-operative period. The aim of the study was to assess the patient's safety and to identify the measures to optimize it.

Methods: Retrospective study on the nurse practice in surgery (SUR; n = 28), continuous care (CCU; n = 17) and gynaecology-obstetric unit (GOB; n = 29) during July-August 2009. Clinical experience, surveillance's criteria [1], safety and assessment's tools of the acute pain have been evaluated. The morphine (po/s.c./i.v.), local anaesthetics (ropivacaine/bupivacaine) and adjuvants (clonidine/epinephrine/morphine/fentanyl/sufentanil) for neuroaxial/peripheral nerve blocks (interscalene/femoral/popliteal/sciatic) in discontinuous/continuous infusion was studied.

Results: Table. Nurse experience and patient safety in nursing practice. 46 on 74 questionnaires were returned. The participation was 65, 88 and 45% for SUR, CCU and GOB unit, respectively.

Units	Years of experience [mean ± SEM]	Nurse-patient ratio/ day [mean]	Nurse's easiness with treatment [%]	Adequate safety's level [%]	Surveillance's criteria controlled by nurse [%]	Nurses favourable to a specialized follow-up [%]
SUR	6 ± 1.1	1:6	38	62	42	100
CCU	7 ± 0.7	1:3	68	97	59	47
GOB	8 ± 1.3	1:3	56	67	54	42

100% of the nurses used VAS and 59% verified the sensory-motor block. Safety and check of surveillance's criteria were the lowest for neuroaxial blocks (18%). Anaesthesiologist was called in 75% of treatment problem.

Conclusions: The safety and effectiveness of acute pain management are insufficient, because the analgesic techniques are complex and require specific expertises. The implementation of an anaesthesiologist-acute pain nurse unit is essential. Moreover, this unit contribute to decrease patient's morbidity and mortality [2] and can participate to control of health care costs. This project has been deposited to the hospital's authority.

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P 12

Effects of Local Anesthetics on Fibroblasts

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Background: Regional anesthesia with lidocaine, bupivacaine or ropivacaine is routinely used to manage perioperative pain. Sparse data exist focusing on the effects of local anesthetics (LA) on fibroblasts, which are actively involved in wound healing. Therefore, we investigated the effect of the three LA on growing human fibroblasts in an *in vitro* model focusing on cell viability, survival and proliferation rate.

Methods: Human fibroblasts were exposed to 0.3 mg/ml and 0.6 mg/ml of each LA for 2 days, followed by an incubation with normal growth medium for another 1, 4 or 7 days (group 1). Alternatively, cells were permanently incubated with LA for 3, 6 or 9 days (group 2). At each time point live cells were counted using trypan blue staining, cell viability was measured by the tetrazolium bromide assay and proliferation tests were performed with the colorimetric bromodeoxyuridine assay. Production of reactive oxygen species (ROS) was determined, measuring the oxidation of non-fluorescent-2',7'-dichlorofluorescin to the fluorescent form of the dye. Three-way analysis of variance and Spearman's correlation was used to analyze data.

Results: Treatment of cells with the three LA showed a concentration-dependent decrease of live cells, mitochondrial activity, and proliferation rate. Group arrangement played a significant role for cell count and proliferation, while exposure time influenced viability. Among the analyzed LA, bupivacaine showed the most severe cytotoxic effects. Increased production of ROS correlated with decreased viability of fibroblasts in lidocaine- and bupivacaine-exposed cells, but not upon stimulation with ropivacaine.

Conclusions: This study shows a concentration-dependent cytotoxic effect of lidocaine, bupivacaine and ropivacaine on fibroblasts *in vitro* with more pronounced effects after continuous incubation. A possible mechanism of cell impairment could be triggered by production of ROS upon stimulation with lidocaine and bupivacaine.

P 13

Potential influence of the anesthetic technique used during open radical prostatectomy on prostate cancer-related outcome

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Background: Recently published studies suggest that the anesthetic technique used during oncological surgery impacts cancer recurrence. To evaluate the effect of anaesthetic technique on disease progression and long-term survival, we compared patients receiving general anesthesia plus intra- and postoperative thoracic epidural analgesia with patients receiving general anesthesia alone undergoing open retroperitoneal radical prostatectomy with extended pelvic lymph node dissection.

Methods: Two sequential series were studied. Patients receiving general anesthesia combined with epidural analgesia (January 1994 – June 1997, n = 103) were retrospectively compared with a group given general anesthesia combined with ketorolac-morphine analgesia (July 1997 – December 2000, n = 158). Biochemical recurrence-free, clinical progression-free, cancer-specific and overall survival were assessed using the Kaplan-Meier technique and compared using a multivariate Cox-proportional-hazards regression model and an alternative model with inverse probability weights to adjust for propensity score.

Results: Using propensity score adjustment with inverse probability weights, general anesthesia combined with epidural analgesia resulted in improved clinical progression-free survival (hazard ratio 0.45, 95% confidence interval 0.27–0.75, p = 0.002). No significant differences were found between the two groups for biochemical recurrence-free, cancer-specific or overall survival. Higher preoperative serum values for prostate-specific antigen, specimen Gleason score ≥7, non-organ-confined tumor stage and positive lymph node status were independent predictors of biochemical recurrence-free survival.

Conclusions: General anesthesia with epidural analgesia was associated with a reduced risk of clinical cancer progression. But no significant difference was found between general anesthesia alone plus postoperative ketorolac-morphine analgesia and general anesthesia plus intra- and postoperative thoracic epidural analgesia in biochemical recurrence-free, cancer-specific or overall survival.

P 14

Determining the ideal location of injection for ultrasound guided suprascapular nerve blocks

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Background: Suprascapular nerve block is a frequently performed intervention for diagnosis and therapy of chronic shoulder pain. This block is increasingly performed for postoperative pain control after minor shoulder surgery. Different blind and image guided techniques of placing the needle to the nerve have been described, of which all target the nerve in the region of the suprascapular notch. This classic target point might not be the ideal location when ultrasound is used, as it is located deep under the skin and the nerve is not always visible.

Objectives: To determine the sonographic visibility and the depth of the suprascapular nerve in the cervical region where it might be located more superficial and compare both to the classic target site in the region of the suprascapular notch.

Methods: We scanned the course of the suprascapular nerve using a SonoSite M-Turbo ultrasound device and a high resolution 13 MHz linear transducer. For identification of the nerve we used the following sonoanatomic criteria: separation from the root C5 when it passes the interscalene gap, passage under the omohyoid muscle, traceable all the way down to the supraclavicular region. The sonographic visibility of the suprascapular nerve and its depth under the skin were determined in the supraclavicular region and compared with the classic target region, i.e. the suprascapular notch.

Results: In this preliminary analysis, data from 30 healthy volunteers bilaterally (60 nerves) were included. The sonographic visibility of the suprascapular nerve in the supraclavicular region was as follows: 51/60 "visible", 9/60 "not visible". Here, the median depth under the skin was 0.8 cm (range 0.25–1.1 cm). In the region of the suprascapular notch, the visibility was as follows: 21/60 "visible", 39/60 "not visible". Here, the median depth under the skin was 3.5 cm (range 2.1–4.5 cm). The differences of the visibility and the depth between the two locations were significant (both P <0.001, Chi-square test) and (P <0.001, t-test), respectively.

Conclusion: In the 30 healthy volunteers examined, the suprascapular nerve was located more superficially and hence was visualized more frequently in the supraclavicular region where it passes under the omohyoid muscle, as compared to the classic target site, i.e. the suprascapular notch region. The cervical region seems to be a valuable alternative for ultrasound guided suprascapular nerve blocks.

P 15

Ultrasound imaging to estimate the risk of conventional stellate ganglion block

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Background: Stellate ganglion block is a frequently performed intervention for diagnosis and management of various vascular disorders and chronic pain states in the upper extremity, head, and neck. The most common technique is the blind approach at the C6 transverse process (Chassagnac's tubercle) after manual lateral dislocation of the carotid artery and the jugular vein. Severe complications have been reported, due to accidental puncture of relevant brain supplying arteries (extraforaminal vertebral artery, ascending cervical artery), or the oesophagus.

Objectives: To describe the sonographic anatomy of the anterior cervical region C6 focusing on hazardous structures.

Methods: The anterior cervical region of 35 healthy volunteers was scanned bilaterally. The presence of the oesophagus or relevant arteries (located within a 1 cm wide band between the thyroid and the carotid artery anterior to the transverse process of C6) were noted before and after manual lateral dislocation of the large vessels. Dislocation was performed with an 11 mm narrow curved array transducer, simulating the dislocating finger.

Results: On the right side, the oesophagus never was located in front of the target point. On the left side, the oesophagus was present in front of the target point in 19/35 cases. After the dislocation manoeuvre, the oesophagus disappeared in 14/35 cases but remained in front of the target point in 5/35 cases and appeared in front of the target point from a previously safe location in 3/35 cases. Relevant arteries in front of the target point could be located in 12/35 and 16/35 cases on the right and left side, respectively. After the dislocation manoeuvre they still were present in 8/35 and 13/35 cases on the right and left side, respectively.

Conclusion: In this descriptive study, both the oesophagus as well as relevant arteries could be located in front of the classic target point of conventional blind stellate ganglion block in a significant number of the 35 examined healthy volunteers. The simulated dislocation manoeuvre had little impact on moving these structures away from the target point and might actually increase the risk of oesophageal puncture in certain individuals. Ultrasound imaging is expected to improve safety of stellate ganglion blocks, as compared to the classic blind approach.

P 16

Ultrasound Guided Percutaneous Tracheal Puncture: A Feasibility Study In Human Cadavers

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Introduction: Ultrasound guided techniques are increasingly used in the daily anaesthesia practice because of the advantages to visualize the tissues underneath the skin and the possibility to accurately place needles close to the targeted structures. To examine the usefulness of ultrasound for possible emergency airway access or for elective percutaneous dilatational tracheostomy, we performed ultrasound guided tracheal punctures in human cadavers, followed by CT-control and evaluation.

Methods: Nine cadavers in legal custody of the Department of Anatomy, Histology and Embryology of the Medical University Innsbruck, Austria, were studied with institutional approval. The trachea was first scanned in a transversal axis to define the midline, using a small curved array transducer. Then the axis of the transducer was tilted to achieve a longitudinal scan of the trachea and to determine the level of puncture with the aim to puncture the trachea between the 1st and 2nd, or 2nd and 3rd tracheal cartilage using an in-plane approach. As soon as a loss of resistance was felt, or air/fluid could be aspirated into the attached syringe, the syringe was disconnected and the ultrasound transducer put away. Thereafter a guide-wire from the pre-assembled cricothyroidotomy kit was inserted via the 18 G needle into the trachea. The needle was then removed, leaving the wire in place and a control CT imaging of the neck and the chest was performed. Primary outcome was successful wire insertion

into the trachea and tracheal midline puncture as described by the dial of a clock between 11:00 and 13:00.

Results: Tracheal puncture and wire insertion was successful in eight of nine cadavers at the first attempt and in one at the second attempt (total of ten attempts, nine successful). In eight of nine successfully inserted wires the wire was placed at the defined midline.

Tracheal Puncture of Nine Cadavers

	n (%) or mean \pm SD
First/ second attempt success	8 (89) / 9 (100)
Cervical puncture level (tracheal ring 1/ between tracheal ring 1-2/ 2-3/ 3-4)	1 (11) / 4 (44) / 2 (22) / 2 (22)
Lesion of tracheal structures (yes/ no)	1 (11) / 8 (89)
Lesion of thyroïdal structures (no lesion/ isthmus/ lobe)	1 (11) / 7 (78) / 1 (11)

Conclusions: Ultrasound guidance can facilitate successful tracheal puncture. However, combining an in-plane approach with a longitudinal ultrasound visualization of the trachea neither guarantees an exact midline puncture, nor allows detection of a misplaced guide-wire.

P 17

Closed tracheal suction and fluid aspiration past the tracheal tube – Impact of tube cuff and airway pressure

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Background and goal of study: It is well known that the application of negative pressure during suction with closed tracheal suction system (CTSS) catheter leads to profound negative tracheal pressures and this might facilitate fluid aspiration past the tracheal tube cuff. We investigated the effect of different tube cuff types and airway pressures on fluid leakage past the tracheal tube cuff during suction with CTSS.

Materials and methods: High volume – low pressure cuffs made from polyvinylchloride (PVC) and polyurethane (PU) of tracheal tubes size 7.5 mm internal diameter (ID) were placed in a 22 mm ID artificial trachea connected to a test lung and inflated to 25 or 50 cmH₂O cuff pressure. Peak inspiratory pressure (PIP) of 15, 20 or 25 cmH₂O and positive end expiratory pressure (PEEP) of 5 or 10 cmH₂O were used. A 14 Fr CTSS catheter was used for 5, 10, 15 or 20 sec under 200 or 300 mbar negative suction pressures. Fluid leakage across the tube cuff and airway pressure at the end of the suction procedure was measured. Fluid leakage and airway pressure changes during different suction conditions was compared using Kruskal Wallis and Mann Whitney test with Bonferroni correction (alpha = 0.0125).

Results and discussion: Airway pressure drop from the preset level when suction force was applied through the CTSS catheter was similar for both the tube cuffs. Airway pressure dropped to -13.3 cmH₂O with -300 mbar suction pressure as compared to -10.6 cmH₂O with 200 mbar suction pressure for both the tube cuff types. PU tube cuff resulted into significantly less fluid leakage than the PVC tube cuff ($p < 0.001$). For PVC tube cuff fluid leakage at transiently increased cuff pressure was significantly less ($p < 0.01$). Varying PEEP and PIP did not change the fluid leakage or drop in airway pressure significantly between respective conditions tested.

Conclusion: The use of PU tube cuffs and transient intermittent increase in cuff pressure during suction effectively reduces fluid leakage past the tracheal tube during suction with the CTSS catheter in a benchtop setting.

P 18

Effect of Lanz™ pressure regulating valve on self sealing mechanism and air leakage across the tracheal tube cuffs in a benchtop model

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Background: Cyclic redistribution of air within high volume – low pressure (HVLP) tracheal tube cuffs during intermittent positive pressure ventilation creates a self-sealing mechanism which allows tracheal sealing, despite tracheal airway pressure being above baseline cuff inflation pressure [1]. Tracheal tubes with the Lanz™ pressure regulating valve have a large compliant pilot balloon that effectively limits cuff pressure to 30 cmH₂O. The aim of the present study was to compare the effect of the Lanz™ system on HVLP tube cuff with regard to tracheal air sealing during cyclic respiratory pressure changes in a bench top model.

Methods: *In vitro* tracheal air sealing was studied in HVLP tracheal tube (internal diameter ID 8.0 mm) cuffs made from polyurethane (PU) (Seal Guard tracheal tube, Covidien, triangular cuff) and from

polyvinylchloride (PVC) (HiLo tracheal tube, Covidien, cylindrical cuff) with and without Lanz™ pressure regulating valve. Tube cuffs were placed in a 22 mm ID artificial vertical trachea and inflated to 5, 10, 15, 20, 25 or 30 cmH₂O cuff pressures controlled by a manual cuff manometer. Pressure control ventilation with peak inspiratory pressure (PIP) of 20 or 25 cmH₂O was applied and air leakage was assessed spirometrically as the ratio of expiratory to inspiratory tidal volumes (VtE/VtI). Non-parametric Mann Whitney test was applied to compare the air leakage between the tracheal tube cuffs with and without Lanz™ system for the PVC and PU cuffs at each cuff pressure and peak inspiratory pressure ($p < 0.05$).

Results: PVC tube cuffs with Lanz™ system resulted in significant air leakage (VtE/VtI ratio) at both 20 and 25 cmH₂O PIP as compared to those without the Lanz™ system, especially at cuff pressures lower than the preset PIP ($p < 0.01$). Although PU tube cuffs with Lanz™ system showed reduced air sealing as compared to cuffs without Lanz™, the difference was not statistically significant.

Conclusion: Tracheal air sealing at cuff pressure below PIP was reduced in all the PVC tracheal tube cuffs with Lanz™ system as compared to those without the Lanz™ system. Rapid cuff pressure correction with the Lanz™ system interferes with the self-sealing mechanism of PVC tube cuffs resulting in air leak across tube cuffs. Air sealing potential of the PU tube cuffs is not significantly altered by the Lanz™ system.

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P 19

Highlights of Airway Management: A Multi-National Survey among Anaesthesiologists

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Background: Highly controversial debates in airway management are: 1. Is Sellick's manoeuvre advisable and how many anaesthesiologists still use it regularly? 2. Should we mask ventilate before applying muscle relaxants (MR)? 3. Do anaesthesiologists check for predictors of difficult mask ventilation (DMV)? We compared the approach to airway management among anaesthesiologists from Austria, Switzerland and the United Kingdom using anonymous questionnaires.

Material and methods: We distributed the same questionnaire during the main session of three anaesthesia meetings in Vienna, Austria (Hands-on Workshop Vienna 2009); Perth, UK (Difficult Airway Society Meeting); and Interlaken, CH (SGAR) in 2009. We checked for participants' awareness concerning predictors for DMV, whether they mask ventilated before applying MR, asked about the use of cricoid pressure (Sellick's manoeuvre), and recorded demographics.

Results: Mean age was 45 ± 9 ys, mean experience 15 ± 9 ys, equally distributed among groups. There were less females in the UK (32%) compared to A (50%) and CH (41%, $p = 0.066$). Answers were similar in A and CH, but different to the UK. Only a minority routinely checked all five predictors for DMV preoperatively (A 8%, CH 9%, UK 15%). Age was more often recognized as a predictor for DMV by anaesthesiologists in the UK (table 1). Anesthesiologists in the UK ventilated patients less often by mask before applying MR.

Discussion and conclusion: Anesthesiologists in the UK more consistently check predictors for DMV and take that into consideration when deciding whether or not to mask ventilate before applying MR. Almost half of anaesthesiologists from Austria and Switzerland never use Sellick's manoeuvre, whereas it is still often applied in the UK. It seems that non-English speaking anaesthesiologists tend to abandon Sellick's manoeuvre because it might add to patients' risks with no evidence of any gained benefit whereas UK anaesthesiologists strongly believe in its effectiveness and apply the technique.

Table 1	A (n = 109)	CH (n = 116)	UK (n = 60)	p-value
Routinely checking predictors for DMV: Age, n (%)	15 (14)	12 (10)	16 (27)	0.015
Always checks if mask ventilation is possible, n (%)	80 (73)	78 (67)	19 (32)	<0.001
Never checks if mask ventilation is possible, n (%)	9 (8)	8 (7)	11 (18)	0.042
Checks when predictors for DMV are present, n (%)	14 (13)	23 (20)	25 (41)	<0.001
Never applying cricoids pressure, n (%)	45 (42)	55 (47)	1 (2)	<0.001
Applying cricoids pressure during RSI, n (%)	53 (49)	36 (31)	58 (97)	<0.001

P 20

Prediction of difficult intubation with advanced face recognition techniques: a preliminary study

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Introduction: Difficult tracheal intubation remains a constant and significant source of morbidity and mortality in anaesthetic practice. Insufficient airway assessment in the preoperative period continues to be a major cause of unanticipated difficult intubation. Although many risk factors have already been identified, preoperative airway evaluation is not always regarded as a standard procedure and the respective weight of each risk factor remains unclear. Moreover the predictive scores available are not sensitive, moderately specific and often operator-dependant. In order to improve the preoperative detection of patients at risk for difficult intubation, we developed a system for automated and objective evaluation of morphologic criteria of the face and neck using video recordings and advanced techniques borrowed from face recognition.

Method and results: Frontal video sequences were recorded in 5 healthy volunteers. During the video recording, subjects were requested to perform maximal flexion-extension of the neck and to open wide the mouth with tongue pulled out. A robust and real-time face tracking system was then applied, allowing to automatically identify and map a grid of 55 control points on the face, which were tracked during head motion. These points located important features of the face, such as the eyebrows, the nose, the contours of the eyes and mouth, and the external contours, including the chin. Moreover, based on this face tracking, the orientation of the head could also be estimated at each frame of the video sequence. Thus, we could infer for each frame the pitch angle of the head pose (related to the vertical rotation of the head) and obtain the degree of head extension. Morphological criteria used in the most frequent cited predictive scores were also extracted, such as mouth opening, degree of visibility of the uvula or thyro-mental distance.

Discussion and conclusion: Preliminary results suggest the high feasibility of the technique. The next step will be the application of the same automated and objective evaluation to patients who will undergo tracheal intubation. The difficulties related to intubation will be then correlated to the biometric characteristics of the patients. The objective in mind is to analyze the biometrics data with artificial intelligence algorithms to build a highly sensitive and specific predictive test.

P 21

Flexible nasopharyngoscopy to assess the dislocation rate of postoperative airway exchange catheters in the post-operative care unit (PACU): Preliminary data from a prospective observational study

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Background and aims: The Cook Airway Exchange Catheter (CAEC) is designed to secure the patient's airway in case there is a need to change the endotracheal tube. It is also used as a post-intubation aid to facilitate quick tracheal access in case of re-intubation. Therefore the correct location of the CAEC in the trachea is of utmost importance. Only retrospective data on its use is available and very little is known about the monitoring of the correct placement postoperatively. The aim of this prospective, observational study was to gather information about the correct tracheal position of a CAEC in the post-anesthesia care unit (PACU).

Methods: With ethics committee approval and informed consent we consecutively included all patients entering the PACU with an oral or nasal CAEC after the extubation of the trachea over the CAEC in the OR. After PACU arrival we continuously measured EtCO₂ from the CAEC until its removal. Additionally, the position of the CAEC was visualized with a flexible nasopharyngoscope (EF-BNI, Acutronic Medical System AG, Switzerland) at PACU admission, at CAEC removal and at changes of the EtCO₂ waveforms indicate no gas flow. The primary outcome was failure rate defined as fiberoptically documented extra-tracheal position of the CAEC. Secondary outcomes are inappropriate EtCO₂ measurement and re-intubation rate.

Results:

Table 1
Results of dislocated CAEC assessed by flexible nasopharyngoscopy.

Oral CAEC n = 20	Nasal CAEC n = 61	p-value
Dislocation rate %, (n) 15 (3)	3.3 (2)	0.09

P 21

Table 2
Relation between EtCO₂-measurement and flexible nasopharyngoscopic verification: Figures are (n).

Endtidal-CO ₂ -curve	CAEC extra-tracheal	CAEC tracheal	Total patients
Absent	2	11	13
Present	3	65	68
Total	5	76	81

Detection of dislocated CAEC by EtCO₂-measuring revealed a sensitivity of 40% a specificity of 85% a positive predictive value (PPV) of 15% and a negative predictive value (NPV) of 95%.

Conclusions: Inexistent or disappearing EtCO₂ curve with the postoperative use of CAEC does not sufficiently predict its incorrect position (PPV = 15%) but the presence of a EtCO₂ curve indicates endo-tracheal position of the CAEC with high probability (NPV = 95%). Fiberoptical visualization revealed a higher dislocation rate in orally placed catheters. Therefore, we recommend endoscopic control of possible CAEC dislocations before its removal to improve patient safety in the case that expected re-intubation problems are probable.

P 22

Ultrasonographic gastric antral area to assess gastric contents in children: comparison with total gastric fluid volume determined by magnetic resonance imaging

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Background: Ultrasonography (US) has recently been proposed for preoperative assessment of gastric contents in adults, using a single, anatomic landmark guided plane for calculation of gastric antral area (GAA) [1]. Supine (SUP), elevated 45° degree supine (E45) and right decubital (RDC) position have been described [1–3]. In children, GAA has not yet been validated.

Method: Healthy volunteers aged from 6 to 12 years fasted overnight. Gastric content was examined before and at various instants up to 120 min after ingestion of 7 ml/kg diluted raspberry syrup. At each instant, gastric fluid volume (GFV) was determined by magnetic resonance imaging (MRI) and GAA were measured 3 times in each of the SUP, E45 and RDC position. Correlation coefficients (Pearson) between GAA and GFV were calculated for each US position. Demographic data are presented as range (median), values for GAA and GFV as mean ± standard deviation.

Results: 16 healthy children aged from 6.4 to 12.8 (9.2) years, weighing 21.6 to 40.7 (31.8) kg, were examined 1 to 3 times. Overall 23 examinations were conducted: 6 after overnight fasting, 3 directly after and 14 with a delay of 74 ± 35 min after ingestion of syrup. GFV was 56 ± 72 ml. Mean GAA was 221 ± 116 mm², 218 ± 112 mm² and 347 ± 188 mm² for SUP, E45 and RDC position, respectively. Variation coefficients for GAA measurements were 20.1 ± 11.6 %, 20.1 ± 12.3 % and 18.9 ± 11.8 % for SUP, E45 and RDC position. Correlation between GFV and mean GAA was R = 0.62 (p < 0.01), R = 0.49 (p < 0.05) and R = 0.73 (p < 0.01) for SUP, E45 and RDC position, respectively.

Conclusion: Overall correlation between GAA and GFV was poor to moderate in children, with the RDC position producing the most reliable results. Interpretation of isolated GAA values could be misleading.

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P 23

A novel puncture sled for ultrasound guided vascular access: Effect on success rates for novices

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Introduction: Most anesthesiologists are familiar with patients who have notoriously difficult intravenous catheter placements. There is growing evidence that the use of ultrasound to visualize and successfully place catheters into peripheral veins is of undisputable value in those patients. However the experiences in using ultrasound guidance for intravenous catheter placement may be limited. The development of a puncture-aid which allows a single, short and effective puncture also in the hand of untrained personnel could be of great value. The aim of this study was to evaluate whether a novel puncture sled would represent an advantage, especially in untrained operators.

Methods: Fifty medical students, novices for ultrasound guided procedures, were randomly assigned (closed envelope) to use

ultrasound combined with the puncture sled (sled group) or ultrasound without the puncture sled (control group). All participants had to perform a sequence of fifteen ultrasound guided phantom vessel (Branched 4 Vessel Vascular Access Phantom, Blue Phantom Products) punctures. The sled consists of a movable mounting for 20 G-catheters allowing only longitudinal axis movements as needed for punctures. Lateral movement will be prevented. The depth of the puncture can be adjusted by moving the position of the calibrated sled along the depth regulator as visualized in figure 1. The movement of the mounting is restricted to limit advancing of the needle tip to any further than exactly under the transducer and thus prevents a puncture beyond the structures visualized by the ultrasound. After the puncture, the sled can be withdrawn and the catheter left in place without further manipulations of the latter. For each of 15 attempts success was rated = 1 and failure = 0. Data are presented as mean \pm SD.

Results: Figure 2 shows overall success count for fifteen attempts in the sled (14.1 ± 1.2) and the control group (11.1 ± 2.7). Box-whisker plots: box: 25 percentile, median, 75 percentile; whiskers: upper and lower fence. Open circle: extreme. ($P < 0.001$, Mann-Whitney U). Figure 3 illustrates success rate in percent for each attempt in both groups (* $P < 0.050$ compared to control, Fisher's exact test).

Conclusions: Ultrasound guided punctures can be learnt quickly. However, a sled as puncture-aid significantly improves the success rate of ultrasound guided vessel punctures in a phantom. It prevents a learning phase with failures and unnecessary needling.

Figure 1

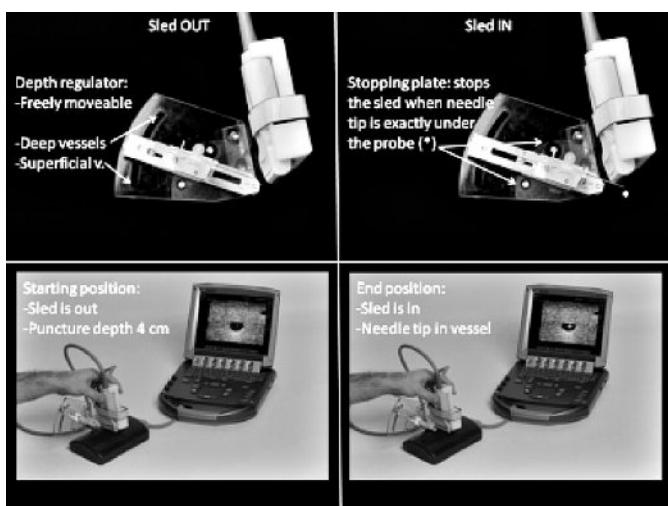


Figure 2

Success of 15 punctures

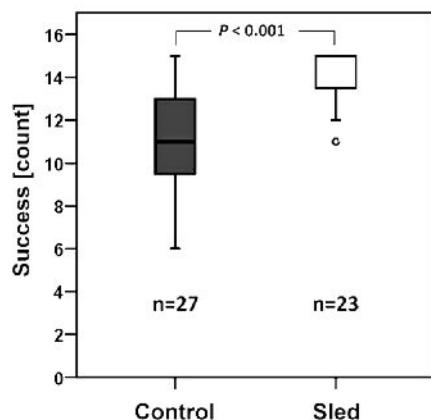
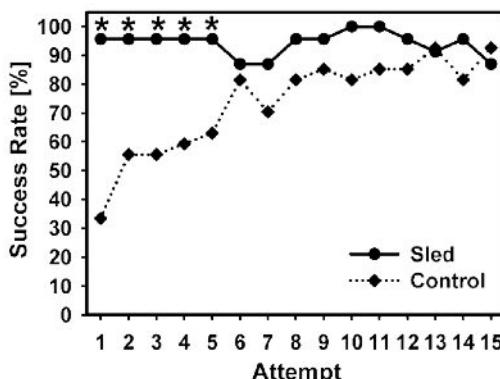


Figure 3

Success at each attempt



P 24

Is a preanaesthetic information form really useful?

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Background: All patients should be fully informed about risks and benefits of anaesthetic procedures before giving a written consent. Moreover, satisfaction level may vary in proportion to given information. We aimed to determine, in a single-blind randomized controlled study, if an information form given before the preanaesthetic consultation could improve perceived information, information gain and satisfaction level.

Methods: Two hundred patients ASA I–III scheduled for elective orthopaedic surgery were randomized in two groups: a group which received an information form before the preanaesthetic consultation (IF group) and a control group (no information form). A standardized questionnaire was submitted after the preanaesthetic consultation, and after the operation. This 17-item questionnaire explored perceived information (5 items), information gain (3 items), and satisfaction level (9 items). The items of each topic were pooled and compared between groups.

Results: One hundred and eighty-five patients (92.5%) completed the study. IF group had a better perceived information (IF group 73% vs. control group 63%, $p = 0.002$), a higher information gain (IF group 75% vs. control group 62%, $p = 0.001$), and a higher satisfaction level (IF group 95% vs. control group 92%, $p = 0.048$).

Conclusions: Our study suggests that an information form given before the preanaesthetic consultation enhances perceived information, information gain, and satisfaction level.

P 25

Quality control in anaesthesia: a retrospective survey

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Introduction: In Switzerland, the SGAR-SSAR encourages the participation with a national project of quality control (ADS) based on anaesthesia data. This data represents a medical point of view, regarding the technical and medical complications. We were interested in a quality inquiry, based on the patient's point of view.

Methods: A questionnaire was created, evaluating the five following anaesthesiological allowances: a) out-patient preoperative consultation b) in-patient preoperative visit c) care in the operating room d) care in the recovery room and e) postoperative medical visit. For 1 month, all surgery patients were included in the protocol. Patients were either contacted at home by phone or interviewed at the hospital.

Results: 733 patients answered the questionnaire.

a) Out-patient preoperative consultation

Out of 331 patients seen, 321 estimated that this consultation was necessary. Ten patients considered it useless. When asked about the fact that the consultant was not necessarily their anaesthetist for the procedure, 281 patients answered that they didn't care, convinced that the record had been transmitted and that the other anaesthetist was competent as well. Thirty-four patients were disappointed not to have been informed of this fact.

b) In-patients preoperative visit

From the 450 patients visited, 437 were satisfied. 9 had no recollection and 4 complained of bad explanations about the anaesthetic technique.

c) Care in the operating room

All 733 patients except one were satisfied. Undesirable postoperative side effects were reported by 15% of patients, mostly nausea/vomiting.

d) Care in the recovery room

Out of the 304 patients staying in the recovery room, 285 were satisfied. Fifteen patients were not satisfied because of bad pain management, noisy environment or the feeling of a premature transfer to the ward.

e) Postoperative visit (post medication)

Only 20% of patients remembered having seen the anaesthesiologist after surgery, but only 6% estimated it was a dereliction of duty. Most patients excused the physician for being certainly busy.

Conclusion: Out-patient preoperative consultation is well accepted by patients. Patients do well accept that another anaesthesiologist will take care of them for the surgical procedure, but such information should be clearly explained. This survey prompted us to take adequate measures in order to improve pain management and noisy environment in the recovery room. Finally a low rate of post medication was established.

P 26

Oxidative Stress and Apoptosis in Alveolar Epithelial Cells upon Exposure to Metal Oxide Nanoparticles

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Introduction: Metal oxide nanoparticles (NP) represent an industrially most relevant class of nanomaterials. With the wide use, concerns over the impact of such materials on human health – especially on airway structures – are growing.

Aims and objectives: We investigated the level of intracellular oxidations and the apoptosis rate in alveolar epithelial cells (AEC) after exposure to manganese(III) oxide-NP (Mn_2O_3 -NP), titanium dioxide-NP (TiO_2 -NP) and cerium dioxide-NP (CeO_2 -NP). We hypothesized that the presence of a high catalytic activity could strongly alter the damaging action of a nanomaterial. Sources of exposure to humans are e.g. occupational environment in metalworking (Mn_2O_3 -NP), glass/ceramic applications (CeO_2 -NP) and cosmetic products (TiO_2 -NP). NP, comparable in their physical characteristics (size, surface area), but different in their catalytic potential were therefore investigated.

Methods: AEC were incubated with Mn_2O_3 -NP, TiO_2 -NP and CeO_2 -NP at concentrations of 5 μ g/ml, 10 μ g/ml and 20 μ g/ml. To quantify the generation of reactive oxygen species (ROS), we measured the oxidation of non-fluorescent 2,7'-dichlorofluorescin (DCFH) substrate to the highly fluorescent form of the dye. To assess the apoptosis rate, we determined the caspase-3 activity. Cells were therefore incubated with the fluorogenic caspase-3 substrate Ac-Asp-Glu-Val-Asp-AMC. After proteolytic cleavage, fluorescence of the reporter group was captured. Cytotoxicity was monitored using DNA Quantitation assay. Statistical analysis was performed with a one-way analysis of variance (ANOVA).

Results: After 24h of exposure to Mn_2O_3 -NP, oxidation of DCFH was increased by 137.6% (5 μ g/ml Mn_2O_3), 110.0% (10 μ g/ml Mn_2O_3) and 125.3% (20 μ g/ml Mn_2O_3) compared to untreated cultures (p values <0.001). Upon exposure to TiO_2 -NP and CeO_2 -NP no significant generation of ROS could be observed. In the case of Mn_2O_3 -NP, caspase-3 activity was increased by 111.52% (5 μ g/ml Mn_2O_3), 115.09% (10 μ g/ml Mn_2O_3) and 96.86% (20 μ g/ml Mn_2O_3) after 24h, compared to untreated cultures (p values <0.001). This could not be found for TiO_2 -NP and CeO_2 -NP. No cytotoxicity could be detected for all three particles.

Conclusions: These results give evidence that acute exposure to metal oxide NP has a different impact on living cells and may be influenced by catalytic activity. Formation of ROS may be a major factor for induction of apoptosis in our experimental setting.

P 27

Metal Oxide Nanoparticles: Interactions with Healthy and Endotoxin-Injured Target Cells of the Lung

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Introduction: We investigated inflammatory and cytotoxic effects of titanium dioxide, cerium dioxide and manganese(III) oxide nanoparticles in healthy and inflamed alveolar epithelial cells (AEC). These metal oxide nanoparticles represent an industrially most relevant class of nanomaterials. Inflammatory and cytotoxic effects were evaluated upon exposure to healthy and inflamed pulmonary cells.

Methods: AEC were incubated with titanium dioxide, cerium dioxide and manganese(III) oxide nanoparticles at concentrations of 5 μ g/ml, 10 μ g/ml and 20 μ g/ml for different time periods with or without the

presence of endotoxins (100 ng/ml lipopolysaccharids, LPS).

Expression of cytokine-induced neutrophil chemoattractant-1 (CINC-1) and monocyte chemoattractant protein-1 (MCP-1) was analyzed by ELISA. Cytotoxicity was monitored using fluorescence DNA quantitation and LDH assays. Physico-chemical characterization of the investigated materials was provided by the Institute for Chemical and Bioengineering, ETH Zurich, Switzerland. Statistical analysis was performed with a one-way analysis of variance.

Results: Upon exposure to the different particles no significant changes in mediator levels were found on healthy AEC. In inflamed AEC, however, a significant increase of CINC-1 levels was observed: incubation with LPS and 20 μ g/ml of manganese(III) oxide nanoparticles caused an increase of 25% after 8h (p value <0.001) and 61% after 24h (p value = 0.001) compared to CINC-1 levels in endotoxin-injured cells. Production of MCP-1 was only moderately enhanced after 8h of exposure to manganese(III) oxide particles in comparison to LPS alone. The increase in lung inflammation could not be shown for titanium oxide and cerium oxide particles. No cytotoxicity could be detected for all three nanomaterials.

Conclusions: These data provide evidence that although belonging to the same group of nanoparticles, manganese(III) oxide has a different impact on AEC than titanium and cerium oxide. Acute exposure to manganese(III) oxide particles might be harmful in patients with inflammatory diseases.

P 28

Fluorinated carbon groups mediate the protective effect of volatile anesthetics in inflammatory tissue injury

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Volatile anesthetics not only provide protection against ischemia-reperfusion events but also modulate inflammatory response upon tissue injury. Whether these protective effects are mediated by the ether basic structure of volatile anesthetics or due to characteristics in their halogenations, is still unclear. We now demonstrate in an inflammation / injury model using lipopolysaccharides, that the fluorinated carbon groups are responsible for the immunomodulatory effects. Conditioning experiments in pulmonary endothelial and epithelial cells with equimolar concentrations of sevoflurane, diethyl-ether and various molecules of different chemical nature (including the sevoflurane metabolite hexafluoroisopropanol.) carrying either a trifluorinated carbon group (CF_3) or methyl group (CH_3) were performed. Both, inflammatory response and the chemotactic activity in either cell line were dose-dependently decreased upon exposure to molecules with CF_3 groups. This was not observed for the corresponding non-fluorinated molecules or diethyl-ether. Cytotoxicity could be excluded.

These findings reveal that the beneficial effects are not limited to volatile anesthetics, but associated with a much broader class of molecules containing at least one CF_3 group. Overcoming limitations of volatile anesthetics (requirement of close patient surveillance), the protective effects could be provided in a hydrophilic, injectable formulation for the future treatment of patients suffering from severe inflammation or ischemia/reperfusion events.

P 29

Ventilatory dependent PaO_2 oscillations and their distribution in the systemic circulation

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Background: PaO_2 oscillations at the brachiocephalic artery have been shown in a rabbit model of lung injury. However, exact relationship with the respiratory cycle and propagation velocity downstream the arterial circulation is unknown. In a porcine lung lavage model (i) we evaluated the temporal behavior of PaO_2 oscillations compared to electrical impedance tomography (EIT) based assessment of ventilation processes and (ii) determined the propagation velocity of aortic PaO_2 oscillations depending on cardiac output.

Method: With IRB approval fast intravascular PaO_2 measurement was performed in 7 anesthetized pigs (25 ± 1.2 kg) by fiber optic, fluorescence-quenching oxygen probes (FOXY-AL300, Ocean Optics,

FL) connected to multi frequency phase fluorimeters (MFPF-100, TauTheta, USA). Respiratory parameters were: respiratory rate 8/min, tidal volume 30 mL/kg, positive end expiratory pressure 5 mbar, FIO_2 1.0. Dynamic changes of regional pulmonary aeration within the respiratory cycles were assessed by EIT (Viasis, Germany). After induction of lavage ARDS, measurements were taken at the ascending aorta (AA) and at the aortic bifurcation (AB). Synchronized fast intravascular PaO_2 measurements were stored with a sampling rate of 10 Hz and electrical impedance tomography data were recorded with 13 Hz. Data analysis was performed with a Matlab application (The Mathworks, Natick, USA). Data are presented as mean \pm SD [median (min-max)].

Results: Figure 1 illustrates a typical example of the tracings of lifetime sampled at AA and at AB with the corresponding EIT in one animal. Peak to peak time for AA vs. AB was 1.5 ± 0.6 sec [1.2 (0.9–2.4)], for AA 7.2 ± 0.5 sec [7.4 (6.2–7.5)], for AB 7.2 ± 0.5 sec [7.4 (6.3–7.5)] and for EIT 7.0 ± 0.8 sec [7.5 (5.6–7.5)]. Amplitude of PaO_2 oscillations for AA was 64.1 ± 16.4 mm Hg [55.8 (50.1–90.4)] and for AB 49.2 ± 18.3 mm Hg [49.2 (26.7–71.8)]. Heart rate was 174 ± 29 beats per minute [172 (140–221)] and cardiac output 5.2 ± 1.4 Lmin $^{-1}$ [5.6 (3.1–7.1)].

Conclusions: PaO_2 oscillations are highly correlated with the respiratory cycle supporting the hypothesis of tidal change of shunt fraction due to recruitment and derecruitment of atelectasis. The impact of heart rate and cardiac output on blood flow velocity and the resulting aortic oxygen partial pressure oscillation distribution seems to be low.

Acknowledgements: All experiments were performed at the Department of Anesthesiology, Johannes Gutenberg-University; funding by DFG Ma2398/7 and SNF POIB-117065/1.

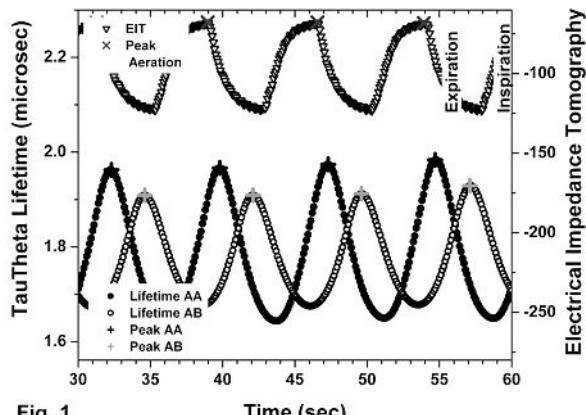


Fig. 1

P 30

Emergent anesthesia for embolectomy in massive pulmonary embolism

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Introduction: Massive pulmonary embolism (PE) has a 90-day mortality of up to 52% [1]. Despite lack of evidence, thrombolysis is still recommended as first line therapy for these patients [2]. However, recent series of surgical embolectomies [SE] in acute massive PE reported excellent outcomes, at a mortality of 8–10% [3, 4].

Nevertheless, anesthetic induction for emergent SE was associated with cardiovascular collapse in 19% [4]. Therefore, the aim of our study was to assess characteristics and risk of anesthesia induction in our institutional series.

Patients and method: With IRB approval, anesthesia records of 40 consecutive patients (m 24/f 16; median age 56 [22–80] y) with massive pulmonary embolism undergoing SE on cardiopulmonary bypass between 02/00 and 12/06 were retrospectively analyzed.

Patients were referred to SE either directly after diagnosis (n = 30) or after medical pre-treatment (e.g., thrombolysis) (n = 10).

Results: After induction of GA, incidence of cardiopulmonary resuscitation (CPR) was 10% (4/39); one patient was already admitted under ongoing CPR; in additional 30% (12/40), vasopressor infusion became necessary. Overall in-hospital and 90-day mortality was 7.5% (3/40) and 10% (4/10), respectively. None of the patients which, after GA induction, required new CPR (0/4) or new vasopressor-infusion (0/12) died during the hospitalization. In-hospital mortality was 3.3% (1/30) if SE was performed directly after diagnosis and 20% (2/10) if conservative treatment efforts preceded surgery.

Conclusion: Anesthetic and surgical risks of SE appear, in our series, to be lower than reported in the literature. Acute hemodynamic

collapse after induction of GA remained a substantial risk, but did not contribute to mortality. We conclude that assumed risks of GA induction should not bias team decisions against proceeding with SE as primary intervention in massive PE, provided cardiopulmonary bypass is available on the spot during and after induction.

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P 31

Inspired oxygen fraction lower than 30% for patients after bleomycin exposition is not associated with perioperative pulmonary complications

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Purpose: The incidence of pulmonary toxicity ranges from 0 to 40% in patients receiving chemotherapy with bleomycin. Hyperoxic exposure during general anesthesia after bleomycin for treatment of germ cell tumors is purported to potentiate bleomycin-induced pulmonary toxicity, however objective evidence is lacking. The aim of this study was to retrospectively assess perioperative pulmonary complications after retroperitoneal lymphadenectomy (RPLND) in patients with bleomycin treatment <6 months before surgery.

Methods: A consecutive series of 47 patients who underwent RPLND after bleomycin treatment for testicular cancer between 1991 and 2007 were reviewed. Patients with preoperative radiotherapy were excluded. Only patients receiving a RPLND within 6 months after completion of chemotherapy were included. Anesthesia was performed with a FiO_2 of 100% for 3 minutes for induction of anesthesia and then with a FiO_2 just under 30% during surgery (median surgical time 240 minutes (120–800)). After extubation, 2–3 l of oxygen were administered for the next 2 days. We assessed all potential risk factors for bleomycin induced pulmonary toxicity (creatinin clearance <35 ml/min, cumulative bleomycin dose >300 000 IU, age >40 years, stage IV disease). Clinical signs for pulmonary damage were documented (dyspnea, tachypnea, non-productive cough, postoperative oxygen saturation problems).

Results: 22 patients with a median age of 26 years (19–49) were finally included. Median bleomycin dose during chemotherapy was 270'000 IU (270'000–540'000). American Joint Committee on Cancer stage groups were as followed: IIa: 4 patients, IIb: 8, IIc: 4, IIIa: 5, IIIc: 1. The majority of patients had mixed tumours 12 (60%), non-seminomatous tumours 5 (25%) and seminomas 3 (15%). No patients had pulmonary disease documented preoperatively. History of smoking was present in 9 patients. Creatinin clearance was normal in all patients. No pathognomonic signs (dyspnea, tachypnea, and non-productive cough) for pulmonary damage could be detected up to 7 days postoperatively.

Conclusion: Administration of 100% oxygen for 3 to 5 minutes during induction of anesthesia and maintaining a FiO_2 <30% during surgery appeared to be safe in this young patient population. We are aware of the limitations of the study especially the lack of pulmonary function assessment, however no clinically relevant pulmonary complications were observed. Prospective, controlled studies are warranted to assess this question.

P 32

Transcatheter aortic valve implantation in high-risk patients: anesthetic considerations

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Introduction: In severe aortic stenosis, mean survival after onset of symptoms is 2–3 years [1]. However, one third of these patients are not admitted to surgical valve replacement because of excessive perioperative risk [2]. In dedicated centres, transcatheter aortic valve implantation (TAVI) emerged as an alternative to surgery in elderly high-risk patients. Aim of our study was to report characteristics and outcomes of TAVI anesthesia at our institution.

Patients and method: With IRB approval, 112 patients (age 83 \pm 5 y; females 57%) with severe symptomatic aortic stenosis (AVA 0.58 cm 2 [0.2–1.0]; NYHA III/IV 80%) at high risk for surgical valve replacement (log. Euro-Score 27 \pm 15%, STS score 9 \pm 7) underwent TAVI between 08.2007 – 05.2009. Systems used were CoreValve Revalving (n = 77) and Edwards-SAPIEN System (n = 35). Vascular access was

transfemorally (n = 86), transsubclavian (n = 2), and transapical (n = 24). TAVI was performed in general anaesthesia (GA; n = 52) or local anaesthesia with sedation (LA-MAC; n = 60).

Results: Device success was 95% (107/112). Mean pre- and postinterventional aortic valve gradient was 50 ± 12 and 7 ± 6 mm Hg, respectively. Major bleeding occurred in 3.7% periprocedurally and in 10% within 30 days. Permanent pacemaker implantation was necessary in 34%. Mortality: periprocedural 2.7%; in-hospital 3.6%; 30-day 8.9%. Anesthetic characteristics see table:

	n (%)	vasopressor infused	converted to GA	CPR (intra-procedural)	extub. p.p. / fit for IMC
LA-MAC	60 (54%)	23 (38%)	4 (6.7%)	4 (6.7%)	56 (93%)
PAVI					
GA	52 (46%)	51 (98%)	n / a	1 (1.9%)	34 (65%)
PAVI	28 (25%)	27 (96%)		1 (3.6%)	22 (79%)
TAPAVI	24 (21%)	24 (100%)		0 (0%)	12 (50%)
Total	112 (100%)	74 (66%)	3 (2.7%)	5 (4.5%)	59 (80%)

LA-MAC: local anesthesia and monitored anesthesia care; GA: general anesthesia; PAVI: percutaneous aortic valve implantation; TAPAVI: transapical aortic valve implantation; Vasopressor: norepinephrine or epinephrine; IMC: intermediate care/step-down unit.

Conclusion: TAVI has good haemodynamic results and a risk-adjusted mortality similar to that of surgical AVR. Transfemoral TAVI can be done in LA-MAC in up to 90% of cases; conversion to GA and/or CPR may be necessary in $\leq 10\%$. Elective GA is required for transapical TAVI and selected indications; it was associated with more vasopressor and resource use, but no different mortality.

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P 33

Survey of neuromonitoring and neuroprotective strategies used by German cardiac anaesthesia groups

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Objective: The primary objective of this survey was to identify current practice in cardiovascular anaesthesia with regard to neuromonitoring and neuroprotection.

Methodology: The dataset is based on a questionnaire sent out to all German cardiac anaesthesia departments between October 2007 and January 2008. The survey enquired about preoperative evaluation of the cerebral vasculature, intraoperative use of neuromonitoring, use of specific interventions aimed at cerebroprotection, perfusion management during cardiopulmonary bypass [CPB], postoperative evaluation of neurological status, and training in the field of cerebral monitoring.

Results: Of 80 mailed questionnaires 55% were answered. Methods used for intraoperative neuromonitoring are (processed) electroencephalography [EEG] (60%), near infrared spectroscopy (40%), evoked potentials (30%), and transcranial doppler (17.5%). EEG is the preferred neuromonitoring modality for type A aortic dissection repair (38%), elective surgery on the thoracic and thoraco-abdominal aorta (34% and 32% respectively), and in carotid surgery (43%). Cerebroprotective measures used comprise CPB-induced patient cooling (100%), external head cooling (65%), the administration of corticosteroids (58%), barbiturates (50%), and antiepileptic drugs (10%). Anaesthetic choice with the goal of neuroprotection consists of inhalation anaesthetics (33%), or using total intravenous anaesthesia (20%). In 85% of departments, targeted CPB flow equals calculated cardiac output [cCO] under normothermic conditions. Target mean arterial pressure [MAP] varies between 60 and 70 mm Hg in 44%, and between 50 and 60 mm Hg in 42%, respectively. At core temperature less than 18 °C CPB flow is reduced below cCO in 70% of the departments, whereas 27% continue to use normothermic flow rates. Target MAP under hypothermia is between 50 and 60 mm Hg in 59% of the centers. In 43% of the centers, postoperative neurological function is assessed by the anaesthesiologist. Continuing education sessions pertaining to neuromonitoring are organized on a regular basis in 33% of the groups.

Conclusion: Results of this survey indicate that intraoperative use and choice of neuro-monitoring techniques and neuroprotective approaches during cardiovascular anaesthesia varies considerably among German cardiac anaesthesia groups. EEG-based neuromonitoring and neuroprotection by induced hypothermia are employed most often.

P 34

Evaluation of planned anesthesia instrumentation and its adequacy for cardiac surgery

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Introduction: In cardiac anaesthesia, instrumentation for hemodynamic monitoring, medication and transfusion is planned preoperatively. Planning considers the patient's cardiovascular risk profile, coexisting diseases, type and potential complications of cardiac surgery (CS) and finally, institutional preferences. Our aim was to study adequacy of instrumentation planning and realization. Here we report the comparison of planned vs. performed instrumentation, and the incidence of unplanned extended monitoring and transfusion in elective CS patients with cardiopulmonary bypass (CPB).

Method: During 1 month, the preanesthetic plan was compared with the performed instrumentation on the day of surgery. Standard anesthesia monitoring consisted of invasive arterial and central venous pressures, ECG (II, V5), SpO₂, end-tidal CO₂, BIS™, temperature and TEE. An 8.5 Fr introducer sheath was planned on expectations by the visiting anesthetist that insertion of a pulmonary artery catheter (PAC) or transfusion of ≥ 3 red cell concentrates be required. A PAC was envisioned when cardiac index $< 2.2 \text{ l/min/m}^2$, mixed venous SO₂ $< 50\%$, ejection fraction $< 40\%$ or pulmonary artery hypertension (mPAP $> 25 \text{ mm Hg}$) were expected. CS performed was categorized as high or low risk procedure according to Fergusson, NEJM, 2008.

Results: All 67 patients (36 high and 31 low risk CS) received standard monitoring as planned. TEE was specifically mentioned in 9/67 patients (13%), and discouraged due to contraindications in 5/67 (7%). In 94% (34/36) of the patients undergoing high risk CS, an introducer sheath was planned and introduced. In 10 of these 34 patients, a PAC was inserted preoperatively, but 6/10 patients did not meet PAC indications. However, 3/24 patients (13%) received a PAC due to hemodynamic instability during ICU stay. In 55% (17/31) of the patients undergoing low risk CS, an introducer sheath was placed. One of these 17 patients (6%) received an unplanned PAC during CPB weaning. Another low risk case (7%) got an unplanned introducer sheath for extended transfusion after CPB. Intraoperative red cell transfusion exposure was 58% in the high and 16% in the low risk group. 52% of all transfused high risk patients received 3 or more blood products.

Conclusion: In high risk patients scheduled for cardiac surgery with CPB, we found instrumentation adequate in 75% for hemodynamic and transfusion management. Instrumentation with introducer sheaths can be reduced in low risk CS patients.

P 35

Comparison of bedside and central laboratory ROTEM®-measurements

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Background and objectives: Major blood loss during surgery can lead to coagulopathy which needs prompt and balanced haemostatic resuscitation. Rotation thrombelastometry by ROTEM® provides a fast and differentiated blood clotting analysis. If ROTEM® measurements are done in the central laboratory, duration until first values are available is delayed. This study aimed to evaluate time savings and reliability of bedside versus central laboratory ROTEM® values.

Material and methods: Blood samples for both bedside and central laboratory ROTEM® delta analysis were simultaneously drawn from children undergoing major surgery with anticipated major blood loss. Blood samples were immediately sent to the central laboratory and analysis was started at the same time in the operating theatre. Time saving between availability of bedside versus central laboratory ROTEM® values was recorded. Paired ROTEM® values were compared using Bland-Altman analysis and Spearman correlation.

Results and discussion: Fourteen patients aged between 0.7–15.3 yrs (median 5.9) weighing 5.5 to 63.0 kg (14.5 kg) undergoing craniofacial (n = 4), spine (n = 7) or tumour surgery (n = 3) were included. Median of time by bedside ROTEM® was 11 min and ranged from 2 to 28 min. Bias and precision of Bland-Altman analysis and Spearman correlation of ROTEM® parameters of 49 paired blood samples were as followed:

	Bias/Precision (median value)	Spearman correlation
EXTEM (n = 48)		
CT [s]	0.4/21.9 (57)	0.629
CFT [s]	-5.0/28.5 (102.5)	0.953
alpha [°]	0.9/6.5 (70)	0.907
MCF [mm]	-1.7/5.7 (56)	0.968

	Bias/Precision (median value)	Spearman correlation
INTEM (n = 46)		
CT [s]	-2.6/23.5 (176)	0.853
CFT [s]	12.8/47.1 (94)	0.975
alpha [°]	-2.3/11.8 (72)	0.915
MCF [mm]	-1.7/5.3 (54)	0.981
FIBITEM (n = 48)		
CT [s]	2.3/86.3 (55)	0.511
alpha [°]	-0.9/8.3 (68)	0.960
MCF [mm]	-0.6/3.1 (9)	0.904
APTEM (n = 43)		
CT [s]	4.5/25.7 (57.5)	0.707
CFT [s]	18.1/36.6 (102)	0.960
alpha [°]	-2.3/7.6 (70)	0.944
MCF [mm]	-3.7/11.3 (55)	0.911

Spearman correlation was very high and ranged from 0.904 to 0.981 ($p < 0.01$), except for CT in all tests, where it ranged from 0.511 to 0.853 ($p < 0.01$). The reliability in our study is comparable to interrater reliability testing of ROTEM® in piglets [1], where CT was also shown to be less reliable than the other parameters.

Conclusion: Bedside ROTEM® measurements save valuable time during surgery with major blood loss. Considerable differences in some of the ROTEM® results demands further studies evaluating rapid versus slow processing of blood samples.

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P 36

Sekt: another tool for the assessment of non-technical skills in simulated pediatric crises

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Introduction: Simulated environments are well-suited to train and assess non-technical skills. Though more or less neglected in traditional medical education, the training and assessment of non-technical skills has now been realized in the recent development of curricula [1]. They still require a validated, reliable, objective, and easily applicable assessment and rating instrument for crisis resource management (CRM). In addition, the rating of performance must provide a reliable assessment tool to facilitate the making of concrete conclusions about the adequacy crisis management. SEKT is an observational assessment tool developed on the basis of the Anesthetists' Non-Technical Skills (ANTS) [3].

Methods: SEKT comprises of 19 specific behavioral markers, which are assigned to four main categories (see below).

SEKT **S** = Situationsbewusstsein (Situation awareness)
E = Entscheidungsfindung (Decision making)
K = Kommunikation (Communication)
T = Teamarbeit (Teamwork)

To investigate validity, reliability, and usability of SEKT as a tool for the assessment of non-technical skills, we conducted 12 observational sessions with interdisciplinary and multiprofessional teams managing simulated pediatric emergencies. The teams were allocated to one of

three pediatric emergency scenarios. The video-recorded simulation sessions were then independently reviewed by ten observers experienced in simulation-based assessment. To ensure their proficiency, the observers completed a defined simulator-facilitator training course. Rating was performed by using a numeric scoring system for each behavioral element. Three months after their first assessment, the same observers rerated all video-recorded scenarios.

Results: The study is currently still in progress. We will be able to present preliminary results.

Conclusion: SEKT indicates a valid, reliable, and easy-to-use assessment instrument to identify observable non-technical skills during simulated medical scenarios. It provides a valuable scoring system to identify good CRM-practice, and provides the framework for structured feedback for the purpose of pediatric simulation courses.

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P 37

No Wrong Site/Patient Surgery for 18 month after Implementation of a Checklist: Is everything all right?

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Introduction: Safety in surgery and perioperative care has evolved as an important quality control measure and outcome over the last decade. In order to improve patient safety at our institution [1, 2] we implemented a surgical checklist called the "4-step-protocol" hypothesizing we would improve team communication and consistency of care.

Methods: We retrospectively reviewed our charts of patients undergoing a surgical procedure over a 52 months period from May 2005 through August 2008 for wrong site/wrong patient surgery. In order to prevent any further incidents we designed and implemented a 13-item surgical safety check-list called the "4-step-protocol" and prospectively we collected data for 18 months from September 2008 through February 2010 for all patients undergoing a surgical procedure at our hospital. The checklist is mandatory for every patient undergoing a surgical procedure in our OR. The primary end-point of this study was the incidence of wrong site surgery. To ensure correct data collection and quality we evaluated the accuracy on 2 different occasions with a sample of 600 surgeries.

Results: The rate of wrong site surgery upon baseline was 5 cases in 52 months resulting in an incidence of 1/4901 cases. None of these patients sustained a noticeable damage. After implementation of a surgical safety checklist the rate declined to 0 cases over the 18 month period or 0/10560 cases using Fisher's exact test ($p = 0.318$). After the rule of three [3] with a confidence interval of 95% our actual incidence of a wrong site surgery is <1/3520 cases.

Conclusion: No wrong site/patient surgery has occurred after the implementation of a specifically designed surgical safety checklist for 18 month. If nothing goes wrong, is everything all right? [3] To be sure that everything is all right, we have to continue error free with 14700 surgeries or another 32 month without a mixed up patient. Since the checklist is part of our daily practice we believe that we are on the road to safer surgery.

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