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YEAR IN REVIEW

A year in review in Minerva Anestesiologica 2019. Anesthesia, analgesia, and perioperative medicine

Franco CAVALIERE [1] *, Massimo ALLEGRI [2, 3], Alparslan APAN [4], Edoardo CALDERINI [5], Massimiliano CARASSITI [6], Edmond COHEN [7, 8], Flaminia COLUZZI [9], Pierangelo DI MARCO [10], Olivier LANGERON [11], Marco ROSSI [12], Peter SPIETH [13], David TURNBULL [14]

[1]Department of Cardiovascular and Thoracic Sciences, A. Gemelli University Polyclinic, IRCCS and Foundation, Sacred Heart Catholic University, Rome, Italy; [2]Unità Operativa Terapia del Dolore della Colonna e dello Sportivo, Policlinic of Monza, Monza, Italy; [3]Italian Pain Group, Milan, Italy; [4]Department of Anesthesiology and Intensive Care, Faculty of Medicine, University of Giresun, Giresun, Turkey; [5]Unit of Women-Child Anesthesia and Intensive Care, Maggiore Polyclinic Hospital, Ca' Granda IRCCS and Foundation, Milan, Italy; [6]Unit of Anesthesia, Intensive Care and Pain Management, Campus Bio-Medico University Hospital, Rome, Italy; [7]Department of Anesthesiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [8]Department of Thoracic Surgery, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [9]Unit of Anesthesia, Department of Medical and Surgical Sciences and Biotechnologies, Intensive Care and Pain Medicine, Sapienza University, Rome, Italy; [10]Department of Cardiovascular, Respiratory, Nephrological, Anesthesiologic, and Geriatric Sciences, Sapienza University, Rome, Italy; [11]Department of Anesthesia and Intensive Care, Henri Mondor University Hospital, Sorbonne University, Assistance Publique -Hôpitaux de Paris, Créteil, France; [12]Institute of Anesthesia and Intensive Care, Sacred Heart Catholic University, Rome, Italy; [13]Department of Anesthesiology and Critical Care Medicine, University Hospital of Dresden, Dresden, Germany; [14]Department of Anaesthetics and Neuro Critical Care, Royal Hallamshire Hospital, Sheffield, UK

*Corresponding author: Franco Cavaliere, Department of Cardiovascular and Thoracic Sciences, A. Gemelli University Polyclinic, IRCCS and Foundation, Sacred Heart Catholic University, Largo Francesco Vito 1, Rome, Italy. E-mail: f.cavaliere@rm.unicatt.it

General anesthesia

Innovations in anesthesia are probably less frequent than in other fields, but new techniques to administer old drugs and the research of secure and reliable monitoring devices have animated the debate in the last year.[1, 2] Drug association is a common practice, looking for positive effects in terms of efficacy and reduction of total doses. The combination of hypnotics like propofol and analgesics like sufentanil can improve anesthesia induction and offer stable maintenance during surgery.[3] A study by Weber and Prasser on 60 patients who underwent sufentanil and propofol target-controlled anesthesia (TCI) offered new insights on the synergism between the two drugs[4] and opened to the possibility of TCI models based on drug interactions.[5] However, even a TCI model that considers the interaction between hypnotics and analgesics are subject to individual variability. Closed-loop anesthesia is aimed at overcoming this problem. An elegant randomized trial by Reboso *et al.* investigated the feasibility of adding a predictor to a controller in a closed-loop system to reach the desired hypnotic effect of Propofol earlier.[6] The combined software showed better performance than the operator's adjustments, reducing the number of anesthetist interventions.

Despite their long history of use, volatile anesthetics are still a topic of interest.[7] In January, MA published an exhaustive Pros-Cons article on Xenon focused not only on pharmacodynamic and pharmacokinetic properties but also on collateral effects, such as the cytoprotective one.[8] Pros included rapid induction and fast recovery

of cognitive function due to low solubility, and cardiovascular stability; Cons were high implementation costs and a MAC value of 0.63, which limits the maximum inspiratory concentration of O_2 to less than 40%. Possible favorable actions on organ preservation and neuroprotective effects are still open issues. The quick recovery of cognitive function following the end of administration makes xenon particularly interesting for anesthesia in asleep-awake-asleep (AAA) craniotomies. Kulikov *et al.* tested the use of this anesthetic in the first asleep phase of AAA craniotomies in 40 patients who underwent removal of cerebral tumors.[9] The authors found that the association of xenon and regional anesthesia alone was adequate to perform craniotomies in 67% of cases; they achieved awareness in few minutes after switching off xenon vaporizer (5±1 min) and performed mapping successfully in 92% of patients.

Nociception is probably the most challenging phenomenon to monitor during general anesthesia. Clinical evaluation based on heart rate and arterial pressure changes in response to surgical stimuli are often inadequate; consequently, new technology has been developed in the last years and is currently under evaluation.[10] In the December issue, Dostalova *et al.* compared the perioperative administration of analgesics based on clinical judgment, Surgical Plethysmographic Index (SPI), or Analgesia Nociception Index (ANI) in 72 patients scheduled for spinal surgery.[11] SPI and ANI groups received less sufentanil during surgery but needed postoperative administration earlier. Time to recovery of spontaneous breathing, postoperative analgesia scores, and plasma cortisol levels did not differ between groups. In May, MA published a systematic review and meta-analysis by Jiao *et al.* on the effectiveness of SPI, ANI, and pupillometry to guide intraoperative opioid administration.[12] In comparison with standard clinical care, SPI monitoring was associated with a significant reduction in opioid doses during surgery, but not in the postoperative period. The excellent editorial by Coluzzi pointed out that, in spite of the important limitations of currently available monitoring systems, there is an urgent need to overcome the management of nociception based on clinical judgment only.[13] A worldwide consensus on the subject would be highly desirable.

Cardiopulmonary bypass (CPB) is associated with the release of pro-inflammatory cytokines that may be involved in postoperative complications.[14, 15] Garau *et al.* tested the hypothesis that hemadsorption (Cytosorb®) during CPB might reduce the levels of pro-inflammatory cytokines and attenuate the inflammatory response.[16] Two groups of 20 patients were studied. The group treated with hemadsoption presented IL-8 and TNFα levels slightly lower than controls, IL-2 levels similar, and higher cardiac index values; the differences disappeared 24 hours after surgery. The authors concluded that hemoadsorption during CPB was feasible and safe, but probably of little clinical significance. A second article on cardiac anesthesia, published in June, was a meta-analysis by Ren *et al.* about the influence of anesthesia (inhalational *vs.* intravenous) on outcome after cardiac valve surgery.[17] The authors found that the choice between sevoflurane and propofol, or desflurane and propofol did not significantly influence the postoperative outcome. That finding differed from what reported by other authors in coronary artery bypass graft (CABG), in which the use of volatile anesthetics was associated with lower postoperative peaks of cardiac troponins I and T.[18]

Thiol-disulfide homeostasis (TDH) plays a significant role in antioxidant defense.[19] In the November issue, MA published a study in which Akin *et al.* evaluated the influence of the type of anesthesia (general *vs*. spinal) on maternal-neonatal TDH in 80 women who underwent elective cesarean operations.[20] The authors registered that "general anesthesia leads to an impairment in TDH when compared with spinal anesthesia."

In this era of opioid-free/sparing anesthesia, dexmedetomidine (dex) is more and more used and appreciated by anesthetists. One possible reason is the broad spectrum of action, which includes sedative, analgesic, anxiolytic, and anti-inflammatory properties.[21] MA published a few articles on the use of dex in anesthesia. In a prospective randomized study on 52 patients who underwent spine surgery, Kim MH *et al.* observed a reduction of epinephrine and norepinephrine levels and a more stable autonomic nervous system

balance associated with intraoperative administration of dex.[22] In patients who undergo total knee arthroplasty, surgeons often apply a tourniquet to minimize blood loss; yet, leg ischemia and local release of inflammatory cytokines may result. Kim SH *et al.* investigated whether dex could attenuate the effects of leg ischemia in 68 patients who underwent total knee arthroplasty.[23] In 34 patients who received dex, they observed lower blood levels of proinflammatory cytokines up to 90 min after tourniquet release, less postoperative pain, and less remifentanil needed for postoperative analgesia. Intranasal (IN) dex has recently gained great popularity due to its favorable pharmacodynamic and pharmacokinetic profile and the lack of significative side effect, but its use remains off-label in Europe and the USA. Mondardini *et al.* reviewed the use of IN dex in pediatric settings: sedation for painful and non-painful procedures, anesthetic premedication, and emergence delirium.[24] The authors claimed that there were still few data from RCTs so that there was not yet a consensus on dosages concerning patient age and clinical scenarios. They concluded that results depict dex as a wild card anesthetists can play in several clinical scenarios.

Hemodynamic monitoring in anesthesia

Physicians of antiquity observed the changes in the pattern of the pulse in health and disease. Harvey described blood circulation in the 16th century as a loop through the various vessels, with the heart acting as a pump and the elastic properties of the arteries creating the dynamics of the pulse. Subsequent refinements in the description of the arterial pressure waveform described the interaction between stroke volume, the compliance of the aorta, and the larger vessels, with the development of simple predictive models for cardiac output.

The development of the pulmonary catheter enabled the direct measurement of hemodynamic indices. Translation of these measurements to the critical care patient did not lead to a reduction in mortality, and this technology has mostly been abandoned, given the complications of pulmonary artery catheters.[25, 26] The development of fast Fourier analysis and computing has enabled a closer inspection of the pulse waves that make up the arterial waveform. The arterial blood pressure waveform has now been elaborated to provide estimations of cardiac output, stroke volume, and other hemodynamic indices.[27]

In 2019, several studies considered the extrapolation of data from close inspection of the pulse waveform complex. These included the "hypotension probability indicator" and "an active decision support system.[28, 29] These systems were trialed in the obese patient, major vascular surgery, and surgery in the prone position.[28, 30] Also, impedance cardiography was applied during liver transplantation to predict hemodynamic values when compared with pulmonary artery catheter values.[31, 32] Finally, through a systematic review, clinical guidelines for hemodynamic targets were reviewed.[33] Direct arterial pressure monitoring and targeted fluid therapy were identified as appropriate in some surgical settings. Nonetheless, each study identified caveats where the information provided was insufficient to support the use of indirect hemodynamic indices to manage the non-cardiac surgical patient.

There are many commercial opportunities to promote the development of tools to measure the indices abstracted from the pulse pressure wave. The translation of the measurement of hemodynamic indices to management and outcomes is a noble objective. We should reflect upon the algorithms behind the calculated indices and the assumptions made. The original observations of the pulse pressure wave registered the influence of systematic factors such as age, and pathological states. Other local factors, such as blood rheology and vessel conductance, influence the pulse pressure wave.

There is the potential for devices that estimate hemodynamic indices from algorithms, being the Emperor's new clothes. The studies reviewed raised issues about the interpretation of hemodynamic indices. The review of the evidence of morbidity reduction with the measurement of hemodynamic indices and or goal-directed fluid therapy was generally supportive but with many issues unresolved.[34] Our enthusiasm for extrapolation of data, beyond the limits of information provided by a pulse pressure waveform or other indirect measures, should be cautioned.

Airway management

Management of difficult airways in adults and children is a core topic and has been the object of recent reviews.[35-37] The authors stated that future research should focus on the development of screening tests useful not only for airway management in anesthesia but also in the prehospital environment, the emergency department, and the intensive care unit.[35] Interestingly, authors have poorly considered gender differences since now. In this regard, MA published a new study on the differences of performance and thresholds of some anatomic predictors for difficult airways in men and women.[38] The authors found that optimal cut-off values differed between males and females. The use of gender-specific values may improve predictivity as suggested by the observation that male patients had larger inter incisor and thyromental distances than female patients, but a higher incidence of difficult airways.

Extraglottic airway devices (EAD) are continually evolving, and MA published some articles on them.[39] Gordon *et al.* reviewed their indications, contraindications, and management.[40] Yoo *et al.* investigated the influence of head and neck position on the performance of the Ambu® AuraGain™.[41] They found that head and neck position affects the oropharyngeal seal, as evidenced by changes in oropharyngeal leak pressure, but not to the extent that prevents positive pressure ventilation. As a rule, the anesthetist can flex the patient's neck to improve the oropharyngeal seal; however, he/she can also extend or right rotate the neck to facilitate endotracheal intubation. That is not the case of laryngeal mask airway (LMA) Protector, a recent supraglottic airway device the pharyngeal seal of which, according to a study by Eckart *et al.* published in January, does not decrease if the neck is extended.[42] Those authors evaluated the performance of LMA Protector, that allows gastric drainage and provides a conduit for tracheal intubation with a fiberscope. Its pharyngeal seal was similar to that of the LMA-ProSeal, whereas its user-friendliness might be superior. The value of EADs in non-operating room anesthesia (NORA) was confirmed by Zamparelli *et al.*, who compared LMA Protector with traditional LMA to perform endobronchial, ultrasound-guided, trans-bronchial needle aspiration (EBUS-TBNA) in a dedicated endoscopic room.[43] The authors found that LMA was a valuable tool that allowed access to higher mediastinal lymph node stations otherwise obscured by an endotracheal tube. Furthermore, LMA Protector shape provided better space for bronchoscopic ultrasound maneuvers so that the procedural time was shorter than with traditional LMA and patient comfort greater.

Postoperative sore throat (POST) and hoarseness are common complications of general anesthesia, mainly caused by airway trauma due to tracheal intubation.[44, 45] Several drugs have been proposed to prevent and treat POST, but the effectiveness was usually limited. A study by Muderris*et al.* published in January showed the superiority of a Flubiprofen spray applied preoperatively on the tracheal tube in comparison with a benzydamine hydrochloride spray and with placebo to improve POST and hoarseness.[46]

The introduction of POCUS (Point-of-Care-Ultrasonography) has become an integral part of anesthesia practice.[47] In this regard, MA published an interesting observational study by Tollinche *et al.* in November.[48] They applied POCUS to confirm correct gastric tube placement in the operatory room and registered a worrying 14% incidence of malposition.

Sedation

Conscious sedation is a technique that facilitates the execution of endoscopic procedures, like gastrointestinal or pulmonary endoscopy. Quality of endoscopy techniques, including their cost-effectiveness, depends a lot on patient comfort and operator ease. In a recent survey, the authors assessed the quality of procedural sedation during gastrointestinal endoscopy.[49] They observed a high correlation between patient-reported intra-procedure discomfort and both clinician assessments of procedural discomfort and patient recall of procedural pain 24 to 48 hours postprocedure. Pulmonary investigations sometimes require conscious sedation for flexible bronchoscopy; this technique should ensure patient comfort without loss of consciousness and respiratory depression. In a randomized, double-blind study, Ibrahim *et*

al. investigated the effects of pregabalin (PRE) premedication in patients undergoing flexible bronchoscopy using dexmedetomidine (DEX) as procedural sedation.[50] In contrast to no premedication, giving PRE (150 mg) one hour before the procedure increased patient and pulmonologist satisfaction and reduced DEX consumption, the cough score, POST incidence, and PACU stay time. Nevertheless, the authors warned that their results needed to be confirmed on a larger scale. Indeed, the use of gabapentinoids during the perioperative period is off-label and raises several questions as Savoia and Scibelli emphasized in their editorial.[51] Besides, the literature on the topic is not entirely consistent. A recent meta-analysis showed that, in comparison to the placebo, PRE improved postoperative analgesia and had an opioid-sparing effect.[52] In contrast, a second meta-analysis concluded that the opioid-sparing effect was negligible in relation to adverse effects such as sedation and dizziness and concluded that there is low evidence to recommend PRE for routine postoperative pain management.[53]

Procedural sedation is increasingly important in children because of the growing number of diagnostic or therapeutic procedures performed outside the operating room. In an editorial, Richa and Chalhoub reminded us how clinical expertise in that field was essential to maximize the benefit and minimize the risk of that technique.[54] They emphasized that the risk of procedural sedation should be assessed based on children's medical history and risk factors mainly related to airways and the cardio-respiratory status. Correct drug choice is essential for pediatric sedation. Mason and Seth reviewed the drugs available and the newest strategies for sedation in the most common procedures.[55] For example, ketamine alone or in combination with propofol or dex is particularly useful for painful procedures. The authors highlighted that oral midazolam (ozalin) indicated for premedication and moderate sedation in children from six to 17 years old is one of the very few new sedatives approved for pediatric use in the past decade.[56] Fortunately, new formulations of propofol, ketamine, etomidate, and benzodiazepines are in development, all striving to improve predictability, safety, and recovery profile.

To achieve and maintain the desired depth of sedation is essential to optimize patient comfort and safety. The Bispectral Index (BIS) has been widely used on this purpose in surgical and critically ill patients.[57, 58] Potential benefits include decreased drug consumption and incidence of cardiopulmonary complications, accelerated recovery, and better patient and physician satisfaction. To investigate these points, Zhang *et al.* performed a meta-analysis on 13 randomized controlled trials.[59] The analysis, which included 1372 patients who underwent endoscopic procedures, failed to confirm positive effects on procedure duration or patient and endoscopist satisfaction; however, BIS monitoring was associated with less hypoxic episodes during the procedure. In an expert opinion on the topic, Dahaba reminded us that BIS could not be considered as a true reflection of the electroencephalography (EEG) signal.[60] In a few conditions, like hepatic encephalopathy, BIS might be used off-label to grade EEG activity, but in general, the interpretation of the Index should be very cautious. In particular, in critically-ill patients, factors affecting BIS values are highly heterogeneous, which makes monitoring not only useless but, most of the time, misleading.

Regional anesthesia

In the last years, technical improvement has deeply influenced the practice of regional anesthesia.[61] Particularly, ultrasound has increased safety and quality of blocks and has become mandatory when landmark identification based on palpation is difficult or impossible.[62] In October, MA published an article by Tubinis *et al.* who studied 150 severely obese parturients and compared ultrasound with palpation to identify midline for epidural needle placement.[63] Following previous findings,[64] the study demonstrated that ultrasound decreased the number of needle orientation, epidural catheter placement, and total procedure time. In another study published in April, Riveros-Peres *et al.* utilized color Doppler mode to confirm the puncture of the epidural space in obstetric patients, and found it useful for visual confirmation of epidural needle and catheter placement.[65] Needle insertion in the epidural space has also been assessed using pressure

changes registered with a trasducer. In a systematic review published in the same month, Hilber *et al.* reviewed the literature on this technique and concluded that the analysis of the epidural waveform is also useful to identify the epidural space both in labor and surgical patients.[66]

Anesthetists often use color Doppler images to detect vascular structures during peripheral nerve blocks. Bereket *et al.* proposed a new application of color Doppler imaging. In 40 patients who underwent an infraclavicular block, they monitored the Perfusion Index (PI) and regional hemodynamic parameters in the ipsilateral limb.[67] Ten minutes after the block execution, Doppler parameters were valid to confirm its success or failure due to the sympathectomy effect. Needles visibility during ultrasound-guided peripheral nerve blocks is vital for procedural success and prevention of possible side effects and complications. Visibility depends not only on needle echogenicity, but can be improved by ultrasound machines.[68] Abad-Gurumeta *et al.* investigated the efficacy of an image enhancement software on standard and ecogenically-enhanced needles in animal and gelatin models.[69] They found that the software was valuable to improve visual performance and quality, mainly when regular needles were utilized.

Along with the advancements in ultrasound technology and the search for optional alternatives for central neuraxial anesthesia, truncal interfascial blocks have become more prevalent in regional anesthesia and pain medicine. Anesthetists widely use the Erector spinae plane block because it can be performed in every segment of the vertebral column, is more reliable than the paravertebral block, and is devoid of many of the epidural anesthesia well-known side effects.[70, 71] In their systematic qualitative review published in March, De Cassai *et al.* described the related anatomy, technique, cadaveric studies, clinical indications, and complications.[72] Better understanding the detail of anatomy may influence the success of regional anesthesia. In their cadaveric study, Vasques *et al.* investigated the transversalis fascia in relation to quadratus abdominis and transversus abdominis plane blocks.[73] They performed macroscopic and microscopic evaluations and described the structure in detail.

The rate of obese population is increasing, and operational requirements seem to rise.[74] Regional anesthesia for morbidly obese patients is challenging for the anesthesiologist. While opioid-free anesthesia is an option, peripheral nerve blocks are recommended whenever possible but pose difficulties.[75, 76] Should we perform transversus abdominis plane block in obese patients? Ruiz-Tovar *et al.* described the two sides of the option as pros and cons and described the possible alternatives.[77] Headache is a well-known complication of spinal anesthesia. Buddenberg *et al.* reviewed this complication, including history, risk factors, pathophysiology, clinics, and treatment options.[78]

Shoulder surgery is one of the most common orthopedic procedures, and regional blocks are the gold standard for perioperative management.[79, 80] Although interscalene block (INB) is the most widely used one for shoulder arthroscopic procedures, its effectiveness has been recently challenged because of hyperalgesia due to the "rebound pain phenomena." Consequently, suprascapular nerve block (SNB) has been suggested as a safe alternative, particularly in patients obese or with pulmonary diseases. Divella *et al.* explored the issue of short- and long-term outcome by performing a retrospective analysis of 140 patients who received INB or SNB.[81] They concluded that "pain scores at rest and during movement two hours after surgery were lower in the INB group"; however, both blocks showed similar functional recovery after six months. Of interest, since the lack of motor impairment, the SNB block favored early rehabilitation. Always on shoulder arthroscopy, Bojaxhi *et al.* compared continuous *vs*. Single-shot interscalene blocks (CIBS and SSISB, respectively).[82] The authors studied 130 patients divided into two groups and found that CIBS was more effective in reducing postoperative pain in the first postoperative day and decreasing opioid requirement.

The debate over the use of perineural catheters in regional anesthesia is still ongoing. In a Pro-Con debate, Capdevila *et al.* addressed that issue.[83] As a matter of fact, continuous local anesthetic infusion provides better analgesia than a single shot without increasing side effects. Moreover, perineural catheters reduce postoperative

pain, increase patient satisfaction, and improve the effectiveness of rehabilitation. There is also evidence that they may reduce the risk of persistent postoperative opioid use and, in some cases, of dependency.[84] Finally, the use of perineural catheters and continuous infusion decreases the incidence of "rebound pain," which in ambulatory patients may carry the risk of hospital readmission.[85] On the other hand, although attractive, there are some concerns about the routine use of continuous catheter infusion. It requires a significant investment in terms of time, cost, necessary infrastructure, and provider training, while multimodal analgesia, which extends the analgesic effect of single-shot regional anesthesia, represents a suitable alternative.

Finally, the debate over single injection or catheter insertion for a regional block is not settled, and it is culture and experience that dictates the practice modality of regional anesthesia in each institution.[86] Interestingly, Hamilton *et al.* conducted a multicenter analysis of almost 60.000 patients addressing the issue of peripheral nerve blocks (PNB) for ambulatory shoulder surgery.[87] They compared patients who received peripheral nerve blockade to those who did not about outcomes, such as readmission rates and costs in the first seven days after surgery. They found that "nerve blockade was not associated with any difference in a composite outcome measure, but was associated with a small increase in costs."

To avoid nerve damage during PNB, monitoring the injection pressure may be beneficial to perform a safer procedure. Carassiti *et al.* addressed this issue by reviewing 15 original studies in which injection pressures were monitored in animals, humans, and *in-vitro* models.[88] They concluded that the pressure was lower in perineural injection than in intraneural injection and identified a limit of 15 psi under which an operator could safely perform a perineural injection; they associated higher values with an increased risk of nerve damage.

Other interesting articles on regional anesthesia published by MA in the last year include the following. Porter *et al.* studied the effects of severe degenerative scoliosis on surface landmarks for lumbar plexus block and recommended preoperative imaging studies and ultrasound.[89] Cappelleri *et al.* compared the advantages of positioning a catheter for lumbar plexus block under the guide of electrical stimulation or not.[90] They found no differences in local anesthetic consumption, pain scores, and muscle strength preservation. Lu *et al.* evaluated the cutaneous sensory blocked area (CSBA) obtained with QLB blocks performed at L2 *vs*. L4 levels and found that the upper-level block produced a more extensive and prolonged sensory blockade.[91] Cuvillon *et al.* failed to register differences about the length of peripheral blocks of upper limbs between diabetic and nondiabetic patients.[92]

Many new papers concerned obstetric anesthesia and analgesia. Epidural volume extension (EVE) is a relatively new technique consisting of the administration of saline in the epidural space after spinal anesthesia to increase the dermatomal spread and expedite motor recovery. The efficacy of this technique is still matter of debate as recently reported in a review by Heseen *et al.*[93] In a randomized trial of patients undergoing short obstetric procedures, Powell *et al.* registered that the group of women treated with EVE showed a shorter time to meet PACU discharge criteria and received less intratechal isobaric bupivacaine.[94] In the accompanying editorial, Brogly and Guasch noted that early transfer to the ward might be related to a lower incidence of side effects, such as arterial hypotension, and that further studies are needed to define the optimal "low dose" of anesthetics for EVE.[95]

Nalbuphine is a mixed synthetic agonist-antagonist, which attenuates the μ-opioid effects and enhances the κ-opioid effects. When used as adjuvant to hyperbaric bupivacaine, it improves the quality of perioperative analgesia with few side effects.[96] Ibrahim *et al.* performed a randomized study in parturients undergoing cesarean section and demonstrated that the addition of nalbuphine to intrathecal bupivacaine plus morphine was associated with a reduction in the incidence and severity of postoperative PONV and pruritus without affecting analgesic potency.[97]

Epidural analgesia is known to prolong the second stage of labor.[98] Zhao *et al.* investigated the effect of the same low dose (0,0625%) of ropivacaine and levobupivacaine given by

patient-controlled epidural analgesia.[99] Unlike levobupivacaine, ropivacaine did not inhibit abdominal muscle activity or prolong the second stage of labor. Moreover, it controlled labor pain well and was not associated with adverse effects on neonatal outcomes. The authors concluded that ropivacaine represents an optimal solution for PCEA during spontaneous vaginal delivery.

Back pain is frequently reported by parturients during labor.[100] Diez-Picazo *et al.* studied the effects of adding programmed intermittent epidural boluses (PIEB) to a background epidural infusion (BEI) of levobupivacaine and fentanyl in 120 nulliparous parturients with early cervical dilation.[101] The addition was associated with a significant reduction of the back pain and rescue analgesic boluses without any increase of adverse events.

Perioperative medicine

Perioperative anemia may negatively influence mortality and morbidity.[102] Patient blood management (PBM) is one of the key interdisciplinary challenges in perioperative medicine enforcing joint efforts of general practitioners, surgeons, anesthesiologists, and intensivists to improve perioperative outcomes. In June, MA published a position paper of the SIAARTI that defined clinical standards for PBM, perioperative hemostasis, and coagulation management.[103] The authors defined three pillars, namely optimization of the hemoglobin content, minimization of perioperative blood loss, and optimization of the patient´s physiological reserve to guarantee tolerability of anemia in the pre-, intra- and postoperative period. Concise decision algorithms, as well as bleeding risk stratifications based on different surgical procedures, were proposed. Point-of-care devices for functional assessment of the coagulation like the thrombelastograph, enable fast and differentiated decision making, especially in highly dynamic situations such as perioperative hemorrhage. Nam *et al.* conducted a retrospective analysis of 534 cardiac surgery patients studied with rotational thromboelastography (ROTEM) and reported that the first derivative curve (V-curve) could predict the risk of perioperative bleeding better than the parameters traditionally used.[104]

Another significant perioperative challenge is the diagnosis, prevention, and therapy of postoperative cognitive dysfunction (PCD) or delirium (POD). While diabetes is a known predisposing factor for POCD and POD,[105, 106] the effects of acute intraoperative hyperglycemia are still unknown. Spies *et al.* conducted a prospective observational study enrolling 87 patients ≥65 years old undergoing elective surgery.[107] The authors found that intraoperative hyperglycemia was independently associated with postoperative delirium, but not with postoperative cognitive dysfunction; also hyperglycemic non-diabetic patients might have an increased risk of postoperative delirium. Members of the same research group carried out an observational study on pediatric patients and found a gap between the 10.5% incidence of emergence delirium detected by a scoring system and 5.7% based on clinical diagnosis by PACU staff.[108] Predictive factors for emergence delirium were age < five years, ASA physical status I, and head/throat surgery. PCD is a relatively frequent complication of cardiac surgery.[109, 110] In an observational study on 59 patients who underwent cardiopulmonary bypass for elective coronary surgery, Kumpaitiene *et al.* showed that impairment of the cerebrovascular autoregulation was associated with a higher incidence of postoperative cognitive disorders.[111]

A consensus paper on anesthesia in urogynecologic robotic surgery was produced by a joined task force of SIAARTI, SIGO, and SIU and published in August.[112] Following a systematic review of the literature, the authors identified nine core contents; recommendations concerned patient position, neuromuscular block, pneumoperitoneum and ventilation strategies, hemodynamic monitoring, fluid therapy, pain management, and prevention of nausea and vomiting, acute kidney injury, postoperative delirium, and cognitive dysfunction. In their accompanying editorial, Skurzak and Robba commended the work of the task force and pointed out that, due to the paucity of randomized controlled trials in that field, most recommendations were still based on case series and expert opinions especially when it came to anesthesiological issues.[113]

In the January issue, Callejas *et al.* reported on a simple predictive model for acute kidney injury

in patients undergoing elective cardiac surgery.[114] The new screening was based on information readily available in the anesthesia consultation (*i.e.*, anemia, age, hypertension, obesity) and showed a better discriminatory ability compared to Thakar and Demirjian's scales,[115, 116] mainly dedicated to hemodynamically unstable patients during emergency surgery.

Cognitive impairment is another crucial risk factor that affects mortality in postoperative geriatric patients.[117] Chen *et al.* evaluated a preoperative cognitive screening tool (Mini-Cog) in a cohort of 551 patients over 65 years old. Patients with cognitive impairment (Mini-Cog Score ≤2) demonstrated a significantly higher mortality rate compared to controls. These results extended the validity of Mini-Cog score also to geriatric patients who undergo general anesthesia for non-cardiac surgery.[118]

Standard chemotherapy for breast cancer, as anthracyclines, trastuzumab, and radiation therapy, increases the incidence of future cardiac events.[119] The study carried out by Zhang *et al.* demonstrated that patients undergoing preoperative chemotherapy before mastectomy were more prone to develop perioperative cardiovascular complications compared to the control group without a history of chemotherapy.[120]

Postoperative shivering is a frequently reported complication after general or regional anesthesia and is associated with increased oxygen consumption. In their meta-analysis, Kang *et al.* compared the effect of the drugs usually administered to prevent or treat shivering. Intravenous (IV) nefopam, IV, and intratechal (IT) meperidine, IV tramadol, and IV and IT dexmedetomidine were ranked high compared to other drugs.[121]

Finally, Brugada Syndrome can precipitate lethal arrhythmias during anesthesia.[122] In the February issue, Espinosa *et al.* published an interesting review on this syndrome and recommended to avoid hyperthermia, electrolytes anomalies, Class IA and 1C antiarrhythmic drugs, beta-blockers and Class II psychotropic substances. They also underlined that the majority of anesthetic, analgesic, and muscle relaxant drugs could be safely used, but recommended caution in the use of bupivacaine and propofol at high doses. An algorithm of perioperative management and treatment of complications was also presented.[123]

Postoperative analgesia

American guidelines on postoperative pain (POP) management underline that to control postoperative pain effectively, we should measure baseline pain in the preoperative period.[124] In fact, adequate preoperative pain management[123, 125] and a personalized plan of pre- and peri-operative antalgic therapy are mandatory on this purpose. Recently, Bastian *et al.* suggested that a single dose of methadone could be more effective than fentanyl to reduce postoperative morphine needs.[126] They randomized 160 patients to receive 0.03 mg/kg fentanyl or 0.2 mg/kg methadone IV before general anesthesia induction for surgery in which they expected severe POP. Unlike previous studies, they found that a single dose of methadone could dramatically decrease morphine consumption in the following 72 hours, even if intraoperative fentanyl consumption was similar in the two groups. As far as methadone pharmacokinetics was concerned, the single administration helped prevent accumulation and possible side effects.[127] These results raise the question of whether this "old drug" could be integrated into the new techniques used in the "opioid-sparing era,"[128] especially in a specific subgroup of patients, such as the opioid-tolerant ones.[129, 130]

Intraoperative antinociception is a crucial issue in perioperative care management not only to reduce opioid consumption but also to prevent pain chronicization.[131] Hence, it is essential to develop new ways to measure intraoperative pain,[132] to obtain the best level of antinociception. In the April issue, MA published a study by Jain *et al.*, who evaluated whether surgical pleth-index (SPI) could improve intraoperative fentanyl dosage in laparoscopic cholecistectomies compared to a conventional protocol.[133] The authors found that SPI monitoring was associated with higher fentanyl doses, less postoperative pain, and fewer rescue analgesia needs; hemodynamic parameters and postoperative side effects such as postoperative nausea and vomit-

ing or respiratory depression were unaffected. That study underlined how important it was to customize our analgesia protocol to our patients also in the intraoperative period, even in surgical procedures that we consider not very painful. Loriga *et al.* carried out a one-year retrospective analysis on 782 patients who underwent vitreoretinal surgery and found that the choice of the intraoperative analgesic technique and surgery duration strongly influenced the levels of POP.[134]

Regional techniques are often optimal choices to control POP and reduce opioid consumption.[135, 136] Ambrosoli *et al.* compared postoperative analgesia between automatic intermittent and continuous adductor canal block after anterior cruciate ligament reconstruction.[137] The authors did not find differences apart from the total quantity of local anesthetics given. Yet, further studies are needed to investigate hypothetical differences on long-term function.[138] In November, MA published a meta-analysis about perioperative pain management of hip fractures through single-shot fascia iliac blocks by Fadhlillah *et al.* The authors found that that block guaranteed reasonable pain control and reduced the incidence of breakthrough pain and the need of rescue analgesia.[139] They observed that, unfortunately, that block was underutilized in clinical practice.

Pain

Acute pain management in the prehospital setting and the emergency departments is still a challenge for physicians. The Italian Intersociety Recommendations suggest a multimodal approach, including regional analgesia (RA) and pharmacological association of opioid and non-opioid analgesics.[140] In the June issue, Saranteas *et al.* reviewed the use of RA techniques in trauma patients. In comparison with systemic analgesia, RA can effectively reduce the stress response, minimize the use of systemic opioids, and prevent chronic pain syndromes.[141] Potential contraindications may originate from the risk of masking acute compartment syndrome and the fear of worsening peripheral nerve injuries. Another critical issue is local anesthetic toxicity, which is more hardly detected in unconscious or heavily sedated patients. In the corresponding editorial, Franchi and Scolletta commented that the more critical trauma patients are, the less likely they are to receive adequate antinociception.[142]

The use of opioids to treat chronic, not oncologic pain has been challenged, particularly in patients with active substance use disorder or at elevated risk.[143] The recent opioid crisis in the United States has raised several questions on the safe use of opioids in chronic pain management.[144, 145] According to the European Pain Federation, the appropriate use of opioids requires an initial accurate clinical assessment, the use of the lowest effective dose, monitoring of outcome at least every 12 weeks, and adequate management of short- and long-term side effects.[146] On the other hand, overly stringent restrictions and regulations intended to prevent illicit, non-medical use of opioids may lead to improper pain management. Pergolizzi *et al.* proposed a series of questions/answers that can help the pain specialist in the decision-making process even in patients with an active opioid use disorder.[147] Further useful strategies for reducing the risk of abuse may be the use of appropriate screening tools and the activation of a government monitoring program of opioid prescriptions.[148]

A significant percentage of women report chronic pain six months after delivery, more frequently after cesarean section, but also after vaginal delivery. The topics were the subject of an expert's opinion by Patricia Lavand'homme published in March.[149] The author highlighted that the role of poorly treated pain since a predelivery history of pain and inadequate per-Partum analgesia was the most reliable predictive factor of chronicization. Unfortunately, physicians often undertreat pain during pregnancy and lactation due to the fear of using drugs that may affect children's safety.[150] However, it should be kept in mind that women who complain about significant pain two weeks after Partum have an increased risk to develop chronic pain at three months.[151]

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