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RESEARCH ARTICLE

Intraoperative management of combined general anesthesia and thoracic epidural analgesia: A survey among German anesthetists

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Abstract

Background: Evidence concerning combined general anesthesia (GA) and thoracic epidural analgesia (EA) is controversial and the procedure appears heterogeneous in clinical implementation. We aimed to gain an overview of different approaches and to unveil a suspected heterogeneity concerning the intraoperative management of combined GA and EA.

Methods: This was an anonymous survey among Members of the Scientific working group for regional anesthesia within the German Society of Anaesthesiology and Intensive Care Medicine (DGAI) conducted from February 2020 to August 2020.

Results: The response rate was 38%. The majority of participants were experienced anesthetists with high expertise for the specific regimen of combined GA and EA. Most participants establish EA in the sitting position (94%), prefer early epidural initiation (prior to skin incision: 80%; intraoperative: 14%) and administer ropivacaine (89%) in rather low concentrations (0.2%: 45%; 0.375%: 30%; 0.75%: 15%) mostly with an opioid (84%) in a bolus-based mode (95%). The majority reduce systemic opioid doses intraoperatively if EA works sufficiently (minimal systemic opioids: 58%; analgesia exclusively via EA: 34%). About 85% manage intraoperative EA insufficiency with systemic opioids, 52% try to escalate EA, and only 25% use non-opioids, e.g. intravenous ketamine or lidocaine.

Conclusions: Although, consensus seems to be present for several aspects (patient's position during epidural puncture, main epidural substance, application mode), there is considerable heterogeneity regarding systemic opioids, rescue strategies for insufficient EA, and hemodynamic management, which might explain inconsistent results of previous trials and meta-analyses.

KEYWORDS
analgesics, enhanced recovery after surgery, epidural analgesia, multimodal treatments, perioperative care

1 | INTRODUCTION

Several guidelines recommend combined general anesthesia (GA) and epidural analgesia (EA) for major abdominal and thoracic surgery[1–4] due to excellent pain control,[5–7] reduced perioperative morbidity,[5,7,8] and even reduced mortality[5,8] compared with systemic analgesia. These beneficial effects are commonly attributed to opioid-sparing and pleiotropic effects of sympatholysis leading to attenuation of the surgical stress response.[9,10] However, recent studies have also reported contradictory results giving impetus to an ongoing debate about the pros and cons of combined GA and EA.[11,12] At closer look, there is high heterogeneity concerning endpoints, study population, and anesthetic management among the available studies. Especially, the anesthetic regimens of both, combined GA and EA and general anesthesia alone (systemic analgesia) deviate significantly regarding substance use, mode of application (bolus vs. continuous; provider-controlled vs. patient-controlled) and timing of EA initiation.[6] Indeed, there is a wide range of possible variation within combined GA and EA and although some aspects have been addressed in trials and meta-analyses,[13–16] guidelines on the optimal performance do not exist. Recently, The Royal College of Anaesthetists published an updated version of their "Best practice recommendations," which refers mainly to organizational aspects of EA.[17] At least, there have been surveys on the management of combined GA and EA several years ago,[18–20] but in the meantime, controversies have shifted due to numerous innovations for anesthetic regimens and perioperative care. The aim of this survey was to assess the current range of approaches for combined GA and EA among expert anesthetists and to unveil a suspected heterogeneity concerning the intraoperative management of the regimen.

Editorial Comment

There is not one widely accepted routine for management of combined general and epidural anesthesia. The results from this German national survey on intraoperative combined general and epidural anesthesia demonstrated that there are some similarities but also large variations regarding the use of systemic opioids, rescue strategies for insufficient EA, and hemodynamic management. Such variability in local routine practice presents challenges for retrospectively exploring outcomes in this context.

2 | METHODS

The Ethical Committee of the University Hospital Wuerzburg, Wuerzburg, Germany approved publication of this survey under the prerequisite of data protection regulations on February 09, 2021 (Ethics Committee No 20201215 01). An online survey was created in German language (English translation available in supplements) using *EvaSys Suite* V8.0 (Electric Paper Evaluationssysteme GmbH).

The questionnaire had six sections comprising mainly multiple-choice questions on:

- Personal information of participants.
- Level of expertise.
- Performance of EA in general.
- Substances for epidural application.
- Anesthetic management.
- Final open question concerning personal rationales and frequent controversies.

The complete translated questionnaire is available as supplementary material. The questionnaire was piloted in terms of comprehensibility and required time to complete by three senior anesthetists who did not belong to the final target group. The final questionnaire was disseminated via e-mail to the 249 members of the Scientific working group for regional anesthesia within the German society of Anaesthesiology and Intensive Care Medicine (DGAI) on February 27, 2020 (reminder: August 14, 2020). The e-mail contained a short description of the project, a hyperlink, and a QR-code to access the questionnaire. The participants were asked to answer the questions according to their personal preferred strategy. Participation was anonymous and the authors received no individual information beyond the questionnaire.

The answers to the multiple-choice questions were summarized descriptively as absolute numbers and frequencies. The answers to the final open question were screened, categorized, and condensed by two authors (TS, PK). Only those comments mentioning a controversial issue or that elucidated topics beyond the closed questions were reported. Descriptive statistics and graphics were created using Prism 8.4.2 (GraphPad).

3 | RESULTS

As of August 27, 2020, we received 94 (38%) responses. Some participants did not answer all questions, especially those on personal data (only 80 respondents reported their age), whereas the specific questions on the anesthetic management were not fully answered by 2 participants. The majority of participants were anesthetists with high expertise concerning the specific regimen of combined GA and EA (Table 1).

The majority of respondents (94%) preferred the sitting over the lateral decubitus position for epidural puncture (Figure 1A). Most anesthetists preferred ropivacaine (89%) over bupivacaine (10%) and chose low concentrations of 0.2%–0.375% and 0.125%–0.25%, respectively (Figure 1B–D). Most participants initiated EA early, i.e., prior to skin incision (80%) and mostly preferred a bolus-based application mode (95%; Figure 1E,F). Opioids for EA were used intraoperatively by 84% (Figure 1G).

Given a sufficient EA, participants agreed with an opioid-sparing (58%) or even an opioid-free (34%) regimen after induction of GA

TABLE 1 Participant's characteristics

Participants, n (%)	94 (100)
Female	20 (21)
Male	71 (76)
Unknown	3 (3)
Median age (IQR) in years	49 (44–56)
Institution, n (%)	
University hospital	31 (33)
Tertiary care hospital (>500 beds)	13 (14)
Secondary care hospital	19 (20)
Primary care hospital (<500 beds)	28 (30)
Outpatient center	2 (2)
Professional experience, n (%)	
<5 years	3 (3)
5–10 years	5 (5)
11–15 years	10 (11)
>15 years	75 (81)
Position, n (%)	
Resident	5 (5)
Consultant	4 (4)
Senior physician	50 (54)
Head of department	33 (36)
Cases of GA + EA per month, n (%)[a]	
<5	12 (13)
5–10	22 (24)
11–15	27 (30)
>15	30 (33)

Abbreviations: EA, epidural analgesia; GA, General anesthesia; IQR, interquartile range.

[a]In how many cases of combination anesthesia (GA + EA) are you involved on average per month in terms of application and intraoperative performance (as an attending physician or supervising consultant, senior physician or head of department)?

while 8% routinely added systemic opioids (Figure 2A). Maintenance hypnotics were sevoflurane (48%), desflurane (31%), and propofol (21%), whereas isoflurane appeared to be obsolete (Figure 2B). The purposes of administering systemic opioids are different with 30% giving opioids exclusively for intubation, 59% only if additional anti-nociception is apparently required and of note, none administers systemic opioids in predefined intervals (Figure 2C). Among the opioids, sufentanil, fentanil, and remifentanil are preferred by 66%, 20%, and 12%, respectively (Figure 2D).

Different strategies are performed in case of suspected EA insufficiency (multiple choices allowed): systemic opioids (85%), EA escalation (52%), and systemic non-opioids such as ketamine or lidocaine (25%, Figure 2E). The majority decided on an individual basis whether advanced instrumentation for hemodynamic management is indicated (85%) considering patient- and/or surgery-related factors. Only 27% consider continuous blood-pressure monitoring (invasive: 13% vs. non-invasive: 14%) to be mandatory and only 5% place a central venous line routinely (Figure 2F).

Among the respondents, 29 (31%) gave an answer to the final open question. We selected relevant comments and allocated them to seven different categories, i.e., pros and cons for EA, alternatives to EA, epidural performance (substances, timing, mode of application), systemic opioids and co-analgesics, technical aspects, hemodynamics, proficiency/standards (Table 2).

4 | DISCUSSION

This survey assessed preferences for individual measures of combined GA and EA among German anesthetists. Consensus seems to be present for some aspects, namely patient's position for epidural puncture, main epidural substance, timing of EA initiation, and application mode of EA. However, for other measures, e.g., the use of systemic rescue opioids and hemodynamic management, there is significant heterogeneity which should be the focus of future research.

Most survey participants prefer a sitting position for epidural puncture which is in contrast to one of the very first descriptions of EA by Dogliotti who recommended a lateral decubitus position over the sitting position to avoid "collapse."[21] Recently, only sporadic investigation on the ideal position for the placement of non-obstetric (thoracic) epidurals has been undertaken. Nishi and colleagues randomized 41 patients to either the sitting or the lateral decubitus position for placement of epidural catheters. They confirmed an increased risk for vasovagal syncope in the sitting position, whereas the lateral decubitus position proved to be more technically challenging.[22] Interestingly, the patient's position seems to have little impact on the longitudinal spread of EA.[23] Therefore, the risk of vasovagal reaction must be weighed against the risk of placement failure.

Further agreement is present regarding the main epidural substance with a distinct preference for ropivacaine. Advantages of ropivacaine over bupivacaine were demonstrated for less motor block ("differential block"),[24–26] less urinary dysfunction,[27] and lower systemic toxicity.[28] Low concentrations (0.2% or 0.375%) of ropivacaine are preferred by most participants, which has been shown to reduce the incidence of motor block, compared with higher concentrations.[29,30]

Most survey participants add opioids to EA intraoperatively, which improves intra- and postoperative pain relief[31] and attenuates EA-induced hypotension by lowering the amount of local anesthetics needed.[5]

The majority initiates EA prior to incision for several reasons. Some anesthetists refer to opioid-sparing and hypnotic-reducing effects, thus decreasing MAC (only MAC awake required) whereas others consider analgesic concepts like "preemptive analgesia."[32,33] Ahlers and coworkers found reduced stress hormone levels if EA was established prior to skin incision compared with postoperative initiation,[9] but the clinical implications, especially with regard to long-term effects and persistent postoperative pain, remain unclear.

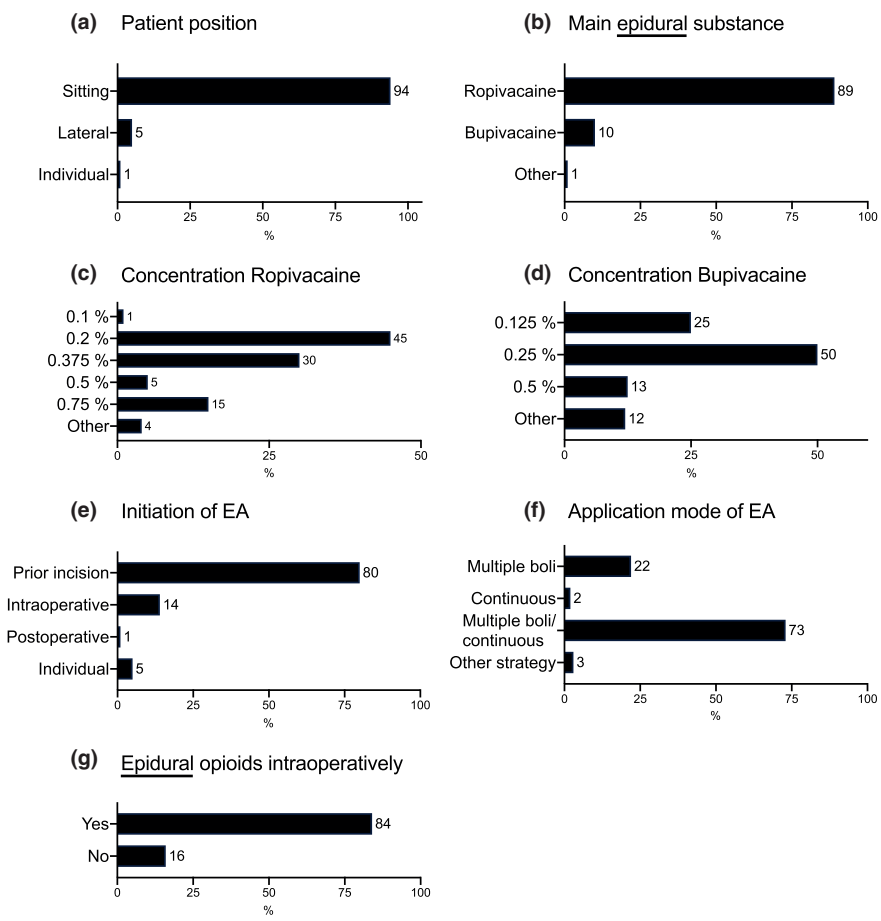

FIGURE 1 Specific management of epidural analgesia. (A) Which patient position do you prefer for epidural catheterization? (B) Which main substance for epidural application do you prefer? (C) Concentration Ropivacaine intraoperatively (rounded). (D) Concentration Bupivacaine intraoperatively (rounded). (E) When do you initiate EA (test dose excluded)? (F) Which application mode for EA do you prefer intraoperatively? (G) Do you use opioids intraoperatively for epidural administration?

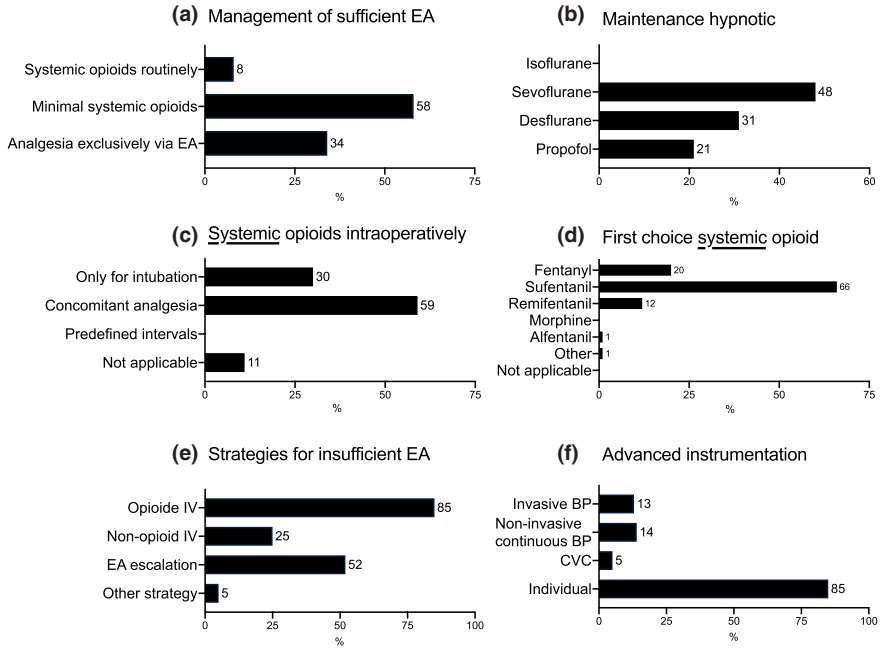

FIGURE 2 Overall management of combined general anesthesia and epidural analgesia. (A) How do you proceed in case of obviously sufficient EA within combined anesthesia? (B) Which maintenance hypnotic do you prefer? (C) In which mode do you apply opioids systemically? (D) Which opioid is your first choice for systemic application intraoperatively? (E) Primary strategy in case of suspected insufficient EA intraoperatively (multiple selection)? (F) Do you perform advanced instrumentation (multiple selection; BP: blood pressure; CVC: central venous catheter)?

Most respondents preferred a bolus-based application mode which has demonstrated to increase the longitudinal spread of substances within the epidural space compared with a continuous infusion[13,15] and thus, providing adequate anti-nociception and postoperative analgesia even in extensive surgery, e.g., median laparotomy.[34] Another advantage may be the fact that individual pharmacokinetics can be better adjusted with an on-demand application rather than giving too much and risking postoperative motor block.

TABLE 2 Final open question: Comments and frequent controversies regarding the management of combined general anesthesia and epidural analgesia

EA: pros and cons
- We observe improved 5-year-survival after colon surgery with perioperative thoracic EA.
- Visceral surgeons don't want EA intraoperatively due to excessive peristalsis.
- Intraoperative continuous EA in (extreme) reverse Trendelenburg position?
- We need basic studies that investigate the effect of perioperative EA on "natural killer cells" regarding infection defence and tumor defence. What is the role of lowered adrenaline and noradrenaline levels on the immune system; does it strengthen or weaken the immune system?
Alternatives to EA
- If EA is contraindicated/not accepted/insufficient lidocaine IV for 24 h off-label (with informed consent)
Epidural performance (substances, timing, modus)
- EA initiation prior to incision *vs.* postoperatively
- Initial bolus with the risk of hypotension and treatment with noradrenaline administration justified?
- The rational for bolus administration (vs. continuous) is the need to cover as many segments as possible, which is especially important for large median laparotomies in order to reach caudal segments.
- Time interval between boluses? 3–4 h? Or bolus + continuous infusion? Or only boluses?
- Analgesia exclusively via EA is appropriate
- Intraoperative EA only concomitantly to opioids. Initiation at the end of surgery for postoperative analgesia
- Which type of sufentanil is suitable for epidural application?
- Test dose – is it really necessary? How often does an unrecognized intrathecal position occur?
Systemic opioids and co-analgesics
- Unnecessary use of systemic opioids despite well-acting EA
- Analgesia preferably via EA, otherwise one misses a big advantage of EA (opioid-sparing, ERAS) and one is not informed whether the EA works well
- IV Opioids only as continuous remifentanil administration, also as delirium prophylaxis according to ESA guideline
- Systemic sufentanil (50–70 µg) for endotracheal tube tolerance with sufficient EA in my view completely obsolete
- Analgesia with piritramide and non-opioid at the end of surgery, even if thoracic epidural catheter in situ
Technical aspects
- occasionally EA insertion at the wrong level and therefore insufficient effect
- EA should always be located at a mid-thoracic level vs. EA at which level?
- subcutaneous tunneling for fixation?
Hemodynamics
- Management of arterial hypotension with vasoconstrictors; no reduction of EA if possible
- Discussion with surgeons: increased bleeding with intraoperative EA?
- Routine norepinephrine to stabilize blood pressure and balance sympatholysis
- Fluid management and vasoconstrictors intra- and postoperatively (within ERAS concept)
Proficiency/Standards
- Additional qualification for anesthesiologists is important, e.g., "Additional qualification in anesthesia in extended visceral surgery". The aim should be to train optimized perioperative neuraxial regional anesthesia and to standardize procedures.
- It is important to have a standardized procedure in accordance with a clinic's internal SOP, to which everyone adheres and which allows comparability.
- Pre-EA antibiotics in case of anticipated antibiotic prophylaxis

Final open question: From your point of view, please add important aspects and/or describe your rationale for specific questions. Frequent controversies or discrepancies between your personal preference and the given standard at your department would also be of interest. Quotes are translated from German.

Remarkably, in many trials the potential of an opioid-sparing regimen has been neglected, which is reflected by the heterogenous answers to our questions. In their meta-analysis, Poepping and coworkers report that only 38% of the included trials excluded patients who required systemic opioids despite EA in situ, whereas 25% of included trials allowed patients with EA to receive systemic opioids and 38% of the trials did not report on additional systemic opioids at all.[5] Unfortunately, sensitivity analyses for concomitant systemic opioids have not been performed and certainly, lumping of these trials likely results in high heterogeneity. However, the postulated EA benefits (e.g., lower incidences of respiratory dysfunction, postoperative nausea and vomiting, and paralytic ileus, early mobilization) strengthen the need to analyze concomitant systemic opioids and co-analgesics in patients with combined GA and EA.

Most participants decide individually whether invasive hemodynamic monitoring and advanced instrumentation is necessary. About one third considers continuous blood pressure monitoring (invasive or non-invasive) to be mandatory and only 5% place a central venous line routinely. Interestingly, the overwhelming majority decides for or against advanced instrumentation on a case-by-case basis. These findings are highly relevant as sympatholysis with subsequent hemodynamic deterioration frequently occurs with EA and can be anticipated.[35] Additionally, since combined GA and EA is recommended particularly for major surgery, advanced hemodynamic monitoring and instrumentation is usually indicated anyway. Taking into consideration, that an individual decision for/against advanced hemodynamic instrumentation is made in most cases, it is obvious that recent studies comparing EA versus systemic analgesia have drawn inconsistent conclusions on cardiovascular endpoints.[7,35]

Rescue strategies for suspected intraoperative insufficient EA are quite different with the majority preferring opioids intravenously followed by EA escalation in terms of further bolus administration and/or increasing continuous application. Intravenous administration of non-opioids such as ketamine or lidocaine is only used by a minority presumably due to the insufficient evidence or the perception that the cumulative dose of local anesthetics may increase the risk for adverse effects.[36] It was beyond the scope of this survey to ask for a ranking of these measures, but it is obvious that administration of systemic opioids impedes subsequent assessment

of EA. However, in case of EA insufficiency differentiation between insufficient analgesia and complete failure, e.g., due to catheter misplacement, is of utmost importance for further action. Therefore, well-defined rescue strategies for insufficient EA are urgently needed to improve pain management, better transparency, and comparability. The free text answers additionally reflect the controversies in several issues.

This survey has several limitations. First of all, the response rate was quite low certainly bearing risk of non-response bias. The participants are exclusively from German-speaking countries who handle numbers of combined GA and EA above-average[20] and who are dedicated to regional anesthesia as members of the scientific working group for regional anesthesia within the DGAI. Information about the number of represented hospitals cannot be given, since participation was anonymous. Therefore, this survey is not definite and likely not representative of all anesthetists performing the regimen. Additionally, there are further modifiable aspects of combined GA and EA, e.g., epidural puncture technique with/without technology assistance, insertion level, catheter tunneling, catheter fixation technique, hemodynamic management, postoperative management etc. which have not been addressed.

In conclusion, the present survey underlines the complexity of combined GA and EA, and the optimal intraoperative management is obviously controversial. To address relevant clinical endpoints such as perioperative morbidity and mortality, development of consensus guidelines would provide a solid basis for improved comparability among clinical trials and meta-analyses. However, this would require rational determination of specific measures within combined GA and EA. Since clinical trials recurrently conclude to be underpowered, some questions might only be clarified by further database analyses, which have proven to be a powerful tool.[37,38]

CONFLICT OF INTEREST

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AUTHORS' CONTRIBUTIONS

Conceptualization: TS, SW, TSt, PK. Data analysis and interpretation: TS, SW, TSt, MS, PM, PK. Drafting the manuscript: TS, SW, MS, PM, PK. Critical review and final approval of the manuscript: TS, SW, TSt, MS, PK, PM.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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