

## YEAR IN REVIEW

## A year in review in Minerva Anestesiologica 2018

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## General anesthesia

**P**ulmonary complications are a significant cause of postoperative morbidity and mortality. The modality of intraoperative mechanical ventilation may damage or protect the lung so that protective ventilation with low tidal volumes and high positive end-expiratory pressure (PEEP) utilized in ICUs has been applied in the operating theatre.<sup>1,2</sup> Atelectasis is a major concern for the anesthetist for its relationship with postoperative pulmonary complications (PPC).<sup>3</sup> In the February issue, a PRO/CON was published, in which two distinguished authors in this field, Goran Hedenstierna and Paolo Pelosi, debated the effective role of PEEP in decreasing atelectasis and PPC and improving the outcome of surgical patients.<sup>4</sup> Readers will draw their conclusions, but PEEP is undoubtedly a vital element of a strategy to optimize driving and transpulmonary pressures.<sup>5</sup> In this context, the best PEEP in anesthesia should not be regarded as a fixed number but should be tailored to each patient and surgical setting. In

the April issue, a study by Wei *et al.* investigated the effectiveness of alveolar recruitment maneuvers with and without PEEP on obese patients scheduled for bariatric surgery.<sup>6</sup> Recruitment maneuvers alone caused lower driving pressure and better arterial oxygenation during pneumoperitoneum and affected less the hemodynamics. The authors stressed the importance to give the right attention to the circulatory effects of mechanical ventilation. Finally, a systematic review by Pang *et al.* on thoracic surgery and one-lung ventilation, pointed out that inhalation anesthesia can preserve intraoperative cardiac function and reduce postoperative pulmonary complications better than intravenous anesthesia.<sup>7</sup> The Authors hypothesized that the anti-inflammatory properties of volatile agents could have a protective action despite the inhibition of hypoxic pulmonary vasoconstriction.

Volatile anesthetics can have a positive preconditioning effect on cardiac damage during cardiac surgery. According to experimental studies, remote ischemic preconditioning may have

similar positive results, but clinical studies failed to confirm them. Yet, the translation of remote ischemic preconditioning as protective strategy in cardiac surgery should face the possible interference of the type of anesthetic agents, whether volatile or endovenous.<sup>8</sup> Benstoem *et al.* carried out a secondary analysis on a Cochrane Systematic Review investigating the interaction of remote ischemic preconditioning and type of anesthesia on cardiac damage in cardiac surgery.<sup>9</sup> They found no significant interaction but concluded that further tightly-focused randomized clinical trials were needed.

Emergency scenarios are always challenging in anesthesia, and severe preeclampsia increases the risks of adverse outcomes for the mother and the newborn.<sup>10</sup> Short-acting agents, such as remifentanyl, allow better control of perioperative hypertension in the mother but may favor hemodynamic instability and respiratory depression in the infant. El Tahan *et al.* compared remifentanyl, 0.1 mcg/kg/min, and dexmedetomidine, 0.4 µg/kg/h, for arterial pressure control during cesarean delivery under general anesthesia in preeclamptic patients.<sup>11</sup> They found that remifentanyl was more useful to control maternal hemodynamics, but more frequently caused maternal hypotension and neonatal respiratory depression. Arterial hypotension is sometimes actively sought to reduce intraoperative bleeding. This is the case of hypotensive strategies for bleeding control during endoscopic sinus surgery, which is nonetheless not always effective, and sometimes even dangerous.<sup>12</sup> In the issue of November, an interesting study by Di Mauro *et al.* was published, in which bleeding control was based on fluid responsiveness, rather than pressure control.<sup>13</sup> The authors found that a stroke volume variation (SVV) >12.5% assessed by the non-invasive hemodynamic monitoring (EV1000 ClearSight) was associated with the most bloodless surgical field during endoscopic sinus surgery.

The GABA system is primarily involved in major depressive disorders (MDD),<sup>14</sup> but is also a favorite target of general anesthetics.<sup>15</sup> By a prospective observational study, Erden *et al.* demonstrated that patients with MDD undergoing laparoscopic cholecystectomy required less sevoflurane than controls during BIS-guided

anesthesia.<sup>16</sup> The authors argued that lowered GABA content and GABA receptor dysregulation might have accounted for the reduced anesthetic requirement. In the accompanying editorial, Aceto and Sollazzi pointed out that patients affected by MDD present decreased EEG power in some cerebral areas and increased EEG power in others.<sup>17, 18</sup> Consequently, a direct effect of MDD on EEG-based monitors is possible and may lead anesthetists to administer lower anesthetic doses to attain the desired BIS values.

Hospitalization and anesthesia can have a substantial psychological impact on children, which may manifest with negative behavioral changes.<sup>19</sup> Berghams *et al.* faced up to the issue of the effects of anesthesia and surgical stress on postoperative sensory processing in toddlers and demonstrated that children who underwent circumcision under general anesthesia were under-responsive to auditory-visual input, particularly in case of pre-existent preoperative emotional/behavioral problems. The authors concluded that clinicians should be aware of this clinically relevant information and should convey it to parents.<sup>20</sup>

Emergence delirium (ED) is a behavioral disturbance that can distress patients and primary caregivers after general anesthesia. The use of Bispectral Index (BIS) may prevent ED by avoiding periods of deep hypnosis (BIS<40).<sup>21</sup> Cotoia *et al.* performed a randomized study in urologic patients investigating the effects on ED of four BIS-guided anesthesia protocols by comparing pre and postoperative mini-mental state exam (MMSE) score; the protocols included automated and manual intravenous propofol-remifentanyl anesthesia and sevoflurane or desflurane anesthesia.<sup>22</sup> The Authors observed that the automated feedback control system outperformed manual systems and reduced ED frequency, probably by achieving a more stable level of hypnosis (40<BIS<60). Another study by Ippoliti *et al.* showed that blueberry juice might act as a protective agent against neuropsychological dysfunction caused by general anesthesia for major surgery.<sup>23</sup> In their editorial, Schneider and Fili Povic argued that during anesthesia EEG based monitors should be used not just as a “monitor for awareness,” but rather as an indicator of an-

esthetic overdose.<sup>24</sup> Low BIS values can identify patients unusually sensitive to anesthesia who are at risk for complications despite low blood pressure, low BIS, and low minimum alveolar concentration of volatile anesthetics (the so-called “triple low”).<sup>25</sup>

The etiopathogenesis of postoperative delirium (POD) and cognitive dysfunction (POCD) is multifactorial and diabetes mellitus (DM) and acute perioperative hyperglycemia may act as potential triggers. In their systematic review, Hermanides *et al.* concluded that both conditions could be associated with POD and POCD; to date, however, it is not known whether lowering perioperative glucose improves neurocognitive outcome and further investigations are needed because of the limited number of randomized trials and the poor definition of DM in many of them.<sup>26</sup> POCD was the object of another study, in which transcatheter aortic valve replacement (TAVR) was compared to surgical aortic valve replacement (SAVR).<sup>27</sup> The Authors found that TAVR patients were characterized by lower values of MMSE but did not undergo any worsening after the procedure, whereas SAVR patients presented a limited decrease of the values after the surgical procedure but recovered six months later.

One of the main goals of anesthesia is to provide adequate analgesia during surgical procedures since the intraoperative perception of noxious stimuli may negatively influence patient outcome. During the last year, MA published several interesting articles on this subject. In a prospective observational study, Stokle *et al.* tested the effectiveness of nociception level index (NOL-Index), a multidimensional index, to detect nociception during tetanic stimulation at various remifentanyl concentrations in patients under general anesthesia.<sup>28</sup> The authors demonstrated that NOL monitoring reflected the degree of nociception better than single clinical parameters as the heart rate and the blood pressure and claimed for randomized studies to confirm their results. In an elegant RCT, Park *et al.* used the Surgical Pleth Index (SPI) to optimize analgesia during direct laryngoscopy; SPI proved to be a useful tool to evaluate the degree of analgesic protection against painful stimuli.<sup>29</sup> An origi-

nal approach to monitoring analgesia has been proposed by Yanabe *et al.*, who investigated the effectiveness of an instrument based on the variation of arterial stiffness (quantified as the K-value) to predict the response to laryngoscopy and tracheal intubation.<sup>30</sup> They found a satisfactory degree of predictiveness and a good correlation between estimated plasma concentration of remifentanyl and variation of arterial stiffness. In the corresponding editorial, Dworschak pointed out that several questions should be answered to weigh the real clinical usefulness of an analgesia monitor based on arterial stiffness; overall, the large K-value inter-individual variability should be explained and related to factors as patient age, sex, body size, and coexisting diseases.<sup>31</sup> Taken together, these researches in the field of nociception monitoring emphasize the importance of a reliable tool to measure pain during anesthesia. Unfortunately, we do not have such a monitor yet, and systems such as SPI, NOL Index, and arterial stiffness represent the first steps of a just-begun journey towards an “intraoperative full monitoring.”<sup>32</sup>

Finally, Glycocalyx, a polysaccharide layer located on the luminal side of blood vessels, is essential for vascular integrity and function. In their excellent study, Belavic *et al.* analyzed the effects on glycocalyx of various fluid delivery regimens in ASA I and II patients who underwent laparoscopic cholecystectomy.<sup>33</sup> Results highlighted a correlation between glycocalyx damage and liberal fluid therapy.

## Muscle relaxants

Since sugammadex has been clinically available, anesthetists have been able for the first time to rapidly and completely reverse rocuronium-induced neuromuscular blocks. Sugammadex is not a magic bullet but a powerful drug even in a clinical situation where the neuromuscular block is challenging. In the August issue, MA published an article in which Abdulatif *et al.* showed that, in a group of Child class A cirrhotic patients undergoing liver resection, sugammadex allowed an 80% reduction of time to TOFr>0.9 in comparison with neostigmine.<sup>34</sup> Another issue about Sugammadex is the poten-

tial interference with coagulation.<sup>35, 36</sup> Carron analyzed sixty morbidly obese patients undergoing laparoscopic sleeve gastrectomy who received sugammadex 2-4 mg/kg to reverse moderate/deep rocuronium-induced neuromuscular block.<sup>37</sup> He observed a slight effect on coagulation without increasing the risk of postoperative bleeding. Bertini, in his editorial, stressed the importance of rotational thromboelastometry as an effective bedside coagulation monitor.<sup>38</sup> Finally, Fuchs-Buder focused his attention on sustained profound neuromuscular blockade during laparoscopic surgery to obtain adequate exposure of the operative field without an excessive increase of the intra-abdominal pressure.<sup>39</sup> Of note, maintaining deep neuromuscular block until the end of surgery would not be possible without quantitative neuromuscular monitoring and sugammadex availability.

### Airway management

Nowadays, extraglottic devices (EADs) represent an essential tool for airway management, alternative to face mask ventilation and tracheal intubation. An interesting review on the topic has been published in the March issue.<sup>40</sup> The authors examined the continuously expanding indications and possible complications. The indications include elective and emergency anesthesia in pre- and in-hospital settings in spontaneously breathing or ventilated patients and the need for a bridge to intubation or extubation.<sup>41, 42</sup> EADs are also precious to rescue ventilation in the “cannot intubate, cannot oxygenate” scenario.<sup>43, 44</sup>

As indications have significantly increased over the last years, EADs design and features are continually evolving<sup>45</sup> and two RCTs published in the April and June issues compared some of them.<sup>46, 47</sup> To orientate yourself in the growing number of devices, it is vital to have a simple and unambiguous classification.<sup>48</sup> Agrò *et al.* claimed that the present generation-related classification may favor confusion and ambiguity and proposed instead to classify EADs in basic and advanced; the latter would be defined by the presence of at least two between high seal pressure, gastric access, and the possibility to intubate.<sup>49</sup>

EADs are less painful and distressing than tracheal intubation. This is particularly important if the surgical procedure can be tolerated with a light plane of anesthesia. In July a study by Fudickar *et al.* was published in which the association of balanced light anesthesia, the use of a laryngeal mask, and no muscular blockade proved to be as effective to perform pars plana vitrectomy as more profound anesthesia with tracheal intubation and neuromuscular blockade.<sup>50</sup>

Although the availability of new rescue devices, unexpected difficult airways remains a leading cause of perioperative morbidity and mortality, but thoughtful preoperative evaluation of upper airway can drastically reduce the incidence of this scenario. For these reasons, there is a constant search for a better way to accurately predict difficult intubation because the degree of precision of the parameters currently used is low.<sup>51, 52</sup> Guo *et al.* used the number of tracheal rings observed by preoperative fiberoptic laryngoscopy to predict difficult tracheal intubation in 994 adult patients.<sup>53</sup> They found that their method had higher sensitivity, specificity, and predictive value than the Mallampati Test or the Wilson Risk-Sum Score.

A recent study showed that replacing direct laryngoscopy with videolaryngoscopy (VL) as the first-choice departmental technique is perceived by operators as beneficial to patient safety, team dynamics, human factors, and quality of care and quality of training.<sup>54, 55</sup> Indeed, a recent Cochrane review concluded that videolaryngoscopy (VL) reduces intubation difficulty, and the associated trauma.<sup>56</sup> On this regard Carassiti *et al.* compared the force and pressure distribution using Macintosh and GlideScope laryngoscopes in normal airway by using film pressure transducers.<sup>57</sup> They found that the use of Glidescope was associated with lower force and, consequently, with a reduced risk of traumatism.

Finally, an exhaustive review on Obstructive Sleep Apnea Syndrome (OSAS) and anesthesia was published in January.<sup>58</sup> The topic is important because the prevalence of moderate and severe forms in the general population is about 10-17%,<sup>59, 60</sup> and many patients may not have a formal diagnosis before surgery.<sup>61</sup> In the corresponding editorial, Riem focused on the dif-

faculty to manage patients affected by moderate OSAS, in whom the results provided by clinical questionnaires also depend on the apprehension of the patient and the way anesthetist asks the questions.<sup>62</sup>

### Regional anesthesia

Comparison about safety profile, and short and long-term complications between general and regional anesthesia for special surgery is an attractive and controversial issue.<sup>63</sup> In their expert opinion, Soffin and Memtsoudis underlined that regional anesthesia and analgesia for total knee arthroplasty present several advantages, which are partially balanced in elderly patients by technical difficulties due to vertebral degenerative changes, obesity, and rheumatologic disorders.<sup>64</sup> May ultrasound facilitate spinal anesthesia in these challenging patients? Elsharkawy *et al.* compared traditional landmark-based blocks to real-time ultrasound-guided blocks, in which they confirmed the correct needle position by colour-Doppler.<sup>65</sup> Ultrasound use was associated with a very small decrease in the number of needle insertions; besides, a higher degree of patient satisfaction was registered at the price of an increased length of the procedure and a larger difficulty score. The same Authors presented their preliminary, successful experience to position perineural and epidural catheters in patients suffering from chronic pain by assessing the anesthetic flow with pulsed wave Doppler ultrasound.<sup>66</sup>

In the last fifteen years, the use of ultrasound proved to be effective in decreasing anesthetic dosage and increasing anesthesia and analgesia quality in many peripheral nerve blocks.<sup>67</sup> In their experts' opinion published in the January issue, Nielsen *et al.* compared ultrasound-guided Shamrock lumbar plexus block to traditional external landmark lumbar plexus block by examining the precision of needle position, the easiness to perform the technique, and the complication rate.<sup>68</sup> They pointed out the greater safety and efficiency of Shamrock block respect to the traditional block, which is commonly reserved to expert operators due to the high risk of complications;<sup>69, 70</sup> a video showing Shamrock block execution was provided as additional material.

The achievement of satisfactory analgesia levels in inguinal surgery often requires the association of multiple peripheral blocks.<sup>71-73</sup> Frassanito *et al.* combined ultrasound-guided genitofemoral nerve block to ilioinguinal/iliohypogastric nerve block in adults undergoing inguinal hernia repair; in comparison with ilioinguinal/iliohypogastric nerve block alone, they registered lower VAS scores and a minor need for additional local anesthetic supplementation.<sup>74</sup> In other cases, the choice of the block may affect anesthetic dosages. In a group of patients undergoing anterior cruciate ligament reconstruction, Lenz *et al.* found no difference between low volume saphenous-obturator block and femoral-obturator block about early and late pain-scores and opioid consumption.<sup>75</sup>

Adjuvant drugs are used to increase the duration and quality of regional anesthesia. In this regard, Dexmedetomidine is recognized as one of the most effective adjuvants in many types of neural blocks.<sup>76-78</sup> In the January issue, MA published a study by Xu *et al.* who investigated the efficacy of dexmedetomidine, 0.5 mcg/kg, as an adjuvant to the local anesthetic mixture in transversus abdominis plane block and rectus sheath block; the addition was associated to decreased opioid demand and consumption.<sup>79</sup> In July, Trifa *et al.* reviewed and recommended dexmedetomidine use by caudal epidural administration in pediatric patients.<sup>80</sup>

Despite the advances in ultrasound-guided techniques, neuraxial blocks are still preferred in clinical practice due to their efficacy in early postoperative analgesia, lower complication rates, and cost-effective profile. In their investigation, Cortese *et al.* presented their 3-year experience in transanal endoscopic microsurgery under spinal anesthesia analyzing perioperative opioid use, operation room occupancy, and length of hospital stay, which were all decreased in patients who underwent spinal anesthesia.<sup>81</sup> Nonetheless, neuraxial blocks are not without complications. Liu *et al.* reviewed physical and pharmacological treatments for shivering that often complicates neuraxial anesthesia for cesarean section.<sup>82-84</sup> Fortunately, other, more severe and devastating complications are seldom observed. Zorilla-Vaca *et al.* reviewed the epidemiology

and history of septic meningitis associated with neuraxial anesthesia.<sup>85</sup> *Streptococcus salivarius* and *Staphylococcus aureus* were the microorganisms most frequently responsible respectively after spinal and epidural anesthesia; prevention requires the observance of strict asepsis, particularly while performing the block.

Perineural catheters (PNC) are widely used to improve postoperative analgesia and are currently recommended to facilitate early mobilization after surgery.<sup>86</sup> For these devices, the definitions of contamination, colonization, and infection remain a question of debate, so that frequency rates vary.<sup>87</sup> In literature, the incidence of PNC infection ranges from 0% to 7% depending on the site of insertion and that of colonization from 6% to 63%.<sup>88</sup> An interesting question is how to distinguish skin contamination from colonization and infection. In the March issue, Blumenthal *et al.* reported on the influence of disinfection before PNC removal on the detection of bacteria on PNC microbiological cultures.<sup>89</sup> In 200 patients who received a PNC for orthopedic surgery, no sign of local or systemic PNC-related infection was observed; alcoholic skin disinfection before PNC removal decreased the incidence of positive PNC cultures from 28% to 14%; signs of inflammation at the PNC insertion were poorly predictive of the cultural positivity. Those findings were in line with a recent systematic review on PNC according to which infection is rare (0-3%) and characterized by signs of systemic infection and inflammation at the catheter entry site, rather than PNC cultural positivity; factors predisposing to infection are trauma, ICU setting, diabetes, immunodeficiency, and catheters that stay for more than 48 hours; colonization rates do not reflect infection, but skin contamination.<sup>90</sup>

The transversus abdominis plane (TAP) block is achieved by injecting the local anesthetic solution between the internal oblique muscle and transversus abdominis muscle.<sup>91</sup> By spreading in this plane, the anesthetic can block neural afferents from T6 to L1 and provide analgesia to the anterolateral abdominal wall. The block is generally used for postoperative analgesia after abdominal surgery, but its effectiveness is questioned, mainly because of its short duration.<sup>92</sup> Continuous infusion or adjuvants have been employed

to increase length and quality.<sup>93</sup> In the March issue, MA published a study aimed to compare the effectiveness of adenosine and magnesium sulfate as adjuvants to bupivacaine in the TAP block.<sup>94</sup> In comparison with bupivacaine alone, the addition of both adenosine and magnesium improved the quality and duration of the block, with a relatively longer length with the second; opioid requirements and the incidence of postoperative nausea or vomiting decreased. Regarding the dosage of the two adjuvants, the authors called for caution for the potential cardiovascular adverse effects (vasodilatation, bradycardia, and negative inotropic effect), but believed that the amounts tested in their study (12 mg of adenosine and 500 mg of magnesium) were probably safe. In the corresponding editorial, Dauri and Lucci invited to be cautious because many of the proposed adjuvants are unlicensed for that use.<sup>95</sup>

Another issue to improve the efficacy and duration of regional anesthesia is at which point of the nerve course the anesthesia is performed. The sciatic nerve courses down the posterior thigh and bifurcates above or within the popliteal fossa into the tibial and common peroneal nerves. Some studies reported that the injection of the local anesthetic distal to the sciatic bifurcation shortens the onset of the block and improves the success rate and the quality.<sup>96</sup> Proximal and distal paths were compared by He *et al.* in an RCT published in May.<sup>97</sup> They performed ultrasound-guided continuous popliteal sciatic nerve blocks for foot or ankle surgery in forty patients with a puncture path proximal to the nerve bifurcation or at the nerve bifurcation and observed that the block at nerve bifurcation provided better postoperative analgesia and patient satisfaction. The authors hypothesized that the anesthetic came in contact with the nerve more easily at nerve bifurcation because the connective tissue surrounding tibial and common peroneal nerves prevents diffusion elsewhere.

Other studies comparing regional anesthesia techniques were published by MA in 2018. Kanadli *et al.* compared the fascia iliaca compartment block (FIB) and the femoral nerve block (FNB) for analgesia after total knee replacement (TKR), observing that FIB resulted in more effective analgesia and less opioid consumption in

the first six hours after the operation.<sup>98</sup> Rodríguez Prieto *et al.* compared distal peripheral nerve blocks (dPNB) with levobupivacaine 0.125% to conventional systemic analgesia after trapeziectomy performed under an axillary block.<sup>99</sup> They found that dPNB provided better postoperative analgesia for the first 48 hours; also, opioid consumption and the incidence of PONV were lower.

Finally, the incidence of peripheral nerve injury associated with regional anesthesia is estimated at 2-4 per 10,000.<sup>100</sup> The injection of the anesthetic into the intraneural space due to needle misplacement is a significant risk factor for nerve injury. Based on the hypothesis that pressure may be used to detect intraneural injection, Krol *et al.* performed an interesting study on human cadavers and developed a map of pressures associated with intraneural and perineural injection during upper and lower limb blocks.<sup>101</sup> They found that intraneural injections required significantly higher pressure.

### Pediatric anesthesia

Pediatric surgical activity carried out in non-specialized pediatric centers with low volume activity is probably at higher risk for inadequate anesthesia management.<sup>102</sup> A task force designated by the two most important Italian Societies of Anesthesia and Intensive Care (SIAARTI and SARNePI) provided expert opinion-based recommendations on organizational, clinical, and training requirements for good clinical practice in pediatric anesthesia.<sup>103</sup> The document was published in the February issue.

### Anesthesia in robotic surgery

In the last decade, we have witnessed a significant diffusion of robotic surgery and the research connected to it.<sup>104, 105</sup> The new techniques have been indeed associated with a better outcome in some thoracic<sup>106, 107</sup> and abdominal<sup>108, 109</sup> surgical procedures. In this context it is essential to optimize anesthesia to match the needs of surgery.<sup>110</sup> In the January issue, a review on anesthesia in robotic surgery was published, which well summarized how to optimize the periopera-

tive treatment in robotic-assisted thoracoscopic lung surgery and to manage emergencies specific to that surgical setting.<sup>111</sup> The authors concluded that anesthetists should be involved in all perioperative phases to maximize the advantages obtained with the robotic technique.

In the October issue, a joint consensus on robotic abdominal surgery by the Italian Society of Anesthesiologists (SIAARTI) and the Italian Society of Surgeons (SIC) was published.<sup>112</sup> The collaboration between anesthetists and surgeons is a mainstay to improve outcome in robotic surgery and the document provides important statements, based on high levels of evidence, that should guide the anesthetists who work in the field of this challenging surgery.

### Perioperative medicine

In 2018 the European Society of Anaesthesiology (ESA) published the updated guideline on preoperative evaluation of adults undergoing elective noncardiac surgery.<sup>113</sup> Besides summaries for risk stratification, this document reviewed a lot of updated evidence-based recommendations helpful for the daily clinical routine.

In MA, Menger *et al.* published an interesting prospective randomized trial comparing the quality of sleep in postcardiothoracic surgery patients with or without the use of earplugs.<sup>114</sup> The authors reported that this easy and cost-efficient intervention significantly improved sleep quality, patient satisfaction, and pain intensity. Although beyond the scope of this study, the authors speculated that by using ear plugs a faster recovery, reduced morbidity and reduced hospital costs might be achieved in postoperative patients. Hoffhuis *et al.* conducted a multinational survey to describe sleep assessment and sleep promoting strategies in adult intensive care units in ten countries.<sup>115</sup> They found that only 18% of intensive care units used earplugs frequently and that sleep management protocols or sleep questionnaires were rarely in place. Beside non-pharmacological interventions, the “sleep hormone” melatonin is known to affect the circadian rhythm directly and may promote sleep in critical care patients by resetting the natural sleeping rhythm. However, a recent Cochrane

Review just found insufficient evidence that administration of melatonin improves the quality and quantity of sleep in critically ill patients due to differences in sedation protocols and methodological issues.<sup>116</sup>

Ferreira Albuquerque Costa *et al.* conducted a systematic review on perioperative ultrasound applied to diagnosis and decision-making in anesthesia.<sup>117</sup> Beside the use of ultrasound techniques for regional anesthesia or vascular puncture, they reported a rapidly growing number of examinations also for echocardiography and neck and a laryngeal, pulmonary, and abdominal ultrasound that frequently (31% of cases) resulted in changes of perioperative management. However, since most studies in this field are observational, prospective randomized controlled trials are warranted to confirm the potential benefits of ultrasound examinations performed by anesthesiologists in perioperative decision making.<sup>118</sup> Van de Putte *et al.* retrospectively analyzed their departmental database containing clinical and sonographic information on elective surgical patients who had been non-compliant to fasting guidelines.<sup>119</sup> They used point-of-care gastric ultrasound and reported a change in aspiration risk assessment and subsequent anesthetic management in almost 65% of the cases. Interestingly, they reported a trend towards a lower number of surgical cancellations and a higher number of proceeds without documented cases of aspiration. They concluded that gastric ultrasound might be a useful tool to personalize aspiration risk assessment and tailor anesthetic management to the individual patient.

Another hot topic is postoperative delirium and cognitive dysfunction. Cascella *et al.* addressed these critical issues in an Expert Opinion and nicely reviewed pathophysiological basics and translational approaches to clinical practice, as well as future research opportunities.<sup>120</sup> Emphasizing the huge incidence and potential clinical impact, the authors focused on pathophysiological basics such as the role of neuroinflammation, microglia activation, surgical stress response, impairment of the complex neurotransmitter system, and direct neurotoxic effects of anesthetic drugs. In an accompanying editorial, Steinmetz and Rasmussen stressed the

importance of distinguishing between postoperative delirium and postoperative cognitive dysfunction.<sup>121</sup> It is worth noting that most of our current knowledge on the pathophysiological basis of postoperative delirium and postoperative cognitive dysfunction is based on animal experiments that may not mimic the complex clinical appearance, especially in elderly patients. Even simple but clinically very relevant questions like the role of regional vs. general anesthesia in the development of postoperative delirium or postoperative cognitive dysfunction need to be further addressed by prospective randomized trials to improve our knowledge.

### Postoperative analgesia

Pain management influences short- and long-term outcome of surgical patients.<sup>122, 123</sup> This is true for patients who undergo cardiac surgery, as pointed out by the review on the topic published in the April issue,<sup>124</sup> and even for those who undergo surgical procedures that are not that painful. Catheter ablation for atrial fibrillation is usually performed under light sedation and local analgesia, and opioids are given as rescue therapy if need be; a study by Ham *et al.* published in June, showed that in this setting the pre-emptive administration of propacetamol provides a significant reduction of opioid consumption.<sup>125</sup>

Regional anesthesia represents an important option to achieve optimal pain relief as well as other potential advantages.<sup>126, 127</sup> On this regard, it is still debated if greater effectiveness can be obtained by preemptive modality. In the July issue, a study by Wenk *et al.* showed that epidural anesthesia in spinal surgery reduces postoperative pain and opioid consumption more effectively if started before surgery without side effects.<sup>128</sup> To optimize intraoperative analgesia, it is useful to quantify intraoperative pain with objective parameters other than heart rate or arterial pressure changes. The Analgesia Nociception Index (ANI) has been introduced to assess intraoperative pain and titrate analgesic administration.<sup>129</sup> Theearth *et al.* evaluated the performance of the index in 60 adult patients who underwent elective supra-tentorial tumor surgery and received scalp block or incision-

site infiltration randomly.<sup>130</sup> Fentanyl administration based on ANI values was significantly less in patients who received the scalp block, which was associated with the higher analgesic effect.

In the last year, MA published other studies on postoperative analgesic regimens. Patient-controlled epidural analgesia (PCEA) is largely used to control labor pain, but modalities are not standardized;<sup>131, 132</sup> Matsota *et al.* showed that the background infusion of local anesthetic and fentanyl decreased breakthrough pain, but did not affect maternal satisfaction and neonatal outcomes.<sup>133</sup> Manassero *et al.* demonstrated that oral slow-release oxycodone was a valid alternative to PCEA with morphine in patients who underwent hip replacement under regional anesthesia.<sup>134</sup> Fusco *et al.* found that continuous wound infusion of levobupivacaine provided better postoperative analgesia and improved rehabilitation compared to local infiltration analgesia after hip arthroplasty.<sup>135</sup> In patients who underwent bariatric surgery, Rupniewska-Ladyko *et al.* observed that a single oral dose of gabapentin, 1200 mg, given one hour before general anesthesia significantly decreased the main pain intensity and opioid consumption in the first 12 postoperative hours while there was no difference about the incidence of nausea and vomiting.<sup>136</sup>

Finally, an intriguing analysis by Karlsen *et al.* on 171 RCTs about postoperative analgesia after total hip and knee arthroplasty was published in March.<sup>137</sup> The Authors focused their evaluation on the control groups, finding extreme heterogeneity in morphine consumption and pain intensity; if neglected, that aspect can condition meta-analyses and lead to incorrect conclusions.

## Pain

To date, opioids are still widely utilized for postoperative analgesia despite their significant collateral effects. Some studies suggest that, at the same dosage, the degree of analgesia obtained can be influenced by the polymorphisms of the genes involved in opioid pharmacokinetic and pharmacodynamics, such as the OPRM1 for mu-opioid receptor (MOP).<sup>138, 139</sup> In August, MA published a study by Zgheib *et al.* on 220

nulliparous women undergoing epidural fentanyl analgesia for labor; the authors found no difference in pain intensity, analgesia duration, side effects, and patient satisfaction in relation to three genetic polymorphisms: OPRM1 118A>G, IVS2+31G>A, and IVS2+691G>C.<sup>140</sup> The intraoperative use of opioids can affect the degree of postoperative analgesia by inducing hyperalgesia and tolerance.<sup>141</sup> Many studies showed that the N-methyl-D-aspartate receptor (NMDA) antagonist, ketamine is useful for both primary and secondary hyperalgesia after a variety of surgical procedures.<sup>142, 143</sup> In an exciting study published in April, Moon *et al.* investigated the mechanical pain threshold in an area distant from the site of surgery in patients who received ketamine at sub-hypnotic dosage during laparoscopic hysterectomy and found that the threshold was higher than in controls.<sup>144</sup> That effects might originate from the crucial role of NMDA receptors in the process of central neuroplasticity, which may also intervene in the transition from acute to chronic pain.<sup>145</sup> In the corresponding editorial, Porter and Schwenk pointed out that many questions remain unsolved, such as what is the appropriate dose of ketamine to prevent severe pain at a site considered remote and unrelated to the surgical trauma and if there is a benefit in continuing ketamine into the postoperative period.<sup>146</sup>

Chronic pain is often undermanaged in children, with a significant impact on sleep, mood, physical activity, school attendance, and quality of life.<sup>147</sup> Inadequate analgesic treatments may be explained by different reasons, first of all, the little or no evidence supporting the use of analgesics in this population. The topic has been reviewed by Vega *et al.* in the September issue.<sup>148</sup> An important recommendation was that considering the multifactorial nature of chronic pain, a multidisciplinary team for pain treatment should include the pain specialist, the psychologist, the physiotherapist, the social worker, the nurse, and should empower the patient himself as an active participant.

Low back pain is the most common cause of chronic pain in adults.<sup>149</sup> In the May issue, Borghi *et al.* reported on a new treatment with ultrasound-guided periradicular infiltrations of meloxicam up to 30 mg performed in the am-

bulatory setting; they registered a dramatic decrease of NRS which was less than three in 82% of the patients treated.<sup>150</sup> In the common practice, however, NSAIDs are the most commonly used first-line drugs.<sup>151</sup> Vuillemier *et al.* reviewed the results of many preclinical studies that suggest a central activity of NSAIDs on inflammatory pain due to spinal cyclooxygenase upregulation and increased prostaglandin E2 production in the dorsal horn; unfortunately, human studies are still not sufficient to translate the results of animal models on humans.<sup>152</sup> The role of cannabinoids as analgesic drugs is still unclear and was reviewed by Pergolizzi *et al.* in the August issue.<sup>153</sup> The authors pointed out that cannabinoids are effective in controlling neuropathic pain, allodynia, medication-rebound headache, and chronic noncancer pain and do not induce tolerance, contrary to opioids. The main limitations are the uncertainty of the delivered dose, the possible psychoactive effects, and the risk of diversion.<sup>154</sup>

### Office-based anesthesia

Office-based anesthesia (OBA) is a field rapidly growing.<sup>155, 156</sup> Patients and surgeons' convenience and reduced costs are clear advantages over surgery performed in hospitals, but safety concerns are present and need strict regulation.<sup>157</sup> The first guidelines produced by the American Society of Anesthesiologists (ASA) and published almost 20 years ago were amended twice, the last time in 2014.<sup>158</sup> MA published a series of expert's opinions on OBA, which was published one manuscript for each issue from August to December. The aspects examined were the need of carers for discharge after office-based anesthesia, obstructive sleep apnea considerations, procedures performed in Interventional Pulmonology (IP) Suites, obese patient peculiarities, and the minimum fasting period.<sup>159-163</sup>

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