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Review article

Epidural anesthesia and pulmonary function

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Abstract
The epidural administration of local anesthetics can provide anesthesia without the need for respiratory support or mechanical ventilation. Nevertheless, because of the additional effects of epidural anesthesia on motor function and sympathetic innervation, epidural anesthesia does affect lung function. These effects, i.e., a reduction in vital capacity (VC) and forced expiratory volume in 1 s ($FEV_{1.0}$), are negligible under lumbar and low thoracic epidural anesthesia. Going higher up the vertebral column, these effects can increase up to 20% or 30% of baseline. However, compared with postoperative lung function following abdominal or thoracic surgery without epidural anesthesia, these effects are so small that the beneficial effects still lead to an improvement in postoperative lung function. These results can be explained by an improvement in pain therapy and diaphragmatic function, and by early extubation. In chronic obstructive pulmonary disease (COPD) patients, the use of thoracic epidural anesthesia has raised concerns about respiratory insufficiency due to motor blockade, and the risk of bronchial constriction due to sympathetic blockade. However, even in patients with severe asthma, thoracic epidural anesthesia leads to a decrease of about 10% in VC and $FEV_{1.0}$ and no increase in bronchial reactivity. Overall, epidural administration of local anesthetics not only provides excellent anesthesia and analgesia but also improves postoperative outcome and reduces postoperative pulmonary complications compared with anesthesia and analgesia without epidural anesthesia.

Key words Postoperative lung function · Cardiac surgery · COPD · Asthma

Introduction

Epidural administration of local anesthetics can provide excellent anesthesia and analgesia for surgical procedures from the neck to the toes. In addition to this primary function of epidural anesthesia, the inevitable sympathetic blockade can have significant beneficial effects on several organ systems [1]. In this way, epidural anesthesia can increase gastrointestinal motility and perfusion, or decrease myocardial ischemia and the systemic stress response [1–4]. All these aspects add to the multimodal concept, or the concept of fast-track surgery, that has been developed over the last 20 years.

However, the impact of epidural anesthesia on lung function can be ambiguous. Effective analgesia, the avoidance of mechanical irritation by airway instrumentation, and no need for mechanical ventilation must be balanced against the possible alteration of lung function by epidural motor blockade of respiratory muscles and the potentially detrimental effects of sympathicolysis, leaving an unopposed vagal tone with a potentially increased bronchial tone and reactivity.

In the course of this review, the physiological effects of lumbar, thoracic, and cervical epidural anesthesia on lung function will be presented, followed by the effects on post-operative respiratory function and the incidence of pulmonary complications.

Finally, studies will be presented to shed some light on the critical discussion about the question of whether the beneficial effects of thoracic epidural anesthesia, in particular on lung function, outweigh the risk of epidural hematoma during cardiac surgery, and whether thoracic epidural anesthesia can be of advantage in patients with chronic obstructive pulmonary disease (COPD), despite a sympathetic and potential muscular blockade.

Physiological effects of epidural anesthesia on lung function

The physiological effects of epidural anesthesia on lung function without any surgical intervention are determined by the extension of the motor blockade. The extension of the motor blockade and its relevance for

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lung function depend on the height of the insertion of the catheter for segmental epidural anesthesia. Furthermore, there is the minor influence of the choice of local anesthetic, and the major influence of the concentration of the local anesthetic that is chosen for epidural anesthesia and analgesia, which will not be discussed in detail.

Lumbar epidural anesthesia

Freund et al. [5] evaluated the effects of the spread of epidural anesthesia from a lumbar catheter up to the midthoracic region in 18 volunteers and patients. Using 2% lidocaine with a volume of 15–25 ml, they found a sensory block level of *T* 3.6 ± 1.2 and a motor block level that was determined electromyographically at *T* 8.2 ± 2.6. With this extensive block, the decrease in inspiratory vital capacity (VC) was only 3%. Usually, a change in vital capacity is felt if it decreases by 10% or more. Therefore, this minor change is not expected to be clinically relevant, and might be even less when the motor block is limited to the low thoracic or lumbar region.

Thoracic epidural anesthesia

With the epidural administration of local anesthetics higher up the vertebral column in concentrations suitable for epidural anesthesia for surgery, some significant alteration to lung function can be expected. With a limited sensory blockade from dermatom T1 to T5, VC is decreased by 5.6% (from 5.4 ± 0.8 to 5.1 ± 0.9 l) and forced expiratory volume in one second ($FEV_{1.0}$) by 4.9% [6]. This effect can be explained by a direct motor blockade of intercostals muscles. This effect increases with the extension of the sensory blockade. Takasaki and Takahashi [7] have shown in 30 patients, that an epidural blockade (mepivacaine 2%) from dermatom C4 to T7 and from T5 to L4 led to a decrease of 25% in VC, and a decrease in $FEV_{1.0}$ of 13% and 12%, respectively. On the other hand, studies in COPD patients have shown that an epidural block with bupivacaine 0.5% (sensory blockade C4 to T8) leads to a decrease in VC and $FEV_{1.0}$ of only 8% from baseline [8]. The difference between these results might be explained by the additional effect of the change in posture. Lung function measurements are usually taken in a sitting position. However, under extensive epidural anesthesia, measurements with high concentrations of the local anesthetic in a sitting position are normally not possible, and therefore these are taken lying down supine with the head, or sometimes the chest, tilted upward. In some study designs, it is not clear whether these measurements under epidural anesthesia have been compared with baseline measurements in a sitting or a supine position. This change in position alone can lead to a decrease in VC and $FEV_{1.0}$ from at least 7% up to 23%, and can explain the discrepancies between different studies [8–11].

Looking at the overall lung function, i.e., gas exchange, concerns about a ventilation/perfusion mismatch by high thoracic epidural anesthesia could not be proven. Neither the arterial–alveolar difference in P_{O_2} (Aa_{DO_2}) nor the direct measurement of shunt showed any significant difference [12,13].

Overall, thoracic epidural anesthesia with a sensory blockade up to the midcervical region did change VC and $FEV_{1.0}$ significantly, but only by an amount which was safe for clinical use. The effect was less than the effect of a supraclavicular plexus blockade, which resulted in reductions in VC and $FEV_{1.0}$ of up to 50% [14]. The ventilation/perfusion ratio remains unaltered under the influence of thoracic epidural anesthesia.

Cervical epidural anesthesia

Finally, cervical epidural anesthesia reduces VC and $FEV_{1.0}$ to about the same degree as high thoracic epidural anesthesia reaching up into the low cervical dermatoms. In patients free from pulmonary disease, epidural administration of ropivacaine (0.75%, 10 ml) led to a sensory blockade from C2 to T3 with a reduction of VC by 17.6%, while administration of bupivacaine 0.25% or 0.375%, with a wider spread of the sensory blockade from C2 to T5 and C3 to T6, led to a decrease of 23% and 33%, respectively, for VC, and 18% and 26%, respectively, in $FEV_{1.0}$ from baseline [15,16]. Unfortunately, the authors do not describe in which position (sitting or supine) their baseline measurements were obtained. The extensive changes with rather low concentrations suggest that they compared baseline measurements in a sitting position with measurements under epidural analgesia in a supine position (see above). Moreover, as well as other parameters, the authors of this study determined movement of the diaphragm and the inspiratory muscle strength based on the forced sniff test. Movement of the diaphragm, as well as the forced sniff test, showed a significant reduction, indicating at least a minor attenuation of diaphragmatic force [16]. The use of cervical epidural anesthesia was evaluated in a series of 324 patients undergoing carotid artery surgery. Following the administration of bupivacaine (0.375% or 0.5%), a sensory blockade resulted from C2 to T4 on average. Three out of 324 patients (0.8%) had to be intubated because of respiratory insufficiency [17], while in another study evaluating cervical epidural anesthesia for the same type of surgery, none of the 215 patients had to be intubated [18]. There were no reports of neurological trauma in any of these studies.

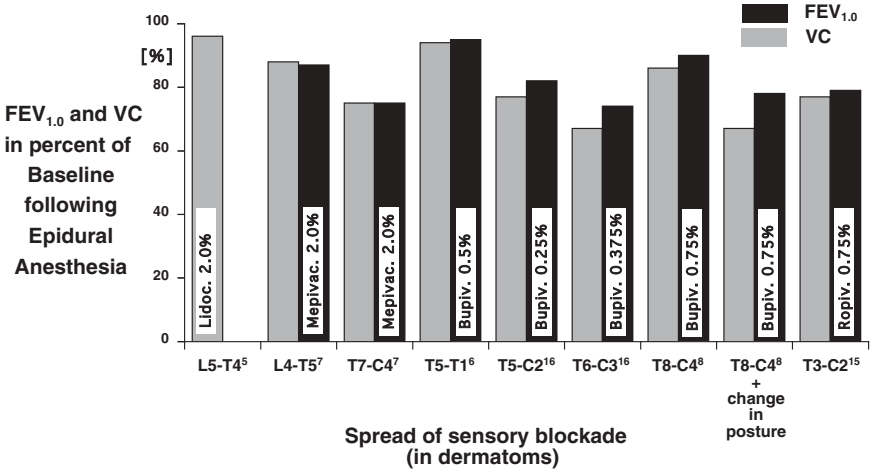

Fig. 1. Synopsis of the effects of epidural anesthesia on vital capacity (*VC*) and forced expiratory volume in 1 s ($FEV_{1.0}$) in 6 studies depending on the spread and concentration of the local anesthetic used. Please note that the change in posture (columns 6 and 7) causes as much or even more of a decrease in *VC* and *FEV1* than epidural anesthesia itself. This could explain why there is a bigger decrease in *columns 5 and 6*, despite lower concentrations of the local anesthetics, compared with the other results. Most likely, the effect of a change from sitting to a supine position was not separated from the effects of epidural anesthesia [16]. (Derived from data from refs. 5–8, 15, and 16.)

Overall, the use of cervical epidural anesthesia seems to be a practical, and so far a safe, alternative to general anesthesia. Only with the use of high concentrations of local anesthetics (bupivacaine 0.5%) is there a 0.8% risk of developing a high muscular blockade with a need for respiratory support.

The effect of epidural anesthesia on VC and $FEV_{1.0}$ is presented in a synopsis with the results of some of the representative studies in Fig. 1.

Postoperative lung function under the influence of epidural anesthesia

Postoperative lung function in general

Early postoperative lung function is influenced by residual muscular relaxation, the time of extubation, pain therapy, and vigilance. Immediately after an operation, the ability to cough seems to be one of the most important aspects of lung function. This might well be represented by the $FEV_{1.0}$ maneuver, which makes $FEV_{1.0}$ one of the preferred parameters for studying postoperative lung function. In this context, it is important to keep in mind that when $FEV_{1.0}$ measurements are performed, the best measurement out of three or more attempts is usually accepted as the actual $FEV_{1.0}$ [19]. However, immediately after an operation with general anesthesia with muscle relaxation, we have to consider the possibility of "rest relaxation," which can be recognized because of the fade phenomenon, i.e., a fading of muscle strength when maximal contractions are repeated [20]. Therefore, in this particular scenario the best $FEV_{1.0}$ does not necessarily represent the reproducible ability of the patient, and in particular not the ability for repeated powerful coughs. In fact, a "fade" of $FEV_{1.0}$ under the effect of rest relaxation has been shown as a result of "rest-relaxation" [21,22]. Thus, postoperative $FEV_{1.0}$ values often overestimate the ability for repeated coughing following general anesthesia with muscle relaxation. In contrast, under epidural anesthesia muscle relaxant agents are not necessarily required, and thus the fade effect is not expected.

In the early postoperative stage, depending on the type of anesthesia, postoperative vigilance and the ability to follow complex commands for lung function measurements are not feasible. It has been shown that patients who undergo major surgery, such as cardiac surgery, under combined anesthesia with epidural anesthesia and epidural postoperative analgesia are able to perform VC and $FEV_{1.0}$ measurements within 1 h after extubation, while patients without epidural anesthesia and analgesia, and treated with intravenous administration of opioids only, were not able to perform lung function tests at this time [23]. This effect was most likely due to reduced vigilance and unsatisfactory pain relief. However, both effects significantly compromise lung function and the ability to cough.

Later postoperative lung function is determined by the type of anesthesia as well as by the type of surgical procedure. In particular, following upper abdominal surgery, VC and $FEV_{1.0}$ can be reduced up to 14 days postoperatively [24,25].

Early extubation under epidural anesthesia

To avoid ventilator-related complications and the use of intensive-care resources, earlier and earlier extubation, even after major surgical procedures such as esophageal resection, abdominal aortic surgery, or cardiac surgery, is desirable [26,27]. As described above, reduced vigilance, rest relaxation, and possibly impaired diaphragmatic function often lead to prolonged mechanical ventilation in the intensive care unit. Several studies have shown that even after these major surgical procedures, patients can be extubated directly at the end

of surgery under combined general and epidural anesthesia. Although there has been no controlled study that proved the reduction of postoperative pulmonary complications by early extubation, there is enough evidence to show that prolonged mechanical ventilation is a risk factor for pulmonary infections and morbidity.

Postoperative analgesia and lung function

Thoracic epidural anesthesia alters lung function and reduces VC and $FEV_{1.0}$ by 15% to 20% of baseline. However, lung function after abdominal surgery can be impaired postoperatively, with a reduction in VC of 60% or more, and lost for up to 14 days until complete restitution [24]. The question occurs as to whether the use of thoracic epidural anesthesia aggravates or attenuates this effect. In fact, thoracic epidural anesthesia leads to an improvement of lung function. In 1975, Whaba et al. [28] demonstrated that the reduction in functional residual capacity (FRC) improved from 21.7% to 15.9%, and the reduction in VC improved from 63% to only 45% when epidural anesthesia was used following upper abdominal surgery. Thirteen years later, Mankikian et al. [29] used epidural anesthesia in patients who underwent abdominal aortic surgery with a complete longitudinal abdominal incision, and demonstrated an improvement in VC from 1380 ± 115 ml to 1930 ± 144 ml.

How thoracic epidural anesthesia and analgesia improve postoperative lung function can not be entirely explained. At least two effects contribute significantly to this improvement. On the one hand thoracic epidural anesthesia improves diaphragmatic function, and on the other it provides better postoperative analgesia than patient-controlled intravenous administration (PCA) of opioids.

Polaner et al. [30] implanted sonomicrometer crystals into the costal and crural regions of the diaphragm in lambs, and found a significant improvement of diaphragmatic function under epidural anesthesia. In the same year, the same authors also demonstrated an improvement in the breathing pattern from fast shallow breathing to slow deep breathing in patients undergoing abdominal aortic surgery. Later, Warner et al. [31] studied the motion of the diaphragm and electromyographic activity in respiratory muscles in volunteers, and found an increase in FRC due to a caudad motion of the diaphragm and a decrease in intrathoracic blood volume. Overall, there seems to be a direct effect on diaphragmatic contractility and breathing pattern under epidural anesthesia.

On the other hand, thoracic epidural analgesia can be superior to systemic analgesia even when compared with a patient-controlled mode of application. Many

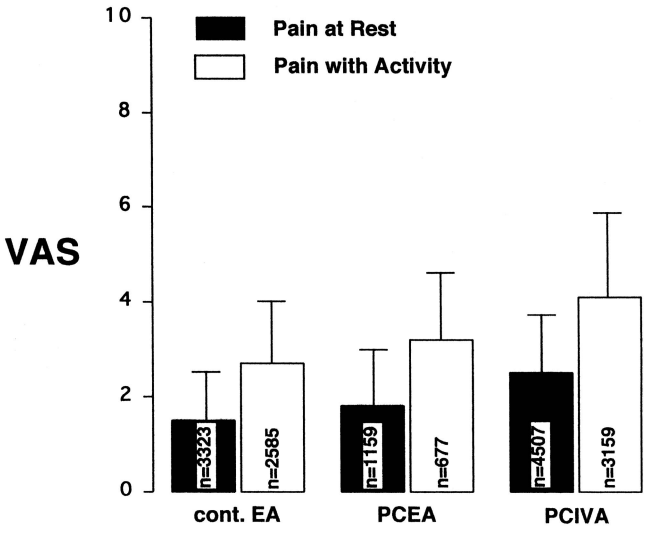

Fig. 2. Average pain at rest and with activity from the day of surgery to the third postoperative day, expressed according to a visual analog scale (*VAS*; mean ± SD), in a comparison of three modes of pain therapy. The patients received either continuous epidural anesthesia (cont. *EA*), patient-controlled epidural analgesia (*PCEA*), or intravenous patient-controlled analgesia with opioids (*PCIVA*). Continuous *EA* was significantly more effective at rest and with activity than *PCEA* and *PCIVA*, and *PCEA* was still significantly more effective at rest and with activity than *PCIVA* ($P < 0.001$). The effects were even more pronounced on the first postoperative day compared with the third day. (Derived from the data in Ref. 32.)

studies have been published on this topic. In 2005, Wu et al. [32] performed a metaanalysis, including 299 randomized controlled trials (more than 15000 patients), looking at the efficacy of postoperative patient-controlled and continuous infusion of epidural analgesia versus intravenous patient-controlled analgesia with opioids. They found that until the third day, epidural analgesia was significantly superior to i.v. PCA. In particular, pain with activity was significantly less with epidural analgesia compared with PCA (Fig. 2) [32].

Postoperative pulmonary complications under epidural anesthesia and noncardiac surgery

The improvement in postoperative lung function can be regarded as a pure academic question or a question of patient comfort (which is not unimportant) as long as there is no effect on the pulmonary complication rate or mortality. In 1997, the first metaanalysis on pulmonary outcome depending on analgesic regimen showed that an epidural analgesia with local anesthetics reduced pulmonary infections to a third, and overall pulmonary complications to about a half, of the infections and complications under systemic analgesia [33]. Moreover, this analysis was followed by an even larger meta-analysis in

2000, including 141 randomised trials and with almost 10000 patients, and analyzing the effects of regional anesthesia on perioperative morbidity and mortality. As well as other effects, these researchers found a reduction in postoperative pneumonia of 39% of the rate under epidural anesthesia compared with a systemic analgesic regimen, and a reduction in mortality of about one third [34].

Thus, the effect of epidural anesthesia improves postoperative VC and FRC, provides better analgesia than any other technique, and reduces the rate of postoperative pulmonary complications.

Cardiac surgery and epidural anesthesia

Because of the need for anticoagulation in cardiac surgery, epidural anesthesia has been used very cautiously for fear of epidural hematoma and possible paraplegia. Over the last 10 years, more and more studies have been published, covering more than 1000 patients, and describing the safe use of high thoracic epidural anesthesia for cardiac, mostly "off pump," coronary artery bypass surgery [35–38]. Epidural anesthesia has been used in combination with general anesthesia, but there have also been reports of cardiac surgery in awake or sedated patients breathing spontaneously without general anesthesia [39,40]. None of these studies found epidural hematoma or persistent neurological damage due to epidural anesthesia.

When cardiac surgery has to be performed on patients with severe COPD, mortality rates increase markedly up to 50% in elderly patients [41]. Therefore, any technique that might improve lung function and allow early extubation is desirable. Epidural anesthesia made early extubation (often in the operating room) possible in all of these studies, and provided superior postoperative analgesia and the benefit of cardiac sympathicolysis with regard to myocardial ischemia. Moreover, it has been shown that the use of high thoracic epidural anesthesia leads to superior postoperative lung function compared with lung function under systemic analgesia with opioids. In 1997, Fawcett et al. [42] found that following cardiac surgery, patients under conventional anesthesia showed a decrease in their VC to 29.1% of their baseline, and a decrease in $FEV_{1.0}$ to 28.4%. In contrast, under a combination of general anesthesia and epidural anesthesia, the VC decreased to only 39.5% and the $FEV_{1.0}$ to 40.4%. Later, in 2000, Tenling et al. [23] presented results that demonstrated a difference in VC and $FEV_{1.0}$ of about 10% from baseline on the first postoperative day, unlike the results of Fawcett et al. [42]. Most importantly, they showed that patients with epidural analgesia were able to perform lung function measurements, including $FEV_{1.0}$, 1h after extubation, while patients without epidural anesthesia were not able to do so [23]. With the idea in mind that the $FEV_{1.0}$ maneuver reflects the ability to cough, this finding might be more important than the absolute numbers of lung function measurements (Fig. 3).

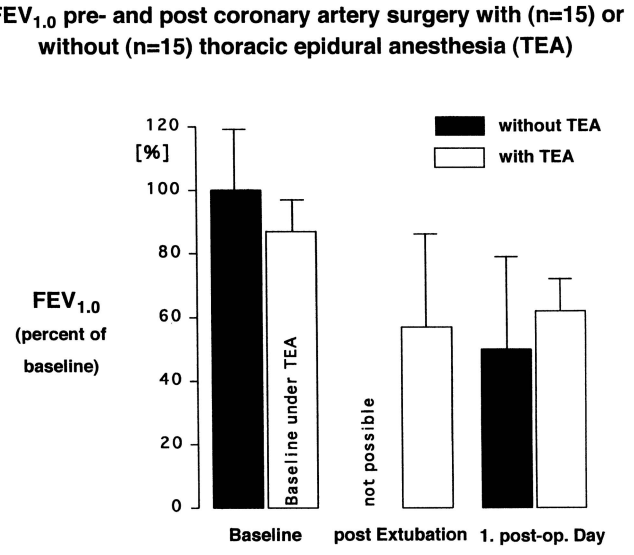

Fig. 3. Pre- and postoperative *FEV1* in patients undergoing coronary artery surgery with and without thoracic epidural anesthesia (means ± SEM). The decrease in *FEV1* of 15% due to thoracic epidural anesthesia (*TEA*) turns into a significantly better *FEV1* postoperatively. Most importantly, for patients without *TEA* it was not feasible to obtain *FEV1* measurements directly after extubation. (Derived from data in Ref. 23.)

In summary, thoracic epidural anesthesia for cardiac surgery offers several advantages, but to date, in contrast to noncardiac surgery, no improvement in overall mortality has been shown. Therefore, there is still a lively debate about the risk–benefit ratio between these advantages and the potential risk of an epidural hematoma and postoperative paraplegia [43].

Epidural anesthesia in patients with obstructive pulmonary disease

The most common obstructive pulmonary diseases are asthma and COPD, which is mainly chronic obstructive bronchitis and emphysema. While asthma is characterized by airway inflammation with bronchial hyperreactivity and most of the time fully reversible attacks of airway obstruction due to bronchial constriction, COPD is characterized by steadily declining, only partially reversible or nonreversible, airway obstruction due to a combination of inflammation, bronchial instability, and bronchoconstriction [44].

General anesthesia with instrumentation of the airways can elicit bronchospasm and life-threatening com-

plications. Undoubtedly, the use of regional anesthesia helps to avoid airway irritation. Therefore, it is not surprising that surgical procedures performed under spinal or epidural anesthesia are associated with fewer respiratory complications as compared with the same procedures under general anesthesia [45–47]. Even open abdominal aortic repair of aneurysm can be safely done under combined spinal epidural anesthesia in patients with severe COPD [48].

However, the use of high thoracic epidural anesthesia in respiratory compromised patients has raised two major concerns. Firstly, the motor blockade that is associated with epidural anesthesia would lead to respiratory decompensation in patients with an already compromised respiratory function. Secondly, the sympathetic blockade, which is also associated with epidural anesthesia, would lead to an increased bronchial tone and airway hyperreactivity.

Effects of high thoracic epidural anesthesia on lung function in patients with obstructive pulmonary disease

High thoracic epidural anesthesia in patients without obstructive pulmonary disease with high concentrations of lidocaine or bupivacaine can reduce VC and $FEV_{1.0}$ by more than 0.5l, which would be detrimental to patients who already start with an $FEV_{1.0}$ of less than a liter. Therefore, there were major concerns about using high thoracic epidural anesthesia in these patients. However, high thoracic epidural anesthesia achieved with bupivacaine (0.75%) with a sensory blockade from C4 to T8 did not change FRC, measured by the helium dilution technique, and reduced $FEV_{1.0}$ and VC by 8%–10% (depending on the individual baseline, i.e., 0.1–0.3l in absolute numbers), which was not felt by the patients as respiratory distress [49]. This effect was no different when ropivacaine was used instead of bupivacaine [8]. Overall, this effect was smaller than the effect of a change in position from sitting to supine, which causes more than 10% decrease in VC and $FEV_{1.0}$, and which is the effect that can be seen following general anesthesia with muscle relaxation. Overall, high thoracic epidural anesthesia seems not to affect lung function more in patients with COPD and bronchial hyperreactivity than in patients free from respiratory diseases. However, these results leave the concern that bronchial reactivity is increased under a sympathetic blockade, and leads to an unopposed bronchial constriction if the system is irritated.

Bronchial reactivity

Bronchial hyperreactivity is defined as an increased bronchoconstrictory response to pharmacological, physical, or chemical challenges [50]. In the US population, increased bronchial reactivity has a prevalence of 10% of the population [51]. Both asthma and COPD have increased bronchial reactivity in common, and can occur in patients with allergic or respiratory diseases, such as allergic rhinitis, during and after viral infections of the upper airway, as well as in heavy smokers [52–57].

Airway instrumentation in patients with increased bronchial reactivity can cause markedly increased rates of intraoperative bronchospasm, and even life-threatening complications postoperatively [55,58–60]. The effect of endotracheal intubation even in symptom-free asthmatics was demonstrated in a study of volunteers with mild asthma [61]. These volunteers underwent endotracheal intubation under local anesthesia, and performed a lung function test before intubation and with the tube in place. Without prophylactic antiobstructive treatment, endotracheal intubation led to a reduction in $FEV_{1.0}$ of more than 50%. Pretreatment with a β2-adrenergic agonist and topical lidocaine application reduced this response to a 20% decrease [61]. The effect of airway instrumentation in asthmatics with severe asthma can only be estimated. In 2001, Warner et al. [55] published a study comparing the rate of respiratory complications in patients (all smokers) with or without signs of a chronic obstructive airway disease. Patients with a preexisting airway obstruction showed a more than 6-fold higher incidence of clinically relevant bronchoconstriction, a higher rate of postoperative pneumonias, and a longer ICU stay postoperatively.

Therefore, regional anesthesia seems to be preferable to general anesthesia with endotracheal intubation. However, concerns about a pulmonary sympathetic blockade and an unopposed parasympathetic tone with the risk of perioperative severe bronchoconstriction remain in cases where high thoracic epidural anesthesia is used, in particular with a spread up to the cervical dermatoms. In fact, following cervical trauma with subsequent complete or incomplete quadriplegia and a sympathetic blockade, patients can show a mild and at least partially reversible airway obstruction [62,63].

Effects of thoracic epidural anesthesia in patients with bronchial hyperreactivity

Tests were carried out to evaluate the effects of high thoracic epidural anesthesia on bronchial reactivity in patients with COPD who received a high thoracic epidural catheter in preparation for upper abdominal surgery [49]. The epidural catheter was placed between the first and second, or the second and third, intervertebral interspace. Following the epidural administration of 7–8ml bupivacaine 0.75%, a sensory block from C4 to T8 developed on average. To determine an increased in

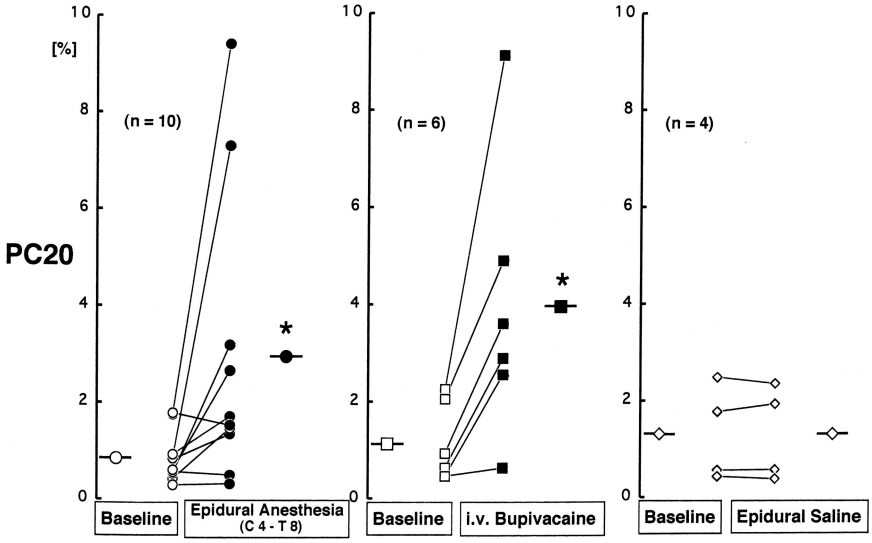

Fig. 4. Effects of high thoracic epidural anesthesia on bronchial hyperreactivity. Compared to baseline, the concentration of acetylcholine inhaled that induces a 20% decrease of FEV1 (*PC20*) has to be increased under high thoracic epidural anesthesia by more than two-fold (*left panel*). The same effect can be seen following intravenous administration of bupivacaine (*middle panel*), while epidural administration of saline does not change the threshold for a 20% decrease of FEV1 (*right panel*; means and individual measurements). High thoracic epidural anesthesia does not enhance, but rather decreases, bronchial hyperreactivity in a similar way to the effect of intravenous administration of bupivacaine [49]

bronchial tone, $FEV_{1.0}$ in relation to VC and airway resistance (oscillometrically) were measured. The results showed no sign of an increased bronchial tone. However, the threat still remains that due to a strong stimulus such as an endotracheal intubation reflex, bronchoconstriction may lead to severe bronchospasm. Therefore, before and during high thoracic epidural anesthesia, an inhalational bronchial challenge with acetylcholine was performed. At first sight the results were surprising, because under high thoracic epidural anesthesia the patients did not show an increased reactivity, but showed an attenuation of their reactivity. The acetylcholine threshold for a 20% decrease in $FEV_{1.0}$ was raised up to three times under high thoracic epidural anesthesia, i.e., the patients became significantly less responsive. The reactivity did not alter following the epidural administration of placebo. The explanation for this result is that intravenous administration of bupivacaine also attenuates bronchial reactivity up to three-fold. Thus, the systemic effect of the local anesthetic significantly attenuates bronchial reactivity and overrides any possible negative effects of the sympathetic blockade (Fig. 4) [49].

The fact that a sympathetic blockade does not alter lung function can be explained by the distribution of β1- and β2-adrenergic receptors in the bronchial tissue. The effect of direct sympathetic innervation is mediated via sympathetic fibers and β1-adrenergic receptors. However, only a small number of β1-adrenegic receptors can be found in the bronchial tissue, and these might be only a phylogenetic rudiment compared with other species, while there is a large number of β2-adrenergic receptors. β2-adrenegic receptors are stimulated not by direct sympathetic innervation, but by circulating catecholamines. Therefore, blockade of β2-adrenergic receptors by nonspecific β-adrenergic receptor blockers can lead to increased airway resistance and acute bronchospasm [64–67]. In contrast, the effect of the direct blockade of the sympathetic innervation seems to be negligible. In fact, in his book about epidural anesthesia, Bromage [68] describes several cases of patients suffering from status asthmaticus who improved markedly following the use of thoracic epidural anesthesia, which most likely can be explained by the systemic effect of the local anesthetic. In addition, Shono et al. [69] describe the improvement of a patient with acute bronchospasm due to the use of epidural anesthesia (or the systemic effect of local anesthetics).

Thus, in patients with increased bronchial reactivity, high thoracic epidural anesthesia seems to attenuate bronchial reactivity rather than to increase it, due to the systemic effects of the local anesthetics.

Clinical implications

In a subsequent study based on the beneficial effects of high thoracic epidural anesthesia in patients with COPD, patients with severe COPD and a history of markedly increased bronchial reactivity underwent ablatio mammae with reconstruction and axillary lymph node dissection under high thoracic epidural anesthesia with mild sedation and no general anesthesia [8]. $FEV_{1.0}$ and VC were measured in a sitting position, a prone position, and under high thoracic epidural anesthesia. The change from the sitting to the prone position caused a bigger change in $FEV_{1.0}$ and VC than the establishment of epidural anesthesia. In addition the ratio of $FEV_{1.0}$ to VC improved, leading to a suggestion that the administration of local anesthetics decreases the bronchial tone rather than increasing it. The use of ropivacaine instead of bupivacaine did not lead to any difference. In none of the cases did epidural anesthesia have to be converted to

general anesthesia, and none of the patients developed postoperative pulmonary complications.

Several studies and metaanalyses have shown a reduction in postoperative complications when general anesthesia was combined with epidural anesthesia and postoperative epidural analgesia [33,34,70]. This effect can be explained as the result of early extubation, better analgesia during mobilization and coughing, attenuation of bronchial reactivity, and improved diaphragmatic function.

Overall, the use of regional anesthesia as the main anesthetic technique, or in combination with general anesthesia, can be recommended in patients with obstructive pulmonary disease [71,72].

Lung reduction surgery

All the studies described above recommend the use of high thoracic epidural anesthesia for a combined general and epidural anesthesia for lung reduction surgery. In 2001, Gruber et al. [73] studied the effects of a combined general thoracic epidural anesthesia for lung reduction surgery in 12 patients with severe COPD. Their baseline $FEV_{1.0}$ was 0.76 ± 0.12 (27 ± 6% of the predicted level). These patients seemed to benefit from this combined anesthesia. However, to date there is not enough evidence to recommend this technique.

The effects of local anesthetics on lung function and bronchial hyperreactivity

Local anesthetics of the amide type attenuate and even block afferent and efferent nerve conduction of autonomic nerve fibers [74,75]. This way, autonomic reflexes such as the coughing reflex or reflex bronchoconstriction can be suppressed with lidocaine plasma concentrations of 1.0–2.0 $\mu g \cdot ml^{-1}$, i.e., far below the toxic threshold of 5.0 $\mu g \cdot ml^{-1}$ [76–78]. In asthmatic volunteers, intravenous lidocaine doses of 1.0–2.0 $mg \cdot kg^{-1}$ body weight significantly attenuated histamine-induced bronchoconstriction [65,67]. This effect is dose-dependent, and can be used to attenuate the response to airway irritations such as endotracheal suction or intubation. This effect is comparable to a moderate dose of a β2-adrenergic agonist such as salbutamol, and leads, in combination with salbutamol, to an additive effect [79]. Therefore, in cases of expected airway irritation, prophylactic treatment with lidocaine and a β2-adrenergic agonist can be recommended [72,77]. As well as its use as a prophylactic agent, intravenous administration of lidocaine has been used successfully to treat bronchospasm [69,80].

Overall, the systemic effect of amide local anesthetics contributes to the beneficial effect of regional anesthesia to maintain, or even improve, lung function, in particular in patients with obstructive airway disease.

Conclusion

Epidural anesthesia with a spread from the lumbar region to the midthoracic region leads to only a minimal reduction in VC and $FEV_{1.0}$, but can help to avoid irritation by endotracheal intubation. Epidural anesthesia with a spread from the midthoracic to the midcervical region (even in high concentrations of the local anesthetics used), including the effect of a change in position from sitting to a supine position, leads to a reduction of VC and $FEV_{1.0}$ of up to 33 %.

However, in terms of postoperative lung function, these effects are still smaller than the effects that can be seen following general anesthesia without epidural anesthesia. As well as the option to avoid general anesthesia and use epidural anesthesia alone, the use of combined general and epidural anesthesia significantly improves postoperative lung function after major abdominal surgery and reduces the risk of pulmonary complications and, according to metaanalyses, even improves overall mortality. The beneficial effects of high thoracic epidural anesthesia on lung function following cardiac surgery have to be weighed against the side effects and a potential risk of epidural hematoma.

Despite concerns about motor blockade and the negative effects of a sympathetic blockade on bronchial tone and bronchial reactivity, high thoracic epidural anesthesia can improve lung function and postoperative outcome in asthmatics and COPD patients.

Although epidural anesthesia alone can reduce lung function, and in gross overdose even block the function of the diaphragm, the overall effect with respect to the systemic effects of the local anesthetics leads to an improvement in postoperative lung function and a reduction in postoperative pulmonary complications.

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