Update S3-guideline: “sedation for gastrointestinal endoscopy” 2014 (AWMF-register-no. 021/014)

Update S3-Leitlinie „Sedierung in der gastrointestinalen Endoskopie“ 2014 (AWMF-Register-Nr. 021/014)

This updated guideline (as in the original version in 2008) is published by the Endoscopy Section of the German Society for Gastroenterology, Digestive and Metabolic Diseases (Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankungen, DGVS), which also has ultimate responsibility for them. Co-publishers are the professional associations and organizations that participated in the preparation of this guideline:

▶ German Association of Gastroenterologists in Private Practice (Berufsverband Niedergelassener Gastroenterologen Deuschlands e. V., bng)
▶ Surgical Task Force for Endoscopy and Sonography of the German Society for General and Visceral Surgery (Chirurgische Arbeitsgemeinschaft für Endoskopie und Sonographie der Deutschen Gesellschaft für Allgemein- und Visceralchirurgie; DGAV)
▶ German Crohn’s Disease/Ulcerative Colitis Association (Deutsche Morbus Crohn / Colitis ulcerosa Vereinigung e. V.; DCCV)
▶ German Society for Endoscopy Assisting Personnel (Deutsche Gesellschaft für Endoskopie-fachberufe; DEGEA)
▶ German Society for Anesthesiology and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e.V.; DGAI)
▶ Society for Legislation and Politics in Health Care (Gesellschaft für Recht und Politik im Gesundheitswesen; GPRG)

Coordination and guidance: T. Wehrmann, A. Riphaus, I. Kopp

* Shared primary authorship.
Introduction

**Background**

In the past decade, interest in sedation for gastrointestinal endoscopy has increased worldwide. It is still the subject of much debate, some of it very lively.

One major issue is the exact indication for sedation. Sedation is not necessary for all gastroenterological endoscopic interventions. Whether it is required, depends on the nature of examination, its duration, its complexity, its invasiveness, and on the individual patient's characteristics. However, sedation can make the examination more comfortable for both the patient and the examining physician. Often it is sedation that makes a successful and low-risk examination possible. This is especially true for complex therapeutic interventions.

In the mid 1990s, sedation was much less often employed for endoscopic examinations in Germany and Switzerland than in the United States (USA) and the United Kingdom (UK); in the USA and the UK patient sedation was performed in up to 88% of endoscopic examinations [1, 2], whereas in Germany and Switzerland this figure was about 9% [3, 4]. However, a recent “nationwide evaluation of sedation in gastrointestinal endoscopy in Germany” has shown a pronounced increase in the frequency of sedation for endoscopic interventions, reaching up to 88% of cases in 2007 [5]. A re-evaluation of this survey was performed after the first German S3-guideline “Sedation for Gastrointestinal Endoscopy” [6] had been published. This follow-up survey showed a continued increase in the frequency of sedation to 90% [7]. This is most likely due to an increase in interventional procedures and patient preferences, e.g., during colon cancer screening. Apart from the long-familiar and most common form of sedation using sedatives such as benzodiazepines – sometimes in combination with opioids – the short-acting hypnotic propofol, with its plasma half-time of 8 – 9 minutes, is increasingly coming into use. The advantage of propofol is that the recovery time is significantly shorter while patient tolerance is equal [8, 9]. In addition, psychomotoric capabilities recover more quickly, as shown by using a driving simulator [10]. However, now and again different sedation depths may be crossed with a single dose of this drug, which can cause sedation to be deeper than intended. Furthermore, in contrast to midazolam, no antagonist exists for propofol.

The performance of propofol sedation by medical assistant personnel was already discussed as a possible option during the development of the German S3-guideline “Sedation for Gastroin...
In 2008, after initial studies of non-physician assisted propofol sedation (NAPS) had been performed in more than 200,000 patients, without the need of endotracheal intubation [11 – 17]. However, these were mostly healthy patients undergoing diagnostic examinations, and the propofol dosages used were on the low side. Thus, uncritical acceptance of this concept is not recommended. On the contrary, in Germany conditions that would make this procedure safe for patients had yet to be defined (e.g. appropriate training in sedation and emergency management).

A training curriculum was therefore developed by the German Society for Endoscopy Assisting Personnel (DEGEA) [18], which was also endorsed by the European Gastroenterological Societies [19]. Its publication in 2013 established the basis for a standardized and certified training strategy, which has been applied to more than 7000 endoscopic nurse assistants in Germany to date. In the meantime, the largest data collection of so called NAAP (non-anaesthesiologist administered propofol sedation) established this practice as being safe, although not completely free of risk [20].

The S3 guideline “Sedation for Gastrointestinal Endoscopy” from 2008 therefore intended to clearly define and summarize individual requirements (personal requirements) and general staffing requirements (personnel-requirements), as well as technical requirements, which are needed for sedation in gastrointestinal endoscopy and for the management of any sedation-related complications. The most recent literature and applicable legal aspects were included in these recommendations and endorsed by several medical associations (including gastroenterologists, surgeons and anesthesiologists), as well as patient “self-help”-organizations and law associations.

**Organizational procedure and fundamental methodology of the consensus process (short version of the guideline report)**

The following starting points were used as a basis for this update of the guideline.

1. Status analysis for the update of the S3-guideline.
2. Systematic literature search for the time frame 2008 – 2012
3. Determination of demands for an updated consensus within the guideline committee

For a detailed description we refer to the methodological report. The update of the S3 guideline “Sedation for Gastrointestinal Endoscopy” was registered at the AWMF in 2014 (AWMF register no.021 – 014). The development process is continuously based on the German instrument for the methodological appraisal of guidelines (Deutsches Instrument zur methodischen Leitlinien-Bewertung – DELBI) [21]:

- Systematic consideration of high-quality international guidelines on the subject of sedation for gastrointestinal endoscopy (systematic literature search, selection according to methodological quality).
- Systematic search, selection and rating of the literature by prioritized questions
- Classification of the studies and formulation of recommendations by criteria of evidence-based medicine.
- Structured interdisciplinary consensus process with involvement of representatives of all addressees.
- Outcome-analysis: Presentation of expected results, pros and cons of varying regimen for sedation and ways of application and monitoring.
- Formulation of quality goals for procedural management.

**Rationale and goals of the guideline**

The main rationale for the preparation of the guideline is the unchanged, increasing role of sedation in gastrointestinal endoscopy. In 2008, the first S3-guideline “Sedation for Gastrointestinal Endoscopy” was published by the DGVS in collaboration with the DGGV. This guideline intended to establish comprehensive, standardized, high-quality patient care based on the current evidence [6]. In order to keep these recommendations in line with the latest scientific developments this guideline is updated in close cooperation with the AWMF.

In addition to optimal patient preparation, which includes not only adequate information about the sedation, but also risk stratification of the individual patient, an overview will be given of the currently most commonly used sedatives and analgesics (with particular emphasis on increasingly used short-acting agents). Furthermore, their mechanism of action and side-effect profile will be reviewed.

Drug therapies with different substances will be compared in terms of their procedural efficacy and effectiveness and their risk profiles (particularly in relation to individual risk groups). In addition, patient preferences, quality management of sedation (appropriate monitoring conditions) and emergency management will be outlined.

The goals of the S3 guideline “Sedation for Gastrointestinal Endoscopy” remain defined as follows:

- To take account of recent advances in evidence-based medicine and recognized sedation and monitoring procedures in the implementation of the guideline.
- To compare drug therapies with various substances with respect to their efficacy and effectiveness and to their risk profiles (especially in relation to individual risk groups).
- To describe patient preferences, and to establish quality management of sedation with appropriate monitoring and incident management.
- To support physicians and patients in medical decision making with evidence-based and formal consensus recommendations.
- To support patient involvement in therapy decisions, taking their individual needs into account.
- To comprehensively implement multidisciplinary, quality-assured, and sector-spanning care of patients who need sedation during endoscopy.
- To support the documentation of complications arising during sedation.
- To systematically consider recommendations in training, further education, and continuing education, and in quality management systems.
- To establish basic contents for targeted training, further education and continuing education for physicians and healthcare staff.
- To systematically consider the recommendations and hence the quality indicators derived from them in external, comparative quality assurance and standardization of documentation standards.
- To comprehensively implement quality-assured patient care during sedation for gastrointestinal endoscopy.
- To optimize patient safety (this amendment is made to existing recommendations for sedation in gastrointestinal endoscopy by non-anesthesiologists, which were included in the 2008 guideline [6], and other guideline sources mentioned below, or projects and measures mentioned above, in order, to assure patient safety in the long-term).
Composition of the guideline committee

An overview of the guideline committee is given in Table 1. On August 27th, 2012, an initial meeting occurred in Bochum, Germany, between the guideline coordinators, PD Dr. Riphaus and Prof. Dr. Wehrmann, who were designated by the DGVS. The following points were established:

To downsize the guideline committee for the updated S3-guideline „Sedation for Gastrointestinal Endoscopy“, as compared to the committee in 2008 [6], without compromising the proportion of each participating medical association.

All medical associations, which were involved in the original guideline, were to participate again. As in the previous guideline, this update omits non-adult, pediatric patients. This topic was again discussed during the initial meeting. Therefore, the following medical associations were asked to pose delegates (the number of proposed delegates in brackets):

- The German Society for Gastroenterology, Digestive and Metabolic Diseases (Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankungen, DGVS), (n = 10; including the two guideline coordinators);
- the German Society for Anesthesia and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesie und Intensivmedizin, DGAI), (n = 2);
- the German Association of Gastroenterologists in Private Practice (Bundesverband Niedergelassener Gastroenterologen Deuschlands, bng), (n = 1);
- the Surgical Work Group for Endoscopy and Sonography of the German Society for General and Visceral Surgery (Chirurgische Arbeitsgemeinschaft für Endoskopie und Sonografie der Deutschen Gesellschaft für Allgemein- und Visceralchirurgie, CAES), (n = 1);
- the Society for Legislation and Politics in Health Care (Gesellschaft für Recht und Politik im Gesundheitswesen, GPRG), (n = 1);
- the German Society for Endoscopy Assisting Personnel (Deutsche Gesellschaft für Endoskopie-Assistenzpersonal, DEGEA), (n = 1);
- the German Crohn’s Disease/Ulcerative Colitis Association (Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung, DCCV), (n = 1).

This guideline is published by the Endoscopy Section of the German Society for Gastroenterology, Digestive and Metabolic Diseases (Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankungen, DGVS), which also has ultimate responsibility for them. Co-publishers are the professional associations and organizations that participated in the preparation of this guideline. The composition and tasks of the guideline steering committee were defined as follows by the coordinators of the professional associations with overall responsibility:

Guideline coordination: PD Dr. Andrea Riphaus, Laatzen
Project management: PD Dr. Andrea Riphaus, Laatzen
Dr. Prof. Till Wehrmann, Wiesbaden
Dr. Prof. Till Wehrmann, Wiesbaden
Dr. Johannes Hausmann, Frankfurt
Birgit Weber, Hannover

Methodological support: Prof. Dr. Ina Kopp, AWMF, Marburg

The tasks of the steering committee included contacting and giving feedback to the professional associations and organizations involved, implementing methodological specifications for stage 3 guidelines using a project plan, administering the financial resources, supporting the work on content by the experts, consolidating and editing the text drafted by the experts of the working groups, and preparing the guideline methodological report.

Dr. jur. H. Bitter (Munich) was invited to support the guideline steering committee with regards to legal aspects.

The guideline group was convened by the coordinators. All professional associations, task forces, and organizations directly relating to the subject of the S3-guideline were contacted. They were asked to appoint experts as members who would represent them in the voting process (consensus process) and who would work on contents in the groups on specific topics.

All experts were chosen and invited according to their expertise and professional qualifications. The goal was to guarantee a multidisciplinarity and multiprofessionality within the guideline group that was appropriate for the guideline with respect to its content and application. Representatives of the co-publishing associations, organisations and working groups were given a written mandate by their respective boards. A representative of “self-help”-organizations was from the beginning actively integrated in the guideline preparation process in order to give a stronger profile to the patients’ perspective. The members of the guideline steering committee, the experts of the participating professional associations and organizations and the experts for legal questions constitute the members of the working groups and are authors of the guidelines (guideline group). In the consensus procedure all experts of the participating professional associations and organizations were entitled to vote (Table 1).

To establish a work-content on specific topics, 5 working groups were appointed during the consensus process. These working

Table 1 Guideline group: Participating professional associations and organizations.

<table>
<thead>
<tr>
<th>professional society/task force</th>
<th>authors entitled to vote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopy Section on behalf of the German Society for Gastroenterology, Digestive and Metabolic Diseases (Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten, DGVS)</td>
<td>Prof. Dr. Joachim Arnold Dr. Angelika Behrens PD Dr. Stefan von Delius Prof. Dr. Dirk Domagk Prof. Dr. Michael Jung Prof. Dr. Alexander Meining PD Dr. Andrea Riphaus Prof. Dr. Dieter Schilling Prof. Dr. Hans Seifert Prof. Dr. Till Wehrmann</td>
</tr>
<tr>
<td>German Society for Anesthesiology and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesie und Intensivmedizin, DGAI)</td>
<td>Prof. Dr. Peter Tonner Prof. Dr. Frank Wapppler</td>
</tr>
<tr>
<td>German Association of Gastroenterologists in Private Practice (Berufsverband Niedergelassener Gastroenterologen, bng)</td>
<td>Prof. Dr. Birgit Kallinowski</td>
</tr>
<tr>
<td>Surgical Task Force for Endoscopy and Sonography of the German Society for General and Visceral Surgery (Chirurgische Arbeitsgemeinschaft für Endoskopie und Sonografie, CAES, der Deutschen Gesellschaft für Allgemein- und Visceralchirurgie, DGAV)</td>
<td>Dr. Anja Schäible</td>
</tr>
<tr>
<td>Society for Legislation and Politics in Health Care (Gesellschaft für Recht und Politik im Gesundheitswesen, GPRG)</td>
<td>Dr. Horst Bitter</td>
</tr>
<tr>
<td>German Society for Endoscopy Assisting Personnel (Deutsche Gesellschaft für Endoskopie-Assistenzpersonal, DEGEA)</td>
<td>Ulrike Beilenhoff</td>
</tr>
<tr>
<td>German Crohn’s Disease/Ulcerative Colitis Association (Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung, DCCV)</td>
<td>Dr. Susanne In der Smitten</td>
</tr>
</tbody>
</table>
Systematic search for evidence

The methodological concept of updating the S3-guideline is outlined in detail in the methodological report. The starting point was a review of current recommendations of the European and American professional associations of gastroenterology and endoscopy, as well as the respective recommendations of the anesthesiological associations and the underlying evidence and citations by the working group leaders. In addition, a systematic literature search was initially performed by the commissioner of the guideline committee (Birgit Weber) and the final evaluation of the cited literature was performed by Dr. med. Johannes Hausmann. These sources were the basis for the updated key points of the guideline. To assure a balanced and goal-oriented update of the guideline, which also considers diverging opinions, a two-step formal consensus process was chosen. For the implementation of the formal consensus process, techniques of the nominal group process (NGP), formal consensus conferences and the Delphi technique were used. The voting process was led by a neutral moderator (Prof. Kopp) with expertise in these consensus techniques. The voting process was documented with all content contributions, results of the voting process and assessment of the grade of evidence (Table 3), including areas in which no consent could be reached. In these cases the reasons (e.g. minority vote) were also documented. The literature search was carried out in a decentralized manner within the working groups with the support of the guideline coordination office. Search strategies for the preparation of the guideline were defined as follows:

- Databases: Pubmed, Cochrane Library
- Search terms:
  - General: “sedation OR conscious sedation” and “endoscopy OR gastrointestinal endoscopy”
  - Working-group-specific (Appendix III)
- Time period: 2007 – 2012

In this way, 4823 publications were identified. After a preview of the abstracts by the heads of the working groups, exclusion of non-English or non-German manuscripts or those with an irrelevant content, 184 sources were chosen for evaluation. In addition, a manual search was done and relevant publications were added by members of the working groups. All sources were entered into a literature database by the guideline coordination office. Publications, which were relevant for more than one topic, were separately evaluated with respect to each topic; some of these therefore have more than one entry in the evidence tables (see methodological report).

International guidelines are the most important sources for guideline development. Therefore, a targeted guideline search was performed in addition to the literature search mentioned above. This was done by the following strategy:
- Database: Pubmed and Guidelines International Network (GIN); www.g-i-n.net
- Search term: Sedation AND Gastrointestinal Endoscopy
- Time period: 2007 – 2012

In this way, 12 publications were identified [6, 22 – 31]. These were used as source guidelines for all working groups. Publications that were not available in English or German language were excluded, as well as withdrawn or unpublished manuscripts and duplicate publications. Finally, the results of this search were matched with those of the literature search to avoid duplication.

For some guidelines a detailed methodological report was not available. Similarly, not all source guidelines complied with the requirements of the evidence base and consensus process, according to DELBI. For these reasons, the source guidelines were indeed used for conceptional comparison, but the guideline group deemed it necessary to perform a systematic literature review for all key questions.

The evidence classification of the present guideline is based on the evidence categories of the Oxford Centre for Evidence Based Medicine [32]. The recommendations were graded according the cur-
rent methodological report of the Program for National Health Care Guidelines. The strength of the evidence is a marker for the methodological validity of the underlying study for each statement/recommendation. The assignment of the evidence grade considers the study design and the quality of its implementation and analysis. The strength of a recommendation was based on considered judgement. The assignment of an evidence grade included explicitly and implicitly valued elements and was done in the context of the final, structured consensus process. It considers the underlying evidence, as well as ethical obligations and the clinical relevance of measures of effectiveness. In addition, it takes the applicability to target patients and the German health care system into account, as well as patient preferences and the implementation into daily practice in varying clinical situations and patient care settings. The terms used in the guideline and the tables, showing the derivation of evidence level and recommendation grade, are summarized and simplified in Table 4.

Whenever possible, the recommendations were formulated in analogy to their grading:

Strong recommendation (grade A): “we recommend” (German: “soll”); recommendation (grade B): “we suggest” (German: “sollte”), recommendation open (grade 0): “may be considered”. Negative recommendations were termed as “don’t” or “not” with the same phrases. Even otherwise “unchanged” recommendations from the previous version of this guideline from 2008 were modified accordingly.

The current update concerns topics I, II, III, IV und V.

In addition to the literature search by Dr. Anja Schaible mentioned above, PD Dr. Andrea Riphaus (Speaker of the gender research task force of the DGVS) subsequently added the search term „gender“ to account for possible, relevant, gender-specific differences in sedation practice. This was done to account for the increasing role of gender-sensitive medical aspects in the establishment of guidelines. Because this search lacked sufficient evidence, no recommendation can be currently given to account for gender-specific differences between men and women in the area of sedation for gastrointestinal endoscopy (see the separately published methodological report for details). For this reason, this guideline uses gender-sensible medical aspects in the establishment of guidelines.

### Measures for quality assurance

To support the content work in the topic-specific working groups and for quality assurance of the working process, the steering committee used the following measures:

- Provision of working materials including all full text articles found in the literature search (reference guidelines, systematic reviews, primary literature)
- Algorithms for literature processing within the working groups
- Strategies for editing and formulating recommendations (structured consensus process or systematic selection and evaluation of the evidence)

### Period of validity and update procedure

The update of the S3-guideline “Sedation for Gastrointestinal Endoscopy” was finalized in April of 2015 and formally implemented and published by the publishing and participating professional associations/organizations in July of 2015. The guideline is valid until December 2020 at the latest. A complete revision and new edition is planned at this time. The guideline groups will watch for new findings that may make the revision of individual sections or recommendations necessary, and the coordinator would be glad to receive relevant information in this regard from users of the guideline. The aim is to produce continual updates as necessary. The date of the publication, the date of the next planned revision, and notification of planned and/or interim revised versions will be displayed in the publicly accessible directory of the AWMF (http://www.awmf-leitlinien.de). The valid version with always be the most recent one according to the AWMF register.

### Funding of the guideline and statement of possible conflict of interest

The preparation of the updated S3-guideline was funded by the German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS). These funds were used for personnel costs (guideline office), costs for strategy meetings and consensus processes (traveling expenses for all participants, rent for meeting

---

<table>
<thead>
<tr>
<th>evidence grade</th>
<th>simplified definition of source</th>
<th>recommendation grade</th>
<th>description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>randomized controlled studies</td>
<td>validation cohort</td>
<td>A</td>
</tr>
<tr>
<td>II</td>
<td>controlled studies without randomization</td>
<td>explorative cohort studies</td>
<td>B</td>
</tr>
<tr>
<td>III – V</td>
<td>observational studies, expert opinion</td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 4 Simplified scheme of derivation of evidence level and recommendation grade.

- Literature evaluation forms and sample tables for evidence
- Scheme for grading of the evidence and recommendations
- Formal, structured correspondence (feedback, reminders)
- Establishment of a (written) protocol for all work sessions and votings.
- Up front determination of process sequences.
- Plans for methods, timeframe and financing.
- Selection and evaluation of sources
- Consensus process and votings
- Transparency of the development process and responsibilities (methodologic report).
- Consultation process for publications
- Delphi process within the guideline group for the complete version, short version and methodological report.
- External review of the short version (publication in peer reviewed medical journals, e.g. German Journal of Gastroenterology/„Zeitschrift für Gastroenterologie“).
- Written consent of the involved organisations and authors for publication, formal implementation by the involved organisations (see Table 1).
- Archiving of the documents for 10 years (until 2025)
- All statements (keypoints and recommendations), regarding the strength of the evidence and recommendations, the primary source-basis of the working groups and the strength of the consensus are declared within the final version of the guideline and the short version.
1. Topic I: Indications/goals/known risks/patients/quality goals

1.1 Recommendation on sedation choice

<table>
<thead>
<tr>
<th>Recommendation 1.1.a</th>
<th>Recommendation on sedation choice</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that sedation should be offered to every patient before endoscopy. The advantages and disadvantages should be discussed in detail.</td>
<td></td>
</tr>
</tbody>
</table>

Evidence level: 5 Consensus (15/16, one abstension)

Comments
Every patient has the right to an endoscopic examination that is as painless and stress-free as possible. It therefore appears ethically unjustifiable to withhold sedation from patients on principle [33]. Endoscopic examinations can be unpleasant, which makes sedation desirable or advisable. Especially during long, difficult endoscopic interventions (e.g., ERCP, difficult resection- or drainage-procedures) it is important to avoid involuntary patient movement. Thus, sedation should on principle be offered to every patient. After the patient has been given adequate information about the facts of sedation, his or her wishes should be taken into account as much as possible.

1.2 Recommendation on indications for sedation

<table>
<thead>
<tr>
<th>Recommendation 1.2</th>
<th>Recommendation on indications for sedation</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
</table>
| Recommendation grade: A | We recommend that the following aspects should be considered when deciding for or against sedation and/or analgesia:  
  - Patient characteristics (risk profile, any co-morbidities, preferences)  
  - Nature of endoscopic intervention (indication, duration, invasiveness)  
  - Structural requirements |                |

Evidence level: 5 Strong consensus (16/16)

1.3 Recommendation on examination quality

<table>
<thead>
<tr>
<th>Recommendation 1.3a</th>
<th>Recommendation for examination quality</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement</td>
<td>No statement can be made on how performance or nonperformance of endoscopic sedation affects the rate of complications related to endoscopic interventions.</td>
<td></td>
</tr>
</tbody>
</table>

Evidence level: 5 Strong consensus (16/16)

<table>
<thead>
<tr>
<th>Recommendation 1.3b</th>
<th>Recommendation for examination quality</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement</td>
<td>Sedation may be considered for gastroscopy and colonoscopy with the goal of increasing the diagnostic yield of the examination.</td>
<td></td>
</tr>
</tbody>
</table>

Evidence level: 2b No consensus (8/16 = 50 %)

Comments
In a large Italian cohort study, which included more than 12,000 patients, it was shown that the diagnostic yield of an examination can be increased with the use of sedation. Polyp detection rates were higher in unsedated patients. In addition, the cecum was reached more frequently (complete exam) [38]. The latter was also demonstrated in another large cohort study. Here, sedation almost doubled the probability of a complete examination [39]. Undoubtedly, sedation is not necessary for all endoscopic, gastroenterological procedures. Ultimately, it depends on the nature of the examination, its duration, complexity, and invasiveness, as well as patient preferences. Sedation contributes greatly to the comfort of the examination for both, the patient and physician. In some cases, especially during complex therapeutic interventions, it may be what allows the intervention to be performed successfully and with low risk. Experiences with previous endoscopic examinations, anxiety, and the patient’s understanding of the procedure all need to be taken into account. In addition, there are often marked cultural variations around the world with regard to sedation for gastrointestinal endoscopy.

For example, in the United States and the United Kingdom, up to 88% of endoscopic examinations are done under sedation [1, 2]. In contrast, sedation was used much less frequently (9% of cases in the 1990s) in Germany and Switzerland [3, 4], although the frequency was higher with complex procedures. However, recent survey results show a pronounced increase in the frequency of sedation for endoscopic interventions in Germany to up to 90% [5, 7]. This is probably due to the increase in interventional...
procedures and to patient preferences (e.g. during colorectal cancer screening). However, studies that compare the safety of diagnostic and therapeutic endoscopy with to those without sedation are almost nonexistent. An American study failed to reach the intended goal of comparison because of lack of patient acceptance (high preference for sedation) [34]. The results of a German study showed that colonoscopy can be done without sedation in more than 90% of cases with a low risk of complications [35]. However, in general the majority of patients prefer sedation [35, 40, 41]. Sedation does not seem to have a major influence on the risk of the endoscopic procedure itself. A prospective study by Dillon et al. [42] of colonoscopy in 136 children under general anesthesia showed that the perforation rate was no higher than for adults under sedation. The claim that fewer perforations occur during colonoscopy if pain perception is maintained has therefore not been confirmed.

1.4 Recommendation on risk assessment

1.4.1. General considerations

Sedating and analgesic drugs can induce overlapping, not always clearly distinguishable sedation states, ranging from minimal sedation (anxiolysis) to general anesthesia. Physicians who are not anesthesiologists are not allowed to perform sedation and/or analgesia procedures that would reach a planned degree of sedation that affects or eliminates life-preserving reflexes. Planned general anesthesia (with loss of consciousness/protective reflexes) should be left to anesthesiologists. If, in the occasional case, it happens that a degree of sedation is reached that affects or eliminates life-preserving reflexes (general anesthesia), and if the intervention is to be continued, anesthesiologist should be called in.

Despite the continuum of sedation/analgesia, with transitions that cannot always be reliably controlled, various levels can nevertheless be differentiated. The degree (depth) of sedation can be assessed and classified using a validated scale. In Germany, the modified Richmond Agitation-Sedation Score Scale (RASS Scale) [43] is commonly used in the anesthesiology community, whereas gastroenterologists/endscopists mostly use the classification of sedation stages issued by the American Society of Anesthesiologists [44]

<table>
<thead>
<tr>
<th>grade</th>
<th>term</th>
<th>description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>alert and calm</td>
<td>not completely alert, but at least awake phases (eyes open, eye contact) lasting at least 10 s when patient is addressed</td>
</tr>
<tr>
<td>−1</td>
<td>sleepy</td>
<td>mild sedation (awake phase (eyes open, eye contact) lasting less than 10 s when patient is addressed</td>
</tr>
<tr>
<td>−2</td>
<td>mild sedation</td>
<td>moderate sedation (movement or eye opening when patient is addressed (but no eye contact)</td>
</tr>
<tr>
<td>−3</td>
<td>moderate sedation</td>
<td>deep sedation (no reaction when patient is addressed, but movement or eye opening when physically stimulated (shaking shoulder or rubbing sternum)</td>
</tr>
<tr>
<td>−4</td>
<td>deep sedation</td>
<td>no reaction when patient is addressed</td>
</tr>
<tr>
<td>−5</td>
<td>no reaction</td>
<td>no reaction when patient is addressed or physically stimulated</td>
</tr>
</tbody>
</table>

Table 5 Modified Richmond Agitation-Sedation Score [43].

<table>
<thead>
<tr>
<th>Recommendation 1.4</th>
<th>Recommendation on risk assessment</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that the type and intensity of the sedation and the drug used should be selected according to the type of intervention and the patient’s ASA grade and individual risk profile. There are particular requirements in respect of facilities, equipment, and qualified personnel. Unless the requirements defined under “structure quality” are met, once the risk-benefit balance and the patient’s wishes have all been weighed, sedation should either be avoided or, if sedation is indicated and/or the patient wants sedation, the patient should be transferred to a facility that does fulfill these requirements.</td>
<td></td>
</tr>
</tbody>
</table>

Evidence level: 5 Strong consensus (16/16)

Comments

The American Society of Anesthesiologists and the American Society of Gastroenterologists [44, 45] recommend carrying out a risk assessment of any cardiovascular and respiratory problems that could occur during endoscopy before the examination begins. This includes a detailed history including questions about the following:

- Reaction to being addressed
- Spontaneous breathing
- Presence of a patent airway
- Patient’s risk assessment
- ASA grade and individual risk profile
- Structure quality

Recommendation 1.4

Recommendation on risk assessment

2008 (unchanged)

Table 6 Stages of sedation. Modified from the American Society of Anesthesiologists [44].

<table>
<thead>
<tr>
<th>minimal (anxiolysis)</th>
<th>moderate</th>
<th>deep</th>
<th>anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>reaction to being addressed</td>
<td>patient reacts appropriately to verbal commands</td>
<td>somnolence, reaction to louder commands with additional tactile stimulation if necessary</td>
<td>somnolence, hard to wake, purposeful response after repeated or painful stimulation</td>
</tr>
<tr>
<td>spontaneous breathing</td>
<td>not influenced</td>
<td>adequate</td>
<td>The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway. Spontaneous ventilation may be inadequate.</td>
</tr>
</tbody>
</table>

Riphaus A et al. Update S3-guideline: “sedation... Z Gastroenterol 2016; 54: 58–95
existing guidelines give recommendations on the assessment of increased risk of airways obstruction [44, 47, 56] in patients with previous problems related to anesthesia or sedation. These are:

1. Patients with stridor, snoring, sleep apnea
2. Patients with malformation of the facial bones, e.g., Pierre-Robin syndrome or Down syndrome
3. Patients with malformation of the mouth, such as small opening (< 3 cm for adults), agenesis, projecting anterior teeth, missing or broken teeth, strongly curved palate with macro-glossia, tonsil hypertrophy, or a uvula that is not visible
4. Patients with abnormalities of the neck, such as obesity involving the neck and face, short neck, restricted neck mobility, reduced hyoid-to-chin distance (< 4 cm for adults), neck tumors, disease or trauma of the cervical spine, tracheal alterations, or advanced rheumatoid arthritis
5. Patients with jaw malformations such as micrognathia, retrognathia, the jaw typical of Down syndrome, or pronounced malocclusion
6. Due to their risk profile, the requirements for sedation are also expected to be higher for persons with alcohol abuse, drug abuse, or on chronic medication, and also for patients with a high ASA grade and/or for persons that are not able to cooperate.

1.5. Recommendation on anesthesia/ intubation

<table>
<thead>
<tr>
<th>Recommendation grade: A</th>
<th>Recommendation on anesthesia/ intubation</th>
</tr>
</thead>
</table>
| Recommendation on anesthesia/ intubation: We recommend that calling in an anesthesiologist should be considered for patients with a high risk profile. These include: high ASA grade (III–IV) and a difficult endoscopic intervention or the presence of pathological anatomical features associated with a higher risk of airway obstruction during the intervention (e.g. craniofacial malformation; lingual, laryngeal, or hypopharyngeal tumor; severely restricted mobility of the cervical spine; severely restricted mouth opening < 3 cm; Mallampati grade 3 or 4; or a restricted hyoid-to-chin distance < 4 cm).

Evidence level: 5 | Strong consensus (16/16) |
|-------------------------|------------------------------------------|

Comments

The risk profile includes pathological/anatomical features that can lead to respiratory problems and could make support by mechanical ventilation or artificial respiration difficult. In addition,
seen in the frequency of pneumonic infiltrates and overall mor-
tality between the intubated and nonintubated groups. However,
deaths due to aspiration were higher among patients who did not
undergo prophylactic intubation (2 % vs. 0 %, respectively).
Because of lack of clarity in such retrospective analyses about
how patients were allocated between the groups, and thus a pos-
sible bias (severely ill patients are more likely to undergo intuba-
tion), these studies are only of limited value.

1.7. Recommendation on patient positioning

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Recommendation on patient positioning</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td>Just as for general anesthesia during</td>
<td>surgery, it is important to ensure</td>
</tr>
</tbody>
</table>
| grade: A       | that sedated patients are positioned | correctly in order to avoid position-
|                | related damage.                     | related damage. |
| Evidence level: | Strong consensus (16/16)            |                 |

Comments
On the whole, damage due to positioning is not a major issue in
gastrointestinal endoscopy. Nevertheless, this should be avoided
as a matter of principle. Especially when under mild sedation, pa-
tients can move involuntarily; they should therefore be secured
appropriately. Damage due to positioning is most likely to occur
in patients undergoing ERCP (prone or left-lateral position) or
when they are being transferred from the examination table to
the bed. There is no direct evidence on the subject of damage
due to positioning in endoscopy; the recommendation is based
on the joint recommendation of the Professional Association of
German Anesthesiologists and the Professional Association of
German Surgeons [45]. Especially during procedures of long
duration (e.g. endoscopic submucosal dissection, retroperitoneal
intervention, peroral myotomy etc.), attention should be paid to
appropriate positioning, including changes in position to relieve
strained areas or pressure points whenever necessary, in analogy
to the approach during surgical procedures. Hypothermia or ocu-
lar dehydration should be avoided by appropriate measures.

2. Topic II: Sedatives/analgesics/adjuvant drugs

2.1. Acceptance by the patient and the endoscopist

2.1.1. Patient acceptance/satisfaction

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Patient acceptance/satisfaction</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td>Sedation increases the patient’s</td>
<td>comfort and hence his or her acceptance</td>
</tr>
<tr>
<td>grade: A</td>
<td>of the endoscopic intervention and is</td>
<td>therefore recommended. The ideal</td>
</tr>
<tr>
<td></td>
<td>therefore recommended. The ideal</td>
<td>sedation seems to be one that leaves</td>
</tr>
<tr>
<td></td>
<td>sedation seems to be one that leaves</td>
<td>no memory of unpleasant sensations</td>
</tr>
<tr>
<td></td>
<td>no memory of unpleasant sensations</td>
<td>but at the same time has a short</td>
</tr>
<tr>
<td></td>
<td>but at the same time has a short</td>
<td>duration of action.</td>
</tr>
<tr>
<td>Evidence level:</td>
<td>Strong consensus (16/16)</td>
<td></td>
</tr>
</tbody>
</table>

Comments
The performance of analgesia and sedation for endoscopy is de-
pendent on several factors. Regional differences, safety require-
ments and reimbursement play a role. More than 98 % of colonos-
copies in the United States and more than 90 % in Canada are
performed with sedation, respectively [40, 60]. Large discrepan-
cies exist in Europe. In Italy, sedation is standard practice and
87 % of colonoscopies and 74 % of esophagogastroduodenoscopies
are performed with sedation in Germany [61, 62]. However, in
the 1980’s sedation was more of an exception for standard endo-
scopic procedures (gastroscopy and colonoscopy). Even nowa-
days, less than 20 % of patients in Spain receive sedation during
colonoscopy [63].

Only 12 % of the endoscopists in the United States would agree to
have their own colonoscopy without sedation. The majority
would prefer propofol sedation [40]. Adequate analgesia and sedation can affect the quality of the pro-
cedure and patient- and endoscopist-satisfaction [64]. The pri-
mary wish of the patients is to have a completely pain-free
exam, followed by the wish to recover quickly from the sedation
[65]. A study by Abraham et al demonstrated that gastroscopies
were less often repeated and had a better patient acceptance,
when performed under sedation [66]. Other studies confirmed
that sedation can increase patient acceptance of endoscopic pro-
cedures [67 – 74]. In a large metaanalysis, patient satisfaction
was generally higher, when sedation was given [75]. Especially
during colonoscopy, patient acceptance is higher when the pro-
cedure is performed under propofol sedation [76].

However, when benzodiazepines are used during upper endosco-
py (gastroscopy), patient complaints may occur (especially re-
tching), which may not be noticed by the endoscopist. In one study
by Walmsley et al. [77] endoscopists did not notice such complaints in 12 % when they occurred. Even in the case of mod-
erate sedation with midazolam, patients can sense pain [34]
which may not necessarily be noticed by the endoscopist. How-
ever, patients frequently do not recall these complaints as a result
of the amnestic properties of midazolam.

2.1.2. Endoscopist satisfaction

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Endoscopist satisfaction</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
</table>
| Recommendation | Sedation increases the practicability and the completeness of the exami-
| 2.1.2a         | nation and thus improves examiner satisfaction (especially in interven-
|                | tional endoscopy).       |                 |
| Evidence level: | Strong consensus (16/16) |                 |

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Endoscopist satisfaction</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td>In interventional endoscopy, propofol is superior to midazolam with respect to endoscopist’s satisfaction.</td>
<td></td>
</tr>
<tr>
<td>2.1.2b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence level:</td>
<td>Strong consensus (16/16)</td>
<td></td>
</tr>
</tbody>
</table>

Comments
Sedation can lead to improved technical success and more com-
plete exams. Therefore, it can increase the satisfaction of the en-
doscopist (especially during interventions) [78]. Similarly, the
combination of benzodiazepines with opioids can improve endos-
copist satisfaction. One study of 107 patients compared midazolam
combined with placebo and midazolam combined with meperi-
dine for EGD [79]. Endoscopist satisfaction was significantly better
with the combination regimen (P < 0.001), whereas little differ-
ence was seen in patient acceptance. Sedation with benzodiazepines leads to sufficient sedation in 85 % of cases and adequate examination conditions in 71 %, respectively. However, patient satisfaction is even higher with propofol mono- or combination-therapy [75].

Especially for longer and more complex interventions, deep sedation may be needed to help ensure that examinations can be done safely without unwanted and uncontrollable involuntary movement of the patient [80]. Especially during interventional endoscopy, propofol is superior to midazolam with regards to patient satisfaction [81]. Better examination conditions may be responsible for the observed trend of an increasing use of propofol. However, increasing the depth of sedation, achieved by raising the dose of the various substances, also increases the incidence of unexpected/unwanted side effects (see dose recommendations in the product information of various manufacturers).

In a recent survey [7], propofol was more frequently given than benzodiazepines. The most common drug combination is benzodiazepines and opioids. A combination of these drugs is used in 38 % of cases. The second study [85]. In Germany, the most commonly used drugs for sedation are midazolam and opioids, which is also seen in incomplete examinations as a result of reduced patient compliance [83].

In a survey of 82 620 endoscopies, propofol sedation was used in 42 % of cases. Adverse events occurred in 0.19 %, with no reported fatalities [84]. Propofol was administered by anesthesiologist in 66 % of cases in an Italian survey [61].

In a retrospective analysis of more than 230 000 patients, sedation and analgesia was determined as a quality indicator for endoscopy, as it was directly linked with the success-rate of a complete exam [39]. These results are also supported by an Italian study [85]. In Germany, the most commonly used drugs for sedation during endoscopy are midazolam (82 %) and propofol (74 %). A combination of these drugs is used in 38 % of cases. The second most common drug combination is benzodiazepines and opioids [62]. Propofol was more frequently given than benzodiazepines in a most recent survey [7].

### 2.2. Monotherapies

#### 2.2.1. Propofol

##### 2.2.1.1. General considerations

Propofol is a sedative with minimal analgesic effect. The sedating effect of propofol is based on the binding of the drug to GABA receptors, resulting in increased binding of GABA to the receptors. The exact pharmacodynamic mechanisms of propofol are still not completely understood.

Propofol is extremely lipophilic and develops its effect within 30–45 seconds. As it is the case with most hypnotics, the duration of action is determined by the redistribution into slow and fast compartments. The duration of action depends on the duration of its application [86]. After short-term continuous application for 30–60 minutes, patients will take 5–10 minutes to awake. The quick onset of action with a short effect duration makes propofol a suitable sedative for gastrointestinal endoscopy [8–10, 78, 87–91]. The effect of propofol is individually variable depending on age [92, 93], body weight, co-morbidity, or concomitant medications. The depth of propofol sedation depends on its dose. Patients who are examined with propofol monotherapy are no more prone to pain sensation than those treated with a standard sedation regimen [76]. This is likely explained by the fact that patients cannot recall painful sensations that might have occurred during the procedure. Even a single dose can take a patient right through several levels of sedation (see Table 9) and trigger short-term apnea [94]. However, in contrast to midazolam, no antagonist exists for propofol. Therefore, all endoscopy teams that use propofol for sedation have to be able to control apnea rapidly (see Section 4 – process quality). Administration of propofol requires vast clinical expertise and attention to the patient. Propofol is administered by anesthesiologists in two-thirds of cases in Italy and 64 % of cases in Greece, respectively [61, 95].

Downsides to propofol are pain during the injection, allergic reactions and hyperlipidemia. Besides possible hypoxia from respiratory depression, hypotension and bradycardia may occur [13] (also see Table 9, section 2.2.3.1.). In isolated cases (intensive care setting) pancreatitis has been reported. As a rare occurrence, bacterial contamination of the lipid based solvent of propofol can result from improper handling, which in turn has the

### Table 9

Comparison of vital signs during sedation with propofol versus midazolam/meperidine for ERCP.

<table>
<thead>
<tr>
<th>author</th>
<th>vital parameter</th>
<th>propofol</th>
<th>Midazolam/Pethidin (meperidine)</th>
<th>differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vargo [164]</td>
<td>SpO2 &lt; 90 %</td>
<td>21/37 (57 %)</td>
<td>14/38 (37 %)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>BP &lt; 75 % of baseline value</td>
<td>7/37 (18.9 %)</td>
<td>6/38 (15.8 %)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>HR &lt; 75 % of baseline value</td>
<td>3/37 (8.1 %)</td>
<td>0/38 (0.0 %)</td>
<td>ns</td>
</tr>
<tr>
<td>Riphaus A [175]</td>
<td>SpO2 &lt; 90 %</td>
<td>7/75 (9.0 %)</td>
<td>8/75 (11 %)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>mean decrease of SpO2</td>
<td>3 % (2 %)</td>
<td>6 % (3 %)</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td></td>
<td>BP &lt; 90 mmHg</td>
<td>4/75 (5.3 %)</td>
<td>6/75 (8 %)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>HR &lt; 50 / Min.</td>
<td>4/75 (5.3 %)</td>
<td>3/75 (4 %)</td>
<td>ns</td>
</tr>
<tr>
<td>Wehmann T [167]</td>
<td>SpO2 &lt; 90 %</td>
<td>8/98 (8.2 %)</td>
<td>11/99 (11 %)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>mean decrease of SpO2</td>
<td>3 % (2 %)</td>
<td>5 % (3 %)</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td></td>
<td>BP &lt; 90 mmHg</td>
<td>2/98 (2.0 %)</td>
<td>7/99 (7.1 %)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>HR &lt; 50 / Min.</td>
<td>2/98 (2.0 %)</td>
<td>5/99 (5.1 %)</td>
<td>ns</td>
</tr>
<tr>
<td>Kruglik P [174]</td>
<td>N</td>
<td>14</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BP &lt; 20 % of baseline value</td>
<td>37.0 ± 30.1</td>
<td>25.2 ± 18.6</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>HR &lt; 20 % of baseline value</td>
<td>48.2 ± 38.0</td>
<td>14.6 ± 25.0</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td>Jung M [165]</td>
<td>N</td>
<td>40</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>decrease SpO2 (%)</td>
<td>–2</td>
<td>–4</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>mean BP decrease (%)</td>
<td>14</td>
<td>17</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>increase HR (%)</td>
<td>+ 3.5</td>
<td>+ 2</td>
<td>ns</td>
</tr>
</tbody>
</table>

BP, blood pressure; HR, heart rate; ns, not significant; **, significant (P < 0.01).
potential for severe septic complications [96, 97]. With such improper handling (e.g. splitting of ampules) series of infections have been described.

The so-called propofol infusion syndrome (PRIS) may occur as a complication, even after short-term application (symptoms include rhabdomyolysis, cardiac arrhythmias, CK elevation; high mortality rate) [98, 99]. However, so far no such case has been reported during sedation for gastrointestinal endoscopy. Propofol is contraindicated in patients with a known allergy to chicken protein, soy protein, or sulfite. Newer formulations of propofol are currently being developed (e.g. water soluble basis) or are in part already in clinical application [100, 101].

The use of propofol generally does not result in higher complication rates than the use of other strategies of sedation, such as a regimen based on benzodiazepines. One metaanalysis even showed that propofol sedation for colonoscopy reduces the overall complication rate [102]. The dosage of propofol can be reduced, when used in combination with other sedatives/analgesics [103, 104]. One metaanalysis of 20 studies showed that propofol was superior to other sedatives with regards to recovery or patient transfer times, and it resulted in higher patient satisfaction rates. However, no differences were observed with regards to complications or technical success [76]. In another metaanalysis, which analyzed 36 studies in 3918 patients who were sedated for endoscopy, propofol led to a shorter recovery time and higher patient satisfaction in comparison to midazolam [75].

2.2.1.2. Techniques of propofol administration

Propofol is initially given as bolus to induce sedation. To maintain sedation, it is then either given as repeated bolus or it is continuously administered using an infusion pump.

Alternative modes of administration to the intermittent bolus mode (currently the most common method for endoscopy in Germany) are administration by infusion pump (with an initial single bolus for initiation), so-called “target-controlled infusion” (TCI), patient-controlled sedation (PCS), and “computer-assisted personalized sedation” (CAPS). Intermittent bolus administration and administration by infusion pump are standard procedures, while the other methods are still experimental in nature, at least with respect to their use for endoscopy.

2.2.1.2.1. Intermittent propofol bolus administration

With the intermittent bolus administration method, sedation is induced with an intravenous bolus adjusted to weight and, if necessary, age and any co-morbidities of the patient (e.g. 40 mg at <70 kg of body weight or 60 mg at ≥ 70 kg of body weight). Thereafter, repeated bolus of, for example, 20 mg according to patient needs are given to maintain the desired depth of sedation [105]. The intermittent bolus administration method was used in almost all published studies on sedation efficacy of propofol for endoscopic examinations/treatments compared to that of other drugs (e.g., midazolam). It is therefore currently the best documented and most often used form of administration in endoscopy.

2.2.1.2.2. Continuous propofol administration using infusion pump systems

For this mode of administration, too, a bolus of propofol adjusted to body weight and, if necessary, age and co-morbidities is given to induce sedation (if necessary, in combination with other drugs). Sedation is then (usually) maintained by weight-adjusted continuous propofol infusion. Dosing is performed according to the desired depth of sedation and the individual patient’s risk profile. Most systems allow additional propofol bolus as needed. Special infusion pump systems for anesthesia automatically calculate the maintenance dose of propofol (1% or 2% solution) required for a specified sedation depth once various patient parameters have been entered (e.g., weight, height, age).

Administration of propofol by infusion pump is currently the method most often used to maintain total intravenous anesthesia worldwide. However, so far there are few studies on its use in endoscopy. A randomized, comparative trial of propofol administration techniques (infusion pump versus intermittent bolus administration) during interventional endoscopy showed no relevant difference regarding the efficacy of sedation or in terms of adverse reactions [106]. However, the authors explicitly stressed the need for a specialized person to adjust the infusion rate of the infusion pump, if necessary. One study in patients older than 80 years, demonstrated that continuous propofol administration has a tendency to cause desaturations in geriatric patients, although the overall complication rate was not higher in comparison to younger patients [107].

2.2.1.2.3. Non-anesthesiologist administered propofol sedation (NAPS)

This type of propofol administration is either termed nurse administered propofol sedation (NAPS) or as a more general term it can be called non-anesthesiologist administered propofol sedation (see subheading above). In a comparison of mild sedation administered by the endoscopist and deep sedation administered by the anesthesiologist, patients preferred the milder sedation and were more willing to repeat the procedure in the future. Again, less complications were noted with milder sedation [74].

One study of patients with obstructive sleep apnea compared NAPS to standard sedation with sedatives and opioids and showed that the duration of the procedure was shorter in the NAPS group, whereas the complication rate was similar between both groups [108]. Because of the favorable safety profile of propofol, the American endoscopist Douglas Rex postulated that propofol may be administered by gastroenterologists or gastroenterological nursing staff [109]. In an analysis (retrospective case series and metaanalysis) of more than 200,000 cases, transient mask ventilation became necessary in only 213 cases. Endotracheal intubation was not needed in any patient and all patients recovered without neurologic deficits. However, due to methodological weaknesses of this study (retrospective analysis), these results are of limited value. Other parameters of potential morbidity were not analyzed. In another epidemiological investigation of 27,000 patients, oxygen desaturations occurred in 2.3% of cases. In patients older than 70 years of age, oxygen desaturations were even documented in 5.5% of cases. Other parameters, such as hemodynamics, were not analyzed in most cases [110].

Detailed data on postprocedural morbidity do not exist.

A sedation task force of the American Association for the Study of Liver Disease (AASLD), the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA) and the American Society of Gastroenterological Endoscopy (ASGE) took the position that NAPS has a safety profile comparable to standard sedation. However, insufficient experience with NAPS precludes firm conclusions regarding its application during EUS or ERCP [111]. In 2005 the AGA sent a petition to the Food and Drug Administration (FDA) to extend privileges of propofol administration from anesthesiologists to also include non-anesthesiologists. However, this petition was finally denied in 2010 [112].
2.2.1.2.4. Patient-controlled (analgo-) sedation (PCS)

Patient-controlled administration of drugs originated from pain therapy and is today a standard in postoperative analgesia. With the help of a programmable infusion pump, patients can self-administer a defined dose of a drug intravenously at the press of a button. To avoid overdoses, a time-delay option can be applied for repeat doses (so-called lockout mechanism) [113]. One downside to this type of dosing is the fact that patients most frequently administer the medication as a response to a painful stimulus. Not infrequently, the action of the applied substance will therefore occur after the stimulus has ended [12]. This will result in milder sedation, but also in insufficient analgesia and lower patient satisfaction [114].

PCS may be useful for endoscopic examinations with relatively short, tolerable episodes of pain, such as is frequently the case during colonoscopy (e.g., passage of the sigmoid colon or splenic flexure). Administration of very short-acting drugs via these systems is ideally suited for these cases. A combination of propofol with short-acting opioids (e.g., alfentanil, remifentanil) is often used [115, 116]. In one randomized study in patients undergoing ERCP, a combined regimen of propofol and remifentanil lead to more cases of respiratory depression and nausea than the combination of propofol and alfentanil [116]. All the other studied parameters, such as used propofol dosages or patient- and endoscopist-satisfaction were the same in both groups. Patients, who received PCS, were less deeply sedated than those who received their sedation from an anesthesiologist. [115].

In a randomized study, patient satisfaction was similar with the use of a PCS system (propofol plus alfentanil) as compared to midazolam and meperidine [117] and also as compared to diazepam and meperidine (called pethidine in Germany) in 2 additional randomized studies, respectively [118, 119]; in two other studies, patient satisfaction with PCS was even higher than for midazolam alone [120, 121]. However, a higher pain score was reported for PCS than for midazolam in another randomized study [117]. Nevertheless, fewer adverse events (oxygen desaturation or drop in blood pressure) were observed with PCS using propofol in comparison to diazepam [118, 119]. In two of these studies, 97% and 78% of the patients who were sedated with PCS for colonoscopy, respectively, said they would be willing to repeat this type of sedation in the future if necessary [122, 123]. Younger age, female sex, and lower patient satisfaction were independent factors for refusal of the PCS procedure. Recently, remifentanil has been the preferred opioid in PCS. However, a randomized, double-blinded comparison between remifentanil and meperidine for colonoscopy showed neither a difference in patient- or endoscopist-satisfaction, nor in terms of procedure duration or time to discharge from the recovery room [124].

In a Swiss study of PCS, 35% of all patients, who were approached, refused to take part in the study, either because they wanted complete unconsciousness or because they did not want to take responsibility for their own drug administration [12]. However, among those patients who did take part, it was observed that a significantly lower dose of propofol was used during colonoscopy when PCS was employed than with intermittent bolus administration by a nurse (NAPS) [12].

2.2.1.2.5. Target-Controlled Infusion (TCI)

The target-controlled infusion (TCI) method allows intravenous administration of propofol (or other drugs) using an infusion pump. The dose and infusion rate are regulated by a computer [125]. The computer system calculates the individual infusion rate of the pump needed to maintain a preset desired drug concentration in the blood, using algorithms that take various patient parameters into account (e.g., age, sex, height, weight, sedation depth). After the initial dose, required to reach the desired blood concentration, has been calculated, the infusion rate is adjusted during the course of sedation.

The potential advantage of the TCI method compared to continuous infusion (with fixed dose and infusion rate) is the ability to avoid accumulation of the drug, since the infusion rate is constantly being changed. However, the current commercially available infusion pump system calculates the dosage based on a pharmacokinetic model which allows a deviation of 20% from the true plasma drug concentration [126]. Despite this fact, TCI provides a more gentle initiation and a more exact titration of the depth of sedation, as well as a shorter wake-up period, as compared with established bolus injection and infusions based on kilograms of body weight [127].

In an evaluation of 205 patients who underwent ERCP under deep sedation (without mechanical ventilation) an open TCI system with propofol was used. The initial desired concentration was 4 μg/ml, followed by a maintenance dose in the range of 2 – 5 μg/ml during that was given by the anesthesiologist in the course of the procedure. In addition, a bolus administration of fentanyl (50 – 100 μg i.v.) was allowed. The endoscopists rated the sedation as excellent in 201 of 205 cases; only four cases of hypoxemia (PO2 < 85%) were observed, and one case where ventilation with a mask became necessary [128].

In another trial, colonoscopy was performed in 16 patients using a closed TCI system where the infusion rate was controlled by means of EEG (bispectral index determination). In this study, a median propofol concentration of 2.3 μg/ml was aimed at; predominantly, a bispectral index of 80 was seen (corresponding to a mild to moderate depth of sedation) [129].

Further studies investigated the combined use of TCI and PCS, as to where the patient was able to modify the administration rate of the TCI pump by pushing a button. Positive sedation effects were reported during colonoscopy and ERCP. However, the case numbers were small (n = 20 – 40) [129 – 132]. In a study by Stonell et al. [132] that compared the TCI/PCS system to repetitive bolus administration of propofol by an anesthesiologist during colonoscopy (n = 40), no significant differences were found in sedation efficacy or complication rates, although the total propofol dose tended to be lower in the TCI group than in the bolus group (233 vs. 288 mg, P = 0.05).

2.2.1.2.6. Computer-Assisted Personalized Sedation (CAPS)

The computer-assisted method of personalized sedation (CAPS) extends TCI dosing of propofol by the addition of various monitoring parameters, in form of both, physiological parameters (heart rate, blood pressure, O2-saturation, and exhaled CO2), and patient reactions to specific verbal (via headphones) and tactile stimuli (via a vibration mouse). Sedation is as such implemented and monitored entirely by computer. A commercially
available system only allows the regulation of moderate sedation depths: deep sedation and anesthesia are not yet envisaged. The system has been available in the United States since 2013 for patients with an ASA risk classification of I or II. The system is licensed in Canada as well and received CE-certification in Europe in 2010 [133].

In an initial two-center evaluation in the US and Belgium, an adequate sedation effect without complications was observed in a total of 96 patients undergoing gastroscopy or colonoscopy. Following an initial bolus administration of fentanyl (25–100 μg), between 20 mg and 350 mg (median 70 mg) of propofol were administered via this system [134]. Here, the CAPS-group had fewer desaturation events than patients receiving standard sedation with midazolam and an opioid [114, 135]. Another system is currently being developed [114].

2.2.2. Benzodiazepines

Benzodiazepines induce anxiolysis, amnesia and sedation. They have both anticonvulsant and muscle-relaxing effects and act by binding to GABA receptors. Different benzodiazepines can have different pharmacologic characteristics (e.g. a stronger sedating effect or a stronger anxiolytic effect) [136].

2.2.2.1. Diazepam

Diazepam was the only available sedative in the early days of sedation for endoscopy, but is now rarely used in the western world for endoscopic examinations. This can be attributed to its relatively long half-time compared to more recent short-acting benzodiazepines such as midazolam [137–139]. As compared to midazolam, diazepam has a markedly longer elimination half-time (30–100 hours for diazepam vs. 1.5–3 hours for midazolam) The main side effects of diazepam are respiratory depression [140], coughing, and dyspnea. Phlebitis may occur at the injection site, especially if water-soluble forms are used [141]. The usual dose is a single injection of 5–10 mg (see also dose recommendation in the manufacturer’s product information).

2.2.2.2. Midazolam

Midazolam is a short-acting benzodiazepine that is still the most commonly used sedative for endoscopy [142]. The sedation potency is 1.5–3.5 times greater than that of diazepam [143]. This substance reaches its maximum effect after 3–4 minutes, although the duration of its effect is between 15 and 80 minutes [144], depending on cofactors such as obesity, advanced age, and liver or kidney disease. It has dose-dependent hypnotic, anxiolytic, amnestic and anticonvulsive properties, similar to other benzodiazepines. The main pharmacologic actions are mediated by an activation of GABA receptors. All effects that are mediated by GABA receptors are reversed by the specific antagonist flumazenil [156, 157]. A study by Mora et al. [158] showed that flumazenil has a stronger antagonistic effect on benzodiazepine-induced sedation and amnesia than on respiratory depression. Neutralization of the midazolam-induced respiratory depression occurs 120 seconds after intravenous flumazenil administration [159]. The half-time of flumazenil is 0.7–1.3 hours, and the average duration of the antagonizing effect is 1 hour. Patients, who initially respond to flumazenil by regaining consciousness, require prolonged monitoring in order to observe and treat a possible medication rebound.

In a study by Andrews et al. [160], 50 patients who underwent gastroscopy with midazolam sedation received either flumazenil or placebo directly after the examination and again 30 minutes later. Those who had received flumazenil showed markedly improved memory, psychomotor function, and coordination after only 5 minutes (p < 0.001). However, a re-evaluation of the same parameters 3.5 hours later showed no difference between the two groups. In contrast, the results of a study by Bartelsman et al. [161] of 69 patients who received flumazenil or placebo after midazolam administration for EGD demonstrated no re-sedation within 6 hours. Routine administration of flumazenil at the end of an endoscopic procedure reduces recovery time [162], but so far no other benefits have been reported for either the patient or the endoscopist. Care should also be taken with patients taking carbamazepine or high doses of tricyclic antidepressants or those suffering from chronic benzodiazepine abuse, as seizures or withdrawal symptoms may occur. For this reason, the routine use of flumazenil cannot be recommended.

2.2.3. Propofol versus Midazolam

<table>
<thead>
<tr>
<th>Recommendation 2.2.3.3</th>
<th>Propofol vs. midazolam</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: B</td>
<td>Because of data on efficacy, recovery and complications, we suggest that propofol should be preferred to midazolam.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 2b</td>
<td>Strong consensus (16/16)</td>
<td></td>
</tr>
</tbody>
</table>

2.2.3.1. Comments

Data on efficacy, recovery and complications suggest that propofol should be preferred to midazolam during sedation for gastro-
intestinal endoscopy. Individual adjustments must be made according to patient criteria and the type of exam, as well as to the personal, personnel, apparative and structural requirements mentioned in this guideline.

Patients and endoscopist similarly judge sedation with propofol to be as good or better than sedation with midazolam [87, 88, 118, 163, 164]. Therefore, propofol has gained importance as a sedative for gastrointestinal endoscopy in recent years. Some have termed this a paradigm-shift in endoscopy, not least as a response to explicit requests for propofol sedation by some patients [78].

Randomized studies suggest that propofol is preferable for EGD, colonoscopy, and ERCP [8 – 10, 78 – 91, 164, 164 – 168]. The advantage of propofol sedation compared to benzodiazepines, for both the patient and the endoscopist, is a shorter time of onset [87], significantly better patient cooperation – especially in interventional endoscopy (such as ERCP) [165 – 167, 169] – and a shorter time for recovery [8 – 10, 76, 87 – 91, 164 – 167], including recovery of psychomotor function [10]. In patients undergoing ESD, a comparison of propofol versus midazolam, showed markedly better endoscopist-satisfaction with the exam conditions in the propofol group [170]. Propofol facilitates the performance of colonoscopy [171], whereby moderate sedation (‘conscious sedation’) is sufficient [76, 172]. The in-depth analysis shows no influence of propofol on patient satisfaction for upper GI-endoscopy [8, 9, 164, 173], but an advantage for propofol during colonoscopies [10, 87, 163].

In a study of 1000 patients who underwent endosonographic procedures, a complication rate of 0.6% was noted with propofol, as compared to 1% in historical controls, who received a combination of midazolam and meperidine, respectively [78]. However, in the propofol-group, one case of aspiration pneumonia occurred and 3 patients required endotracheal intubation [78]. Endoscopist satisfaction was higher in the propofol-group and examination times were significantly shorter.

### 2.2.3.2. Cardiorespiratory complications

Comparative data on complications from 12 randomized studies were compiled in a meta-analysis by Qadeer et al. [102] that described the relative risk of sedation with propofol compared to benzodiazepines. The use of propofol for colonoscopy was associated with significantly fewer side effects. For other interventional endoscopies (EGD, ERCP) no significant difference was seen. A more recent meta-analysis included 20 studies and found higher satisfaction rates with propofol, but no increase in complication rates [76]. When propofol is used for ERCP there is in some cases a significantly higher risk of arterial hypotension compared to midazolam/meperidine [164, 165, 167, 174, 175]. There was also a tendency for oxygen saturation to drop below 90% with propofol sedation, although this was not statistically significant (Table 9).

In a risk factor analysis by Wehrmann and Riphaus [176] in 9547 patients who received propofol sedation for interventional upper endoscopy over a period of 6 years (EGD, n = 5374, ERCP, n = 3937, EUS, n = 236), 3151 patients had monosedation with propofol and 6396 patients sedation with a combination of propofol and midazolam. A total of 135 severe complications were reported (1.4%), leading to discontinuation of the intervention. Short-term mask ventilation was necessary in 40 patients (0.4%) and endotracheal intubation in 9 patients (0.09%). Eight patients needed additional observation in the intensive care unit (0.3%) and four patients died, three of whom had adverse events that could have been sedation-related (mortality rate 0.03%). After multivariate analysis of the data, emergency interventions and a higher propofol dose were assessed as independent risk factors for cardiorespiratory complications [176]. In a comparative study of propofol monotherapy versus propofol after sedation with midazolam in patients undergoing ERCP, less episodes of oxygen desaturation were noted in the combination group, as well as lower doses of propofol and less anxiety of the patients prior to the procedure [177].

### 2.2.3.3. Amnesia

#### Diazepam versus midazolam

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Amnesia</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2.3.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommendation</td>
<td>grade: B</td>
<td>If benzodiazepines are used for sedation because of their stronger amnestic effect, we suggest that midazolam should be preferred to diazepam because of its shorter half-time.</td>
</tr>
<tr>
<td>Evidence level: 2a</td>
<td>Consensus (14/16, 2 dissenting votes)</td>
<td></td>
</tr>
</tbody>
</table>

#### Comments

Amnesia following the use of midazolam has been well studied [178] and in all studies has been shown to be significant. If amnesia is not desired, midazolam should not be used. An alternative benzodiazepine is diazepam [138, 139]. The longer half-time of diazepam has not been reported in studies as a disadvantage compared to midazolam [139, 143, 179]. However, in some studies patient comfort was lower after diazepam than after midazolam. With respect to amnesia midazolam has the highest potency of all sedation methods.

### 2.2.4. Other drugs as monotherapeutics

#### 2.2.4.1. Introduction

Other drugs are additional either sedating/hypnotic or analgesically active substances that do not fall into the usual substance classes. These include opioids and ketamine (as monotherapeutics), inhalation anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs) and neuroleptanalgesics. The few studies from the past that exist on these substances show at a moderate level of evidence that these drugs are in principle suitable for sedation. Evaluating the existing literature, the following points stand out:

1. The frequency of adverse events is much higher than for the usual sedation methods.
2. Some of these methods (such as neuroleptanalgesia) no longer have a role in modern anesthesia.
3. Scientific evidence is lacking for ketamine; specific side effects make this drug unsuitable for the use as a monosubstance. Only a few studies with small patient numbers exist on the use of ketamine in combination therapy (e.g. in combination with midazolam or propofol); they suggest a positive effect. However, further evaluation in randomized studies with larger patient numbers is required.
4. Inhalation anesthetics require special equipment, monitoring procedures, and standards of safety in the workplace. It is impossible to adhere to MAC values (maximum allowable concentrations) of the substances used because open inhalation systems are almost always used in endoscopy and routine protection of the airways (intubation, airtight laryngeal mask) is not usual practice.
5. On the basis of the current data, there is not enough evidence for the routine use of NSAIDs for endoscopic interventions.
2.2.4.2. Opioids as monotherapeutics

2.2.4.2.1. Fentanyl

2.2.4.2.1.1. General considerations

Fentanyl is a lipophilic synthetic morphine derivative that is chemically related to meperidine. It is about 600 times more potent than meperidine and 100 times more potent than morphine. The effect starts only about 20 seconds after intravenous administration as the substance binds to specific opiate receptors in the brain and spinal cord. The maximum effect is expected after 6 minutes and the duration of effect is 20–30 minutes. The initial dose is usually 50–100 µg. In older patients the dose should be reduced. The most common adverse effect is respiratory depression, which may be expected with a dose of as little as 100 µg (for adults) because of the strong potency of the drug. In addition, thoracic rigidity may occur, which can make it more difficult to ventilate the patient, should that prove necessary. The effects on blood pressure and heart rate are fairly mild, usually causing a drop in these parameters due central inhibition of the hypothetic nervous system. Smooth muscle spasms of the bile duct and pancreas and constipation can also occur. Nausea and vomiting under fentanyl is comparable to other opioids. Although fentanyl is usually used for general anesthesia (often in combination with other drugs) or for chronic pain (usually transdermally), there are few studies with small patient numbers on its use as an analgesic for endoscopy.

Studies, that compared the use of fentanyl during EGD and sigmoidoscopy to unsedated procedures, showed better patient acceptance and tolerance with fentanyl. Cardiorespiratory complications were not observed [180, 181]. A recent study comparing fentanyl and meperidine during endoscopic procedures showed shorter examination times when fentanyl was used. A more rapid patient recovery was reached with the use of fentanyl. However, meperidine showed a better analgesic effect in postprocedure pain scores [182].

2.2.4.2.2. Remifentanil

2.2.4.2.2.1. General considerations

Currently, data on the routine use of remifentanil, a highly potent synthetically synthesized opioid with an extremely short half-time (2–3 min), are sparse. Regardless of renal and liver function, remifentanil is cleared hydrolytically within a few minutes by non-specific esterases in the blood and tissue. Therefore, no accumulation occurs, even after prolonged, continuous application [183]. As it is the case with other opioids, remifentanil can lead to respiratory depression. In addition, muscular rigidity may occur, especially within the respiratory musculature. These side effects mainly occur after bolus administration. Therefore, this substance should only be applied as a continuous infusion in patients who are breathing spontaneously. Its application (according to the product information) is limited to settings, which are completely equipped for monitoring and support of cardiorespiratory functions (such as intensive care units and surgical operation rooms).

In a randomized study by Akcaboy et al. [184], 100 patients received a continuous infusion of remifentanil (bolus 0.5 µg/kg, then 0.05 µg/kg per minute continuously) or propofol (bolus 0.5 mg/kg, followed by 50 µg/kg per minute) for colonoscopy. The duration of the examination was longer and the oxygen saturation after bolus administration was lower after remifentanil than after propofol. Although the recovery time was shorter for remifentanil, the time to hospital discharge was comparable. Nausea and vomiting were observed much more frequently in the remifentanil group. Fanti et al. performed a randomized, double-blinded comparison of remifentanil and meperidine for sedation during colonoscopy. After an initial bolus, remifentanil was administered by patient controlled application. Patients in the meperidine group received a bolus and a pump with normal saline for self-administration. Satisfaction scores of patients and endoscopists were not different in both groups. In addition, no differences were observed with regards to procedure duration and discharge times [124]. In another study, remifentanil was compared to a combination of midazolam and meperidine for colonoscopies. It showed a more rapid recovery and better hemodynamic stability of patients receiving remifentanil, as compared to the control group [185].

2.2.4.3. Ketamines as monotherapeutics

2.2.4.3.1. General considerations

Ketamine is an intravenously or intramuscularly injectable general anesthetic with strong analgesic effects. It is mainly used as a “monoaesthetic” for short diagnostic and therapeutic interventions in children and for special situations in adults. After intravenous bolus administration ketamine has a rapid onset of action (<1 min) and an effect duration of about 10–15 minutes [186]. It causes a so-called dissociative anesthesia without cardiorespiratory depression [187]. The analgesic effect starts at sub-hypnotic doses and lasts longer than its anesthetic effect. The sedative and hypnotic properties of ketamine, however, are much less pronounced. Muscle tone is maintained or increased under ketamine anesthesia so the protective reflexes are generally not affected. Because of its sympathoexcitation, ketamine leads to a rise in blood pressure and heart rate which in turn causes an increase in myocardial oxygen consumption and concomitantly increased coronary perfusion. Myocardial ischemia may occur [188]. Ketamine displays a negative inotropic and antiarrhythmic effect on the heart itself. Moderate hyperventilation is observed after ketamine administration. It has a relaxing effect on the bronchial muscles. Contraindications for the use of ketamine include insufficiently treated or untreated arterial hypertension (systolic/diastolic blood pressure above 180/100 mmHg at rest) and patients for whom a rise in blood pressure would constitute a substantial risk (e.g. history of cerebrovascular insult). Relative contraindications include unstable angina pectoris or myocardial infarction in the preceding 6 months. Since the pharyngeal reflexes are maintained in general, mechanical irritation of the pharynx should be avoided when ketamine is employed as a monoanaesthetic. One adverse side effect is the frequent occurrence of hallucinations, nightmares, and delirious states in about 10–30% of cases. These reactions can be reduced by giving midazolam in addition [187, 189]. Besides racemic ketamine, an s-isomer, so called “s+ketamine”, is commercially available in some countries, including Germany. This “s+ketamine” is twice as potent as racemic ket-
mine and is supposed cause less side effects. However, the literature regarding this topic is still ambivalent [189, 190]. For the reasons given above, ketamine is not recommended as a routine monotherapeutic for endoscopic examinations. Most studies on the use of ketamine relate to its use in combination therapies – mainly with midazolam – for endoscopic interventions in children [191, 192]. It was shown that adequate sedation can be achieved without cardiorespiratory complications. Although the data on the use of ketamine in adults are limited, there are some indications that adjunctive use of ketamine, in combination with midazolam, can be beneficial for certain patients (all contraindications considered). A double-blind, placebo-controlled study by Rosing et al. [193] that compared midazolam/placebo with midazolam/ketamine for colonoscopy in 129 patients showed that patients receiving the combination therapy needed fewer repeat injections (40 % vs. 27 %), had better sedation and analgesia, and were more willing to agree to undergo another similar procedure. A randomized study by Ong et al. [194], that compared ketamine combination sedation (ketamine plus midazolam, pentazocine, propofol) with propofol monotherapy in ERCP, demonstrated that especially in younger patients the benefit of the combination sedation was a better patient tolerance. However, patient satisfaction was similar in both groups. In addition, hypoxia occurred more frequently when the combination therapy was used.

### 2.2.4.4. Inhalation anesthetics as monotherapeutics

#### 2.2.4.4.1. Nitrous oxide

Nitrous oxide (laughing gas) is a gas at room temperature and must only be applied using suitable inhalation and anesthesia equipment. It has a mild sedative effect and a strong analgesic effect. Although it normally affects the circulation only slightly, a drop in blood pressure, decreased stroke volume and increased pulmonary vascular resistance may occur. Possible adverse side effects are nausea and vomiting. The occurrence of euphoria, dreams, and fantasies has been described. The methionine-, folic acid- and vitamin B12-metabolism can be affected [195]. If the dose is too high, hypoxia, circulatory depression, agitation, or somnolence and even unconsciousness may occur. Occupational safety measures must be enforced. In addition, its oxidizing capacity must be enforced. In addition, its oxidizing capacity must be considered (see statement of the BDA and German Society for Anesthesiology and Intensive Care Medicine; DAGI) [196].

In a metaanalysis of 11 studies, including 623 patients who had a sigmoidoscopy or colonoscopy, nitrous oxide was compared to procedures that avoided the use of an analgesic [197]. There were no differences with regards to pain during exams that avoided analgesics, but also no differences with regards to colonoscopies with intravenous sedation. The use of nitrous oxide led to a more rapid discharge, as compared to intravenous sedation. A Cochrane-metanalysis analyzed the use of nitrous oxide during colonoscopy [198]. In total, 16 studies with 547 patients were included. Four studies showed that nitrous oxide has similar analgesic effects as conventional sedation. One study showed superiority of conventional sedation and one study showed an advantage of nitrous oxide. Two studies showed a more rapid recovery of the patients with nitrous oxide and one showed no difference. Finally, two studies showed improved safety with the use of nitrous oxide, whereas one study showed improved safety with sedation [198]. The authors concluded that nitrous oxide appears to have the same efficacy as conventional sedation for colonoscopy and a better safety profile, but that more data are required. In one recent study it was found that nitrous oxide lead to more rapid recovery, as well as better pain control and patient satisfaction, however in another study no difference was observed between nitrous oxide and iv-sedation, when both were applied on demand [199, 200].

Overall the evidence is still insufficient as to make any firm conclusions regarding the use of nitrous oxide for endoscopic procedures. It has to be pointed out that occupational safety measures must be enforced when nitrous oxide is administered.

#### 2.2.4.4.1.2. Dexmedetomidine

Dexmedetomidine is a specific α2-adrenoreceptoragonist with sedating and weak analgetic properties. In contrast to other sedatives/hypnotics, dexmedetomidine does not cause respiratory depression. This substance has been licensed in Germany since 2011 for sedation of adult intensive care patients with a RASS-3 grade of sedation. However, application of this drug for endoscopy would be considered an off-lable use. Alpha2-adrenoreceptoragonist shows, such as dexmedetomidine, show a typical hemodynamic profile after rapid intravenous administration. Initially, this will lead to an increase in blood pressure, followed by a mild phase of hypotension [201]. As a result of these pronounced hemodynamic effects, dexmedetomidine should not be given by rapid intravenous infusion or bolus administration [202]. Alpha2-adrenoreceptoragonists should not be used in patients with bradycardia or those who require a sufficient mean blood pressure [203]. In the setting of hypovolemia, hypotension may occur. For this reason hypovolemic states should be assessed and volume substitution should be performed as necessary. This drug should only be used by experienced physicians and continuous monitoring must be ensured. Dose adjustments must be made in older patients or those with impairment of renal or hepatic function.

To date, only a few studies exist regarding the use of dexmedetomidine for sedation in endoscopy. One study compared dexmedetomidine with a combination of midazolam and fentanyl for colonoscopy. No difference in blood pressure was observed, whether dexmedetomidine (1 µg/kg followed by 0.5 µg·kg⁻¹·hr⁻¹) or midazolam (0.05 mg/kg)/fentanyl (1 µg/kg) was used, but an increased in heart rate and a decrease in oxygen saturation was found in the dexmedetomidine-group [204]. Another study analyzed 30 patients who received dexmedetomidine, midazolam or propofol for endoscopic mucosal resection, respectively [205]. Patients in the dexmedetomidine-group showed less movement during the procedure than patients within the other groups. The duration of the...
procedure was shorter in the dexmedetomidine-group. However, in patients undergoing ERCP, a study by Muller et al. showed greater hemodynamic instability and a delayed recovery with dexmedetomidine as compared to propofol/midazolam [206]. One study that compared dexmedetomidine with midazolam and meperidine or fentanyl, respectively, had to be terminated early as a result of hemodynamic adverse events, such as bradycardia and hypotension [207].

2.3. Combination therapies

2.3.1. General considerations

Combination therapies are usually comprised of a sedative and an analgesic or a combination of different sedatives. As a general principle, opioids and sedatives mutually potentiate their action, leading to an increased risk of possible side-effects [50, 208, 209]. By combining different substances, dose reductions can lead to more rapid recovery after the procedure [63, 87, 210, 211]. Although combination therapy causes hypotension and oxygen desaturation more frequently than monotherapies [212 – 214], the occurrence of accidental overdosing is reduced [105, 109] (see also Section 2.3.3).

Because of the synergistic effects of propofol, midazolam and opioids, the dosage of propofol can generally be reduced in combination with these substances (mainly shown in studies of general anesthesia) and side effects can therefore be reduced [215, 216]. In addition, combination therapy more safely reaches the goal of moderate sedation, rather than deep sedation. [168, 215, 217, 218]. In elderly patients with comorbidities, the combination of midazolam and propofol leads to a shorter recovery time and better patient satisfaction than midazolam monotherapy [219]. These results are confirmed by a metaanalysis from 2010 that showed more occurrences of deep sedation with propofol monotherapy as compared to benzodiazepine monotherapy. However, propofol in combination with other substances showed no difference in the level of sedation, as compared to benzodiazepines alone [76]. However, anesthesiologists voice concerns of overdosing with the use of combination therapies [220].

Both, midazolam and propofol are sedatives/hypnotics, which primarily elicit their action by binding to GABA-receptors. For this reason, they have additive effects. The dosages of propofol and midazolam can be reduced, when used in combination. However, the effect on GABA receptors remains similar. Propofol and midazolam have synergistic effects, at least with regards to cardiorespiratory function. These can lead to corresponding hemodynamic changes. Midazolam has a longer half-time and a longer duration of action than propofol. Therefore, a prolonged recovery time must be expected, as compared to propofol monotherapy. See chapter 2.3.2.3 for details and recommendations regarding the use of this combination for endoscopy.

2.3.2. Specific combinations

2.3.2.1 Combination of benzodiazepines plus opioids

A study by Milligan et al. [209], comparing a combination of alfentanil/midazolam with midazolam alone for upper endoscopy, showed an improvement in examination conditions for the endoscopist, increased patient acceptance and a shorter recovery time. Another randomized, double-blind study by Radaelli et al. [221], that compared midazolam to midazolam/meperidine for colonoscopy in 253 patients, reported significantly less pain and a higher rate of willingness to repeat the intervention under combination therapy. The recovery time and the fall in oxygen saturation were comparable in both study groups. A study, comparing midazolam alone to a combination of midazolam and meperidine in 74 patients, showed no difference in the quality of analgesia, recovery or procedure time [222]. The combination of midazolam and fentanyl, on the other hand, had a similar analgesic effect but a shorter recovery time than midazolam plus meperidine [223].

2.3.2.2 Combination of propofol plus opioids

In a randomized, controlled study by Van Natta et al. [103], 200 patients undergoing colonoscopy were given propofol alone to reach deep sedation or a combination treatment with propofol/fentanyl, propofol/midazolam, or propofol/midazolam/fentanyl to reach moderate sedation. Recovery time, patient satisfaction, and vital signs were compared. Patients with propofol sedation alone needed significantly higher doses and showed deeper sedation stages than those given the other combination treatments (p < 0.001). The time to discharge was significantly shorter after the combination treatments than after propofol alone (median 13.0 – 14.7 min versus 18.1 min, P < 0.01).

Vital signs and patient satisfaction were comparable in all study groups. In a study of 222 patients undergoing complex endoscopic procedures, the combination of propofol and opioids was as safe as the combination of benzodiazepines and opioids [224]. In addition, the study showed that the use of propofol markedly increased patient satisfaction.

2.3.2.3 Combination of sedatives plus propofol

In 64 patients who underwent two consecutive, long (> 30 min) endoscopic examinations, and who initially received propofol and then a combination of midazolam and propofol, the advantage of combined sedation was the significantly lower dose of propofol required (reported as 59 % compared to monotherapy). However, the postinterventional recovery time was twice as long for the combination regimen (4 vs. 8 min) [225]. Furthermore, it was demonstrated in 239 consecutive patients undergoing therapeutic endoscopy (EGD and endoscopic ultrasonography) that the combination of propofol and midazolam led to a lower dose of propofol compared to monotherapy (0.20 ± 0.09 mg/min per kilogram body weight vs. 0.25 ± 0.13 mg/min per kilogram, respectively, P < 0.01) with otherwise comparable efficacy [211]. However, the combination regimen was also associated with a longer recovery time (25.8 ± min vs. 19 ± 7 min, P < 0.05). Another study showed a similar effect of dose reduction with the use of a combination of propofol with midazolam and a shorter postinterventional recovery time, as compared with propofol monotherapy (13.0 – 14.7 versus 18.1 min, P < 0.01) [103]. Overall, all studies in the endoscopic field failed to show a definitive advantage of a combination of propofol plus midazolam over propofol monotherapy regarding the efficiency of sedation and the safety profile. Combination therapy has the disadvantage of a significant prolongation of the recovery time. In addition, the long half-time of midazolam (several hours) leads to the recommendation for a prolonged abstinence from active participation in traffic (see topic V). The routine use of a combination of propofol and midazolam can therefore not be recommended.
2.3.2.4 Combination of a sedatives plus spasmolytics
A prospective, double-blind, placebo-controlled study by Mui et al. [226] investigated the use of the spasmolytic hyoscine N-butylbromide (Buscopan) for sedation in patient-controlled sedation with propofol/alfentanil for colonoscopy. The study demonstrated a longer cecal intubation time, significantly lower endoscopist satisfaction, a significantly higher dose of sedative/analgesic, and significant hemodynamic instability. The combination of spasmolytics with sedatives increases the rate of cardiovascular side effects and reduces both patient satisfaction and the endoscopist's evaluation of the examination. The use of spasmolytics in sedation for endoscopy should therefore be carefully considered. Because the focus of this guideline is sedation and not spasmolysis, no firm recommendation is given.

2.3.3. Side effects of combination therapies

2.3.3.1 General considerations
Even if the recommended dose reduction for combination therapy is followed, respiratory function is compromised more frequently than under monotherapy [212–214]. Based on the existing studies, it cannot be stated whether life-threatening situations occur more often under combination therapy. In a randomized, double-blind, placebo-controlled study, 71 patients were sedated with diazepam or a combination of diazepam plus meperidine. Patient satisfaction was similar in both groups, but the endoscopists preferred the combination therapy because of better patient tolerance. However, with combination therapy oxygen saturation dropped twice as often as with diazepam monotherapy (P = 0.008) [214]. Another study randomized 35 patients to either a combination of alfentanil/midazolam or midazolam alone [212]. Again, a fall in oxygen saturation, resulting in a need for oxygen administration, was more common with the combination treatment. Patient tolerance, patient satisfaction, recovery time, and blood pressure were comparable in both groups.

A randomized, double-blind study investigated the addition of remifentanil to sedation with propofol in 50 relatively healthy patients (ASA grades I and II) undergoing colonoscopy. Blood pressure and oxygen saturation dropped significantly more often in the remifentanil/propofol group. Although the addition of remifentanil allowed for a dose reduction of propofol, recovery time was significantly shorter (P < 0.01) and patient satisfaction significantly higher (P < 0.01) with propofol monotherapy [213]. In a comparative study of the combination of propofol/alfentanil or remifentanil, respectively, more episodes of respiratory depression and nausea were noted in the remifentanil group [116].

2.4. Influence of comorbidities

2.4.1. General considerations
A higher ASA-classification is assigned to patients according to the severity of their comorbidities. Patient with comorbidities have a higher rate of adverse events as compared with healthy subjects [92, 227, 228]. Older patients and patients with pre-existing coronary or pulmonary diseases in particular are at higher risk of complications during endoscopy with sedation [92, 229, 230]. Hepatobiliary diseases in which drug elimination is reduced, or age-related slower metabolism, can also lead to potentiation of side effects [145, 231, 232]. A multiplicity of physiological processes contribute to increased sensitivity towards the various drug substances, leading to a correspondingly increased sedation risk [233]. Age-related diseases and rapid or excessive doses contribute more strongly to cardiorespiratory complications than age per se [233].

### 2.4.2. High-risk patients

<table>
<thead>
<tr>
<th>Recommendation 2.4.2</th>
<th>High-risk patients</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: B</td>
<td>Patients with a higher ASA grade and/or older patients are at higher risk of sedation-related side effects (cardiorespiratory depression). We suggest that the dose of the sedative/analgesic used should be adjusted/reduced accordingly.</td>
<td></td>
</tr>
</tbody>
</table>

**Evidence level: 2b Strong consensus (16/16)**

### 2.4.3. Substance type

In accordance with the modified recommendations of the American Society of Gastroenterology for elderly patients undergoing gastrointestinal endoscopy [234], fewer substances given more slowly and at a lower cumulative dose should be administered [234, 235]. Older patients are frequently sedated with midazolam and/or other opioids or narcotics. Since benzodiazepines increase the risk of hypoxemia in older patients, overweight patients and anemic patients, a dose reduction is also recommended here [236]. Especially older patients carry an increased risk of postinterventional hypoxemia [175].

Since propofol has a limited therapeutic range, it can lead to more cardiorespiratory complications in older high-risk patients than in younger patients [92, 237]. Low initial doses of propofol (in general half the recommended dose for adults), slow, gradual titration and careful monitoring are recommended for sedation of older patients [238–240].

It has been shown that, used with due care, propofol can be safely employed for sedation in this age group [175, 237, 240]. A study in older patients, who received propofol for endoscopic procedures, showed that patients who are > 70 years required less propofol for sedation than those < 70 years. The frequency of major and minor side effects was similar in both groups. [240]. In a cohort of 27000 patients oxygen desaturation occurred in 2.3% of cases, even though 2 liters of oxygen were given routinely during the procedure. In patients > 70 years this even occurred in 5% of cases [110]. In these patients hemodynamic parameters were infrequently assessed and therefore the frequency of such complications remains speculative. There also was no monitoring of ventilation. Therefore, the occurrence of hypoventilation or hypercapnia also remains speculative. The continuous administration of propofol in patients older than 80 years led to a tendency of increased episodes of oxygen desaturation, although the overall rate of complications was not higher than in younger patients [107]. A cohort study by Vargo et al. [227] analyzed risk factors for cardiopulmonary events during propofol sedation for upper and lower endoscopy. The overall risk of a cardiopulmonary event during 528 gastroscopies and 1683 colonoscopies was 11.7 per 1000 cases. A higher risk was found in patients with increasing ASA grade who were undergoing colonoscopy.

In a randomized study by Riphaus et al. [241], 60 patients with known liver cirrhosis and portal hypertension were sedated with either propofol or midazolam. Before and 2 hours after the examination all patients took a number connection test (ZVT-A) and a portosystemic encephalopathy syndrome test (PSE). Twenty patients without liver cirrhosis who did not undergo gastroscopy were the control group. Recovery time and the recovery score were also determined. Compared to sedation with midazolam, patients sedated with propofol had a significantly shorter...
recovery time (18.4 ± 6.7 min vs. 7.8 ± 2.9 min, respectively). Propofol also affected the PSE score less than midazolam, the use of which led to transient exacerbation of the existing subclinical hepatic encephalopathy. Hence, sedation with propofol tends not to cause exacerbation of subclinical hepatic encephalopathy in patients with liver cirrhosis and is therefore an alternative sedative for use in these patients. Likewise, another study compared a combination of propofol with midazolam or fentanyl in patients undergoing upper gastrointestinal endoscopy and found propofol-based sedation to be more effective with a more rapid recovery, as compared to midazolam [242]. Because of its shorter duration of action, better controlability and fewer complications, with regards to hepatic encephalopathy in cirrhotic patients, propofol should be preferred over benzodiazepines and/or opioids in such cases [241 – 245].

### 2.4.4 Obesity
Data on the effect of obesity on sedation for endoscopy are still limited. Morbid obesity can result in a number of comorbidities, such as obstructive sleep apnea, restrictive lung disease and pulmonary hypertension. Diseases of the lung or upper airways increase the risk of complications during sedation. In a study in obese patients, who received propofol sedation for upper gastrointestinal endoscopy, 2 of 69 patients had to be treated for hypoxemia [246]. Multivariate analysis of another study also showed a correlation between body-mass-index and problems with sedation, when propofol was used [247]. An analysis of 799 patients identified BMI and higher ASA-classification as predictors for respiratory and cardiac complications [248]. A multivariate analysis identified ASA-class III or greater, as well as an elevated BMI, as independent risk factors for mechanical, respiratory support [249].

### 2.4.5 Elderly patients
A number of studies found a positive effect of music with regards to the reduction of sedative and analgesic doses. These results were also confirmed by several metaanalyses. A recent, randomized, controlled study confirmed this advantage of music during colonoscopy. Pain was reduced in the group receiving music. Furthermore, patients were more satisfied and the performance of the procedure was easier. In addition, the required doses of midazolam and meperidine were lower as compared with the control-group and anxiety-levels were positively affected by the use of music [257]. In contrast, another study of 180 patients showed that patient age and the type of examination did not influence anxiety levels. However, again music reduced anxiety-levels significantly [258]. Another study in 307 patients showed no influence of music on pain-scores during an endoscopic procedure [259].

### 2.4.6 Comorbidities
An increased risk can also be found in younger patients with comorbidities who undergo sedation. As a result, higher ASA classification appears to predict more frequent complications [11, 249, 253 – 256]. One study of propofol sedation for endosonography included patients of all ASA-classes and found no correlation of ASA-class and risk of complications. However, sedation was performed by an anesthesiologist [78]. It should be considered that patients with multiple comorbidities and high-risk patients, pose particular staffing requirements (see chapter 3.3).
ed music in addition to drug therapy (midazolam, meperidine, or propofol/alfentanil). This significantly reduced the need for analgesics by 29.7% (P = 0.001) and the need for sedatives by 15% (P = 0.055). Another meta-analysis of 8 studies included a total of 722 patients undergoing colonoscopy. A reduction in examination time was found, whereas other parameters, such as pain, blood pressure and recovery times were only minimally influenced by music. However, no unfavorable effects of music were noted, aside from the acoustic isolation of the patient from the endoscopy personnel [260]. A third meta-analysis of 8 studies included 712 patients. Here, no difference was found regarding diverse endpoints whether music was used or not. However, overall satisfaction-scores were significantly higher in the music-group [261]. In summary, current data suggest that music during endoscopic procedures leads to shorter examination times and to a possible reduction in sedative doses. Since the implementation of music is not cumbersome and it does not lead to any side effects, it can be recommended depending on the patient’s wishes.

3. Topic III: Structure quality: personal/personnel/equipment/requirements

Since there are currently only limited prospective studies on the topic of structure quality, almost all recommendations are based on previous guidelines and recommendations of other professional associations [6, 22 – 31, 45, 48, 49, 51, 55, 238, 279], as well as the current S2k-guideline “Quality-Requirements for Gastrointestinal Endoscopy” (AWMF-register no. 021 – 022).

Introduction

The endoscopic examination and/or treatment and the sedation procedure are distinct medical interventions. If one physician performs the diagnostic or therapeutic intervention and at the same time also carries out the sedation, he or she takes on full responsibility not just for the intervention but also for the sedation and/or analgesia, including monitoring and, if required, restoration of vital functions.

Special theoretical and practical knowledge of sedation and/or analgesia is necessary not just for physicians, but also for supporting nurses and other ancillary staff. A physician cannot perform the invasive intervention and at the same time be monitoring the sedation and/or analgesia procedures. Therefore, all personnel involved in sedation and monitoring should be familiar and trained with the particular sedation technique used, as well as its monitoring and complication management (see point 3.3.1). Whether the physician performing the sedation can be substituted by qualified, specially trained, non-physician personnel (e.g. nurses) in individual cases, has to be decided on a case by case basis by the physician who performs the diagnostic or therapeutic intervention (endoscopist). This physician takes the responsibility, and he or she must perform an assessment on-site under consideration of the structure of the working place, the patients overall condition and the complexity of the procedure (also see point 3.3.3.1). The examining physician (endoscopist) must ensure that such a substituting person (non-physician) is sufficiently qualified and capable of carrying out their tasks appropriately.

The problem of organization/transfer of liability rests on general legal principles based on civil, criminal, and occupational law. The detailed manufacturer's information for the used drug(s), especially in respect of structure quality (e.g. equipment and personnel requirements) must be followed.

3.1. Personal requirements

<table>
<thead>
<tr>
<th>Recommendation grade: A</th>
<th>Personal requirements</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend that the physician who performs and is responsible for the sedation should be experienced in intensive care medicine. He or she should be trained and proficient in the use of sedatives and analgesics. This includes knowledge, recognition, and treatment of expected side effects, including cardiopulmonary resuscitation, maintaining upper airway patency, intubation, and assisted ventilation.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Evidence level: 5 Strong consensus (15/15)

Comment

As in the guidelines of other professional associations [6, 22 – 31, 45, 48, 49, 51, 55, 238, 279 – 282] personal prerequisites for carrying out sedation analgesia include knowing how to deal with an emergency situation by correcting circulation problems and being proficient in endotracheal intubation.

3.2. Education and training courses

<table>
<thead>
<tr>
<th>Recommendation grade: A</th>
<th>Education and training courses</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>As part of quality assurance, we recommend that physicians and non-physician ancillary personnel should participate in specifically designed training for sedation.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Evidence level: 5 Strong consensus (15/15)

Comments

So far, only isolated special training guidelines exist on sedation and management of emergency situations. However, they show that specific training courses, such as those based on simulators, improve physicians' confidence in handling emergency situations [283].

A much more comprehensive training program for non-physician ancillary personnel (nurses) was the subject of several studies using propofol [11, 94]. The German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS) has developed a structured curriculum for a combined one-day team training for physicians and nurses [284]. For training of qualified, non-physician ancillary personnel (nurses or physician assistants) a 3-day curriculum is sponsored by the DEGEA and accredited by the DGVS [284]. In addition, a training curriculum of the ESGE and ESGENA exists since 2012 [19], which was developed in accordance to the German recommendations. All curricula rely on the use of simulators based training.
**3.3. Personnel requirements**

**3.3.1. Education requirements**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Education requirements</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>grade: A</td>
<td>We recommend that the qualification of physicians and nonphysician assistant personnel who are involved in sedation, monitoring, and follow-up should be ensured by periodical participation in structured educational curricula. In addition to theoretical knowledge, these curricula transmit practical competencies including complication management (e.g. simulation training).</td>
<td></td>
</tr>
<tr>
<td>Evidence level:</td>
<td>Strong consensus (16/16)</td>
<td></td>
</tr>
</tbody>
</table>

**Comments**

Annual training course in cardiopulmonary resuscitation (e.g. "megacode" training) for all hospital-nurses is still generally recommended. The training curriculum for sedation is no substitute for these annual courses. How frequently such training curricula for sedation must be held, is quite variable and depends on the individual prerequisites of hospitals or office-based institutions (experience/training of physicians and nurses, number of sedations performed, experience in complication management etc. Therefore, no definite statement about the required frequency of repeating such training curricula can be made in this guideline. The individual frequency (e.g. every 3 years) should be determined in each endoscopy unit as part of the quality management process. Ideally this should be done as a peer-reviewed process and the results should be documented in writing. The DGEA recommends repeated training for nurses every 3 years.

**3.3.2. Monitoring of sedation**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Monitoring of sedation</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>grade: A</td>
<td>For every endoscopy under sedation we recommend that one person should be solely responsible for the performance and monitoring of the sedation. This person should have received special training for the monitoring of sedated patients.</td>
<td></td>
</tr>
<tr>
<td>Evidence level:</td>
<td>Consensus (15/16)</td>
<td></td>
</tr>
</tbody>
</table>

**Comments**

The guideline of the German Society for Anesthesiology and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin, DGAI) [48] states: “Since the examiner is usually unable to watch the patient’s vital functions with sufficient care while doing an endoscopy, it is necessary for a second, specially trained and qualified person to reliably take over the patient monitoring.”

It was shown in several studies that patients with greater comorbidities (ASA class ≥ III) have an increased sedation-risk during emergency endoscopies [20, 179, 285, 286]. Questions regarding the composition of endoscopy teams or persons involved in endoscopic procedures or interventions, respectively, are addressed in the DGVS-guideline “Quality Requirements for Gastrointestinal Endoscopy” (AWMF register no. 021 – 022). There is adherence to the initial statement that one person should be exclusively responsible for the performance and monitoring of the sedation.

Requirements for training are outlined in the training curricula of the European Society of Gastrointestinal Endoscopy (ESGE) and German Society for Endoscopy Assisting Personnel (DEGEA), respectively [19, 284]. In principle, as a prerequisite to training in sedation and emergency management, assistants should have received formal training in a medical profession (nurses, physician assistants etc.).

**3.3.3. Carrying out the sedation**

**3.3.3.1 Requirements for nursing staff or medical assistants who perform propofol sedation (non-physician-administered propofol sedation/NAPS)**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Requirements for the delegation of sedation to non-physician ancillary personnel</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>grade: A</td>
<td>For simple endoscopic examinations of low-risk patients, we recommend that sedation should be initiated by a properly qualified physician.</td>
<td></td>
</tr>
<tr>
<td>Evidence level:</td>
<td>Consensus (10/12)</td>
<td></td>
</tr>
</tbody>
</table>

**Comments**

A number of prospective complication registries [20, 179, 285, 286] showed increased complication rates in patients with an ASA-class of III or higher in the setting of interventional, as well as emergent endoscopies. In a single-center prospective case series of patients undergoing interventional endoscopy (primarily upper gastrointestinal hemorrhages and ERCP) an increased mortality and morbidity was found in those patients with higher ASA classification. The highest risk was found in those receiving emergency interventions.
Comments
For the delegation of the physicians’ tasks, such as the mentioned delegation of monitoring responsibilities, the presence of the responsible physician is mandatory.

<table>
<thead>
<tr>
<th>Recommendation 3.3.3.1c</th>
<th>Requirements for the delegation of sedation to non-physician ancillary personnel</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that the person responsible for monitoring must not have any other tasks during this time.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Consensus (10/12)</td>
<td></td>
</tr>
</tbody>
</table>

Comments
The European guideline addresses this demand more openly as it states that “it is recommended that patients be continuously monitored by a person dedicated” to the sedation [24] and this also holds true for the ASGE guideline [27]. Here, it is noted that (in simple procedures) such person can assume “minor, interruptable tasks”, which do not compromise safety [24, 26]. One possible example is handing the biopsy forceps to the physician (e.g. when a biopsy for H. pylori is performed during gastroscopy). A more comprehensive definition of such short interruptable tasks is not given [26]. However, the German guideline group remains stringent regarding the statement above, as a result of a legal expert opinion from 2006, regarding the delegation of intravenous sedation for endoscopy, by Prof. Dr. Dr. A. Ehlers (see www.dgvs.de; homepage of the German Society for Gastroenterology, Digestive and Metabolic Diseases).

Table 10  Observed cardiorespiratory complication rates during NAPS procedures.

<table>
<thead>
<tr>
<th>author</th>
<th>n</th>
<th>procedures</th>
<th>assisted ventilation</th>
<th>hypotension (BP syst. &lt; 90 mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex DK et al. [14]</td>
<td>2000</td>
<td>EGD and colonoscopy</td>
<td>0.2 %</td>
<td>0 %</td>
</tr>
<tr>
<td>Heuss LT et al. [11]</td>
<td>2547</td>
<td>EGD and colonoscopy</td>
<td>0.002 %</td>
<td>0.08 %</td>
</tr>
<tr>
<td>Sieg A et al. [287]</td>
<td>3641</td>
<td>EGD and colonoscopy</td>
<td>0.14 %</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Rex DK et al. [15]</td>
<td>36743</td>
<td>EGD and colonoscopy</td>
<td>0.2 %</td>
<td>n. i.</td>
</tr>
<tr>
<td>Tohda G et al. [16]</td>
<td>27500</td>
<td>EGD and colonoscopy</td>
<td>0 %</td>
<td>2.0 %</td>
</tr>
</tbody>
</table>

n. i.: not investigated; BP: blood pressure.

3.3.4. Monitoring after the endoscopic procedure

<table>
<thead>
<tr>
<th>Recommendation 3.3.4a</th>
<th>Monitoring after the endoscopic procedure</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that patients should receive continued monitoring with respect to their sedation after the examination is over.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

Comment
Postinterventional monitoring is necessary to detect any sequelae of sedation. The duration of the postinterventional monitoring phase depends on the expected risk [50]. The duration of action and the half-time of the substance used should be taken into account.

Close monitoring of the patient by qualified personnel should be continued until the patient has completely recovered. This should be done irrespective of the substance used, and with the use of a pulse oximeter if thought desirable. Patients can be released from the monitoring area when their vital signs are stable and they are oriented [48]. The vital signs and level of alertness of the patient must be documented upon discharge from the recovery area. Please refer to topic V of this guideline for details regarding the outpatient and inpatient setting.

Table 10  Observed cardiorespiratory complication rates during NAPS procedures.

<table>
<thead>
<tr>
<th>author</th>
<th>n</th>
<th>procedures</th>
<th>assisted ventilation</th>
<th>hypotension (BP syst. &lt; 90 mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rex DK et al. [14]</td>
<td>2000</td>
<td>EGD and colonoscopy</td>
<td>0.2 %</td>
<td>0 %</td>
</tr>
<tr>
<td>Heuss LT et al. [11]</td>
<td>2547</td>
<td>EGD and colonoscopy</td>
<td>0.002 %</td>
<td>0.08 %</td>
</tr>
<tr>
<td>Sieg A et al. [287]</td>
<td>3641</td>
<td>EGD and colonoscopy</td>
<td>0.14 %</td>
<td>0.3 %</td>
</tr>
<tr>
<td>Rex DK et al. [15]</td>
<td>36743</td>
<td>EGD and colonoscopy</td>
<td>0.2 %</td>
<td>n. i.</td>
</tr>
<tr>
<td>Tohda G et al. [16]</td>
<td>27500</td>
<td>EGD and colonoscopy</td>
<td>0 %</td>
<td>2.0 %</td>
</tr>
</tbody>
</table>

n. i.: not investigated; BP: blood pressure.

3.3.4. Monitoring after the endoscopic procedure

<table>
<thead>
<tr>
<th>Recommendation 3.3.4b</th>
<th>Monitoring after the endoscopic procedure</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation Grade: A</td>
<td>We recommend that patients monitoring during the recovery phase should be done by appropriately trained and qualified personnel.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

Comment
The monitoring person must always be present in the recovery area or have the recovery unit in view (telemetric monitoring via cameras etc. is not recommended).

He or she may, however, for example use the telephone or file reports (i.e. perform tasks that can immediately be terminated). This prevents patients from leaving the area on their own while still under the influence of sedation [see verdict of the German Supreme Court (Bundesgerichtshof), reference no. VI ZR 265/02].
3.4. Facility requirements
According to the DGAi guideline [48], “the location and the equipment of the treatment and monitoring area should be geared to the needs of patients with relevant comorbid diseases (ASA grade III and higher).

The recovery unit should be equipped with monitoring devices (pulse oximetry, blood pressure, ECG), drugs, oxygen supply, and a pipeline outlet for suction, together with all the auxiliary material and equipment needed for resuscitation. In case of severe complications, suitable transport to a qualified treatment unit (e.g. intensive care unit) must be possible (e.g. an elevator large enough to take a bed). Currently, no evidence-based data relating to the current recommendations and standards are available. We refer to the guideline “Quality Requirements for Gastrointestinal Endoscopy” (AWMF-register no. 021 – 022) for further details.

<table>
<thead>
<tr>
<th>Recommendation 3.3.4c</th>
<th>Monitoring after the endoscopic procedure</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that sedation should only be carried out in a place that is adequately equipped for monitoring and support of respiratory and cardiovascular function. There should be an additional, separate recovery area.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

Comment
A verdict of the German Supreme Court (reference no. VI ZR 265/02) criticized the seating of patients in the hall outside the treatment room after endoscopy under sedation. The recovery area must be defined as such and the patients must be under constant observation.

3.5. Equipment
3.5.1. Clinical monitoring / standard monitoring

<table>
<thead>
<tr>
<th>Recommendation 3.5</th>
<th>Equipment</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>Mandatory monitoring during endoscopy includes pulse oximetry and blood pressure measurement.</td>
<td></td>
</tr>
<tr>
<td>Recommendation grade: B</td>
<td>In addition, we suggest that ECG monitoring should be done for those patients who have severe heart disease or expected arrhythmic problems.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

Comment
The person in charge of monitoring checks breathing clinically by observation, palpation of thorax and abdominal wall movement and possibly palpation of the expiratory airstream. The endoscopy personnel must have appropriate emergency training and must be proficient in cardiopulmonary resuscitation.

According to the recommendations of various national and international professional associations, pulse oximetry is required for monitoring during all examinations [6, 22 – 31, 34, 44, 47 – 49, 279, 281]. For sedated patients and high-risk patients, continuous blood pressure monitoring and an ECG monitoring are also demanded.

In addition to clinical monitoring, pulse oximetry is required for sedation nowadays (especially since the introduction of quality assurance agreements for colonoscopy in Germany according to §135 SGB V). Oxygen saturation and heart rate are measured continuously. According to a survey in Switzerland in 2012, 100% of endoscopies with propofol sedation were monitored by pulse oximetry [288]. Similar studies in other countries, such as Germany [7, 60 – 62] show comparable rates of such monitoring in 96%-97% of cases. For propofol sedation, blood pressure must also be monitored. The best monitoring devices show oxygen saturation, heart rate, and blood pressure on one screen that can be placed right next to the endoscopy monitor, so that the endoscopist can watch both. Documentation of the measurement parameters is desirable as well. In Germany, the rate of blood pressure monitoring doubled within 3 years after the implementation of the first national sedation guideline in 2008 [7].

3.5.2. Extended monitoring
3.5.2.1. Capnography

<table>
<thead>
<tr>
<th>Recommendation 3.5.2.1a</th>
<th>Capnography</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement</td>
<td>Capnography may be used for early detection of apnea.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 1b</td>
<td>Strong consensus (9/9, 3 votes excluded because of potential conflicts of interest)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation 3.5.2.1b</th>
<th>Capnography</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement</td>
<td>The use of capnography for monitoring of ventilation during endoscopic procedures is associated with earlier detection of episodes of apnea. Whether this improves patient-safety remains unclear.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 1b</td>
<td>Strong consensus (9/9, 3 votes excluded because of potential conflicts of interest)</td>
<td></td>
</tr>
</tbody>
</table>

Comment
Capnography records the concentration of CO2 in the breath. Breathing activity can be graphically displayed. Apnea can be detected earlier than with pulse oximetry by observing the continuous graphic display of the expiratory CO2-concentration on the monitor. The time difference of detection between these methods lies in the range of 1 minute [289 – 294]. Measurement of the absolute CO2-tissue concentration (e.g. by transcutaneous measurement) or in the exhaled air has less of an importance, as compared to capnometric measurements in patients receiving general anesthesia (the main focus should be on the continuous capnographic monitoring).

In a prospective study by Vargo et al. [295] of 49 adults undergoing gastroscopy with therapeutic intent, twice as many apnea episodes were diagnosed by capnography than by pulse oximetry or clinical observation. In a retrospective study by Koniaris et al. [296] 4846 patients were monitored without and 600 patients with capnography during endoscopy. In the patient group not monitored with capnography, there was a tendency toward oversedation, especially in older patients and those undergoing long examinations, although this was not significant.

In the capnography group no case of oversedation was reported. In a prospective, randomized study by Qaedaer et al. [297] 247 patients were sedated with benzodiazepines and opioids for ERCP or EUS, respectively. The study showed a significant reduction in the rate of hypoxemia as detected by pulsoximetry (pO2 <90%), as well as in the rate of pO2 desaturations to less

than 85% when capnography was used during sedation. Another randomized, multicentric study [298] confirmed these results in 760 patients who received propofol sedation for colonoscopy. Overall, a number of studies demonstrated [297–299] that approximately two-thirds of all apnea episodes will be missed by using pulseoximetry alone. However, none of these studies have shown that the earlier detection of apnea episodes (and the reversal by appropriate measures such as increasing the oxygen supply, use of the Esmarch grip – also called jaw-thrust maneuver – or tactile stimulation of the patient etc.) improves outcomes with regards to hard clinical endpoints (such as death, neurologic deficits, intensive care measures or need for endotracheal intubation), when compared to the usual monitoring (pulseoximetry, blood pressure and ECG). All studies were not adequately powered to answer these questions [297–299]. In addition, it must be noted that the advantages of capnography over pulseoximetry were only demonstrated for longer lasting endoscopic procedures (duration > 10 minutes) so far [289, 291, 294, 300, 301]. On the basis of currently available data, routine use of capnography generally cannot be recommended. However, its use may be useful in selected cases during long lasting procedures.

### 3.5.2.2. EEG monitoring

**Recommendation**

**EEG-Monitoring**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>EEG-Monitoring</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statement</strong></td>
<td>A benefit of EEG monitoring with respect to relevant parameters in gastrointestinal endoscopy has not been demonstrated.</td>
<td></td>
</tr>
<tr>
<td><strong>Evidence level: 1b</strong></td>
<td>Strong consensus (9/9, 3 votes excluded because of potential conflicts of interest)</td>
<td></td>
</tr>
</tbody>
</table>

**Comment**

The electric activity of the human brain correlates with the level of alertness and cerebral perfusion. For this reason, measurement of the electrical activity of the brain via EEG can be useful during general anesthesia or deep sedation. Bispectral monitoring is used to evaluate sedation depth in intensive care medicine and in surgical patients. A pilot study described bispectral monitoring as part of a closed monitoring cycle for the continuous infusion of propofol in 16 patients sedated for colonoscopy [129]. However, the majority of subsequent studies [302–311] failed to demonstrate a significant decrease in the use of propofol, mostly in the setting interventional endoscopy. In addition, BIS-Monitoring mostly did not reduce surrogate parameters of patient safety (hypoxemia, hypotension) [306]. Furthermore, some studies reported insufficient and untimely evaluation of sedation depths of the patients, when clinical evaluation of sedation depth was compared to BIS-Monitoring [308]. However, when compared to another method of EEG monitoring, namely the detection of auditory evoked potentials, BIS-Monitoring was superior with regards to the assessment of sedation depth under propofol sedation [312].

In a randomized, controlled study, a significant reduction of the propofol dose for ERCP procedures was possible with the use of another EEG monitoring technique, the Narcotrend system [167]. However, this reduction of the propofol dose during sedation for ERCP was not confirmed in a more recent, randomized study using the Narcotrend system [313], although a lower rate of hypoxemia and hypotension was noted when Narcotrend monitoring was applied.

In summary, these studies mostly did not demonstrate significant advantages for the use of EEG monitoring in the setting of gastrointestinal endoscopy. Therefore, the use of such monitoring systems currently cannot be recommended.

#### 3.5.2.3. Sleep apnea screening prior to endoscopic procedures with sedation

**Comments**

The presence of obstructive sleep apnea increases the possible risks of sedation [314]. A case-control study included 231 patients who received propofol sedation for ERCP or EUS. This study showed that 43% of patients in the USA had sleep apnea, when evaluated by the so called “stop-hang questionnaire” prior to their endoscopic procedure. In the same study, an increased rate of hypoxemia with a need of ventilatory support measures was found in these patients [315]. More studies are required to confirm these findings in larger collectives.

### 4. Topic IV: Informed consent/prerequisites for performance of sedation/preservation of vital functions/clinical monitoring/emergency management

#### 4.1. Informed consent

**Recommendation**

<table>
<thead>
<tr>
<th>Informed consent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation grade:</strong> A When patients are being given information about the endoscopy, we recommend that they should also be told about side effects of sedation, especially anterograde amnesia and the possibility of restricted psychomotor capability after the sedation.</td>
</tr>
</tbody>
</table>

**Evidence level: 5** Strong consensus (12/12)

#### 4.1.1. General and legal aspects

The adjudication on medical interventions, the physician’s duty to inform, and patient information are very complex. According to permanent adjudication of the German Federal Supreme Court, every medical intervention constitutes a personal injury offense according to paragraph 223 ff. StGB, 823 I BGB [316]. The consent (“informed consent”) that is necessary for these procedures is only valid if the patients have been given sufficient information and are competent to exercise their right to self-determination. If patients are not competent to give their consent (e.g. children, severely mentally retarded persons), the physician must give the information to their representative (guardian, agent for health care matters, or other responsible person) [317].

To be competent to give their consent, patients must also be able to understand the implications of the intervention. Aside from the legal background, a well-performed consent procedure with information and explanation increases patient satisfaction [51]. Patients should receive the information even if they have already undergone a similar endoscopic intervention and they claim to have been given plenty of information the first time. Many patients are not good judges of their own level of information and understanding. Moreover, information received earlier may have been forgotten or details might remain misunderstood.
4.1.2. Informed person

<table>
<thead>
<tr>
<th>Recommendation 4.1.2</th>
<th>Informed person</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that a competent and experienced physician should provide information about the procedure to the patient in a form he or she can understand.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (12/12)</td>
<td></td>
</tr>
</tbody>
</table>

**Comments**
The physician must be competent and experienced in sedation. Informing the patient, who is usually uneducated in medicine, must be done gently and comprehensibly. It is important that the patient understands the impact and implications of the intervention, and the physician must make sure that the patient does have this understanding. Delegation, e.g. to a nurse, is not permissible by law in Germany.

4.1.3. Informed consent procedure

<table>
<thead>
<tr>
<th>Recommendation 4.1.3</th>
<th>Informed consent procedure</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>The foundation of the consent procedure should be a discussion between the physician and patient. We recommend that the content and range of the discussion should be documented. The patient should receive the information within appropriate time.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (12/12)</td>
<td></td>
</tr>
</tbody>
</table>

**Comments**
The information about and discussion of the proposed procedure must be conducted in a patient-centered manner, i.e., dependent on the patient’s ability to comprehend and on how much information he or she wants. Standardized patient information forms can be used in addition to help convey the information and for documentation purposes, but they are not a substitute for the personal discussion. Written documentation is essential, because according to civil law physicians have to be able to prove that the information procedure was followed correctly [316].

Patients should not be told that they may waive their right to information, and should certainly not be urged to do so. However, if they refuse the information of their own accord, this refusal should be documented and signed by the patient [317]. The importance of the patient’s right to decide dictates that they should have enough time to give their consent before the procedure [318] and this involves an informed consent process that starts early enough for their decision to be made without time pressure. The right time for the information interview depends on the individual situation. Even in an emergency, responsive patients should have as much explained to them as time permits before giving their consent [317]. Altogether, the information procedure should proceed as soon as possible; ideally it should be started when the appointment for the endoscopic intervention is made [317].

4.1.4. Content of the patient information interview

<table>
<thead>
<tr>
<th>Recommendation 4.1.4</th>
<th>Content of the patient information interview</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that the discussion should include information on the preparation for sedation, various sedation methods, and their possible complications. It should also include making the patient aware that it is possible to perform the intervention without sedation.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (12/12)</td>
<td></td>
</tr>
</tbody>
</table>

**Comments**
In almost all types of endoscopic interventions, adverse effects of sedation are responsible for at least 50% of complications [319]. Complications of sedation (aspiration, arterial hypotension, bradycardia, apnea, etc.) are therefore typical complications and must be discussed with the patient in detail. The patient should be informed about the typical sedation risks irrespective of complication rates. Severe atypical risks must also be discussed. The physician should advise the patient on the “if and how” of sedation. In addition to sex and age, it is wise to take into account the patient’s level of anxiety/fear when setting the sedation dose, because these three factors have been shown to predict the patient’s cooperation during the intervention, and on his or her satisfaction afterwards [153, 320, 321]. On the whole, the tendency should be to offer sedation to younger and more anxious patients as well as to women [34, 37, 50, 65, 153]. However, as sedation usually seems necessary to avoid unwanted involuntary patient movement, especially during long examinations and difficult interventions (e.g., ERCP, difficult polypectomy), this too should be explained to the patient [49, 138, 322, 323]. If the patient suffers injury after withholding consent to a necessary intervention as a result of an information interview that was too “tough,” the physician is responsible [324].

Sedation can be refused if either the patient has a very high ASA risk class [51] or if the hospital and personnel are not adequately equipped to perform sedation according to the required standard. The physician must then explain to the patient why sedation is not possible. Whether patients should be informed of the possibility of dying as a result of the intervention is debated. In two judgments of the Regional Appeal Court Stuttgart, Germany [324, 325] and one of the Regional Appeal Court Zweibrücken, Germany [326] it was required that the patient be gently informed before colonoscopy of the possibility of dying as a result of perforation. In another case, it was required that the patient be informed that she could die as a consequence of an ERCP.

In the case of very urgent or emergent procedures the extent of information can be adjusted to the situation.

4.1.5. Safety information (patient do’s and don’ts after endoscopic sedation)

<table>
<thead>
<tr>
<th>Recommendation 4.1.5</th>
<th>Safety information</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that patients should be informed about what is safe for them to do or not to do after sedation and discharge from outpatient care, and should be given an information leaflet.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (12/12)</td>
<td></td>
</tr>
</tbody>
</table>
The next day was more effective than a written reminder [327].

4.2. Requirements for carrying out sedation

Recommendation 4.2 Requirements for carrying out sedation 2014 (new)

Recommendation grade: A A permanent intravenous access is a prerequisite for sedation and/or analgesia.

Evidence level: 2b Strong consensus (12/12)

Comment
Peripheral venous access is a fundamental requirement for the administration of sedatives. A comparative study by Smith et al. [328] investigated the functionality of a butterfly versus indwelling catheters 1 hour after endoscopy, a time when most benzodiazepines and opioids have not even reached their half-time. Only 44% of the butterflies, but 98% of the indwelling catheters, were still functional.

4.3. Protection of vital functions

Recommendation 4.3 Protection of vital functions 2008 (unchanged)

Recommendation grade: A We recommend that sedated patients should prophylactically receive oxygen via a nasal cannula.

Evidence level: 2b Strong consensus (12/12)

Comment
Incidents due to sedation are usually cardiopulmonary events [319]. These make up about half of all complications in endoscopy, and depending on the patient’s risk level can also occur during gastroscopy without sedation [329]. Earlier publications reported a 5% incidence of cardiopulmonary events with benzodiazepine use [179] and recent studies with propofol report an incidence of 0.1%, respectively [20].

Older patients in particular are at risk of hypoxia under sedation [12, 151].

Prophylactic oxygen administration via a nasal cannula can significantly reduce the frequency of hypoxic events [330 – 333]. However, there are also indications that prophylactic oxygen administration can delay the early detection of hypoxic events using pulse oximetry [50]. Despite this fact, the authors consider the „safety-buffer“-effect of prophylactic oxygen administration to be more important than its possible disadvantage of a delayed detection of hypoxemia.

4.4. Management of sedation-related emergencies

4.4.1. Hypoxemia

Hypoxia is present if oxygen saturation declines below 90% as measured with a pulse oximeter. Most pulse oximeters indicate the level of oxygen saturation by the pitch of the impulse. Thus, if the tone frequency becomes lower or the digitally visible oxygen saturation drops continuously, counteractive measures must be taken. Initially this means asking patients in a loud voice and stimulating them by touch to breathe deeper. If the patients are on their back their chin can be pulled up using an Esmarch grip (also called jaw-thrust maneuver), allowing them to breathe freely again through the mouth. Placement of a Guedel- or a Wendl-tube may be of help. In addition, the oxygen flow should be increased (e.g. from 2 to 4–5 L/min) and the application of sedatives should be paused.

Should the patient fail to develop spontaneous breathing with these measures, ventilatory support must be performed via bag-mask. Under given circumstances, the airway should be finally secured instrumentally (e.g. endotracheal intubation). If the patient was sedated with benzodiazepines, the antagonist flumazenil should immediately be given intravenously (naloxone is used as an antagonist for opioids) in addition. This often makes ventilation unnecessary. Otherwise the procedure for hypoxia under benzodiazepines is the same as for propofol.

4.4.2. Cardiac arrhythmias

4.4.2.1. General considerations

Endoscopic intubation of the colon is enough by itself to cause excessive activation of the sympathetic autoregulatory nervous system in unsedated patients [334], thus increasing the probability of cardiovascular events. The influence on heart rate variability is enhanced further by sedation [335]. However, cardiopulmonary events can also be observed in unsedated patients during gastroscopy [336, 337].

4.4.2.2. Tachyarrhythmias

There are only a few reports of occurrences of supraventricular or ventricular tachyarrhythmias during endoscopic procedures [338 – 341]. In emergencies, class Ia–IV antiarrhythmics and a defibrillator should be kept at hand [342 – 344].

4.4.2.3. Bradyarrhythmias

Occasionally bradycardia occurs, especially during colonoscopy with or without sedation. The incidence is reported at 0.5% [287]. However, drug intervention was only necessary in one third of the patients. The intervention consists of giving 0.5 mg of atropine intravenously This can be repeated if necessary up to a dose of 3 mg, and/or adrenaline 0.02 – 0.1 mg can be given intravenously. In life-threatening situations cardiopulmonary resuscitation should be done [342 – 344].

4.4.3. Arterial hypotension

The incidence of arterial hypotension during colonoscopy varies between 0.3% [287] and 3%–19% depending on the definition [334]. In the case of arterial hypotension, volume resuscitation with cristalloid infusion should be the initial intervention, followed by administration of vasoactive substances if hypotension persists. Prophylactic infusion in all colonoscopies is not recommended [345] but may well be a good choice in older dehydrated patients.
patients. Prophylactic intravenous administration of crystalloid fluids can also be useful for long procedures carried out under propofol sedation, because of the pronounced blood pressure-reducing properties of propofol.

### 4.4.4. Myocardial ischemia

Myocardial ischemia may occur during endoscopy with or without sedation. In a prospective study ST-segment depression was described in 7% of patients undergoing colonoscopy. However, three-quarters of these events occurred before the actual endoscopy [346]. ST-depression can be significantly reduced by oxygen supplementation during endoscopy [332]. There is one published report of a case of myocardial infarction during colonoscopy [230].

### 4.4.5. Rare events during sedation

Allergic reactions are rarely observed in patients who are sedated for endoscopy. In 80,000 colonoscopies, one allergic reaction to midazolam was observed [319].

Localized pain at the injection site, especially in small-caliber midazolam was observed [319]. In 80,000 colonoscopies, one allergic reaction to midazolam was observed [319]. Localized pain at the injection site, especially in small-caliber midazolam was observed [319]. In 80,000 colonoscopies, one allergic reaction to midazolam was observed [319].

### 5. Topic V: Quality goals: internal quality assurance/discharge criteria/fitness for road traffic/ability to work/documentation/benchmarking

#### ▼ 5.1. Internal quality assurance

<table>
<thead>
<tr>
<th>Recommendation 5.1</th>
<th>Internal quality assurance</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that there should be a written and easily comprehensible procedure plan for carrying out sedation and/or analgesia, monitoring the patient after sedation, the criteria for discharge to the outpatient or general inpatient area, and the management of any complications. The respective responsibilities should be clearly defined.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

#### 5.2. Discharge criteria

##### 5.2.1. Patient instructions

<table>
<thead>
<tr>
<th>Recommendation 5.2.1</th>
<th>Patient instructions</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>We recommend that patients should have an accompanying person when they are being discharged. They should also receive written instructions, including a 24-hour emergency telephone number in case of complications.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

#### 5.2.2. Minimum criteria for discharge

<table>
<thead>
<tr>
<th>Recommendation 5.2.2</th>
<th>Minimum criteria for discharge</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>The use of minimum criteria for discharge after sedation and/or analgesia from the recovery area is sensible. The use of a standardized discharge checklist is recommended.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation 5.2.2b</th>
<th>Minimum criteria for discharge (outpatients)</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>For outpatients, we recommend that the discharge criteria listed in Table 11 (modified according to Ead et al [351]) should be met and documented.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation 5.2.2c</th>
<th>Minimum criteria for discharge (inpatients)</th>
<th>2014 (new)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: A</td>
<td>For inpatients, we recommend that the discharge criteria listed in Table 12 should be met and documented.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 5</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

#### 5.2.3. Use of scoring systems for discharge

<table>
<thead>
<tr>
<th>Recommendation 5.2.3</th>
<th>Use of scoring systems for discharge</th>
<th>2008 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation grade: B</td>
<td>We suggest that scoring systems (e.g. Aldrete score) should not be the sole basis for decisions as to whether patients can be discharged, because they do not evaluate psychomotor function.</td>
<td></td>
</tr>
<tr>
<td>Evidence level: 1b</td>
<td>Strong consensus (13/13)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 11 Minimum criteria for discharge after outpatient endoscopy with sedation/analgesia (modified according to Ead H. [351]).

- stable vital signs for at least 1 hour
- alert and oriented to time, place and person (for patients with initially reduced mental state, the initial state must be reached)
- complete (or near-complete) resolution of pain
- ability to get dressed independently and to walk with assistance (for patients with initially reduced functional/mental state, the initial state must be reached)
- discharge with an accompanying, vested adult
- written and verbal instructions, regarding diet, activities, medications, participation in traffic, judgement ability, typical signs of complications, follow-up appointments and a phone number to be called in case of complications.

### Table 12 Transfer after inpatient endoscopy with sedation/analgesia.

minimum criteria for transfer from the recovery room to the hospital ward after endoscopy with sedation/analgesia (according to DGI 2009 [352]):

- level of alertness: awake or same as prior to the endoscopic procedure
- protective reflexes present or same as prior to the endoscopic procedure
- sufficient spontaneous breathing without treatment or same as prior the endoscopic procedure
- stable cardiac circulation without therapy or same as prior the endoscopic procedure.
Comment

Various scoring systems devised for the assessment of postsurgical recovery have been used after sedation for endoscopy, the most popular systems being the modified Aldrete score (for early or phase I recovery) and the postanesthetic discharge scoring system (PADSS, for intermediate or phase II recovery) [353, 354]. Despite limitations of PADSS, inherent to its focus on surgical procedures (e.g., one of the five criteria in this system is “surgical bleeding”), it has been shown to allow safe discharge after digestive endoscopy in a relatively small prospective study [355]. A checklist (Table 11) is proposed to assess home-readiness of patients after outpatient endoscopy under sedation (modified according to Ead et al [351]). At a minimum, criteria proposed by the ASA should be met [44]. Commonly used tests to evaluate psychomotor functions are the coherent response to questions, ability to stand on one foot, and ability to walk in a straight line for 5 m without instability.

The use of the modified Aldrete score [356] only allows statements about patients’ vital functions, but not about their psychomotor performance, which may be considerably impaired even when a maximum score is obtained [357]. Even if patients have stable vital signs and seem sufficiently awake after sedation, it is known that after the use of intermediate–acting substances (e.g., midazolam, meperidine) patients have a prolonged phase of amnesia and impairment of reflexes and judgement. Patients undergoing colonoscopy, who are sedated with a frequently employed combination of midazolam plus an opiate, show impairments of reaction time, fine motor skills, and perception for at least 30 minutes after the procedure.

Study data show that the remaining after-effects of midazolam impair various aspects of psychomotor function for at least 1 hour after administration [357, 358]. Midazolam seems to be the main reason for the persistent impairment of psychomotor function after sedation in these cases [359]. A study by Thapar et al. [359] comparing the effect of midazolam with fentanyl and propofol gave similar results.

5.3. Fitness for road traffic

5.3.1. Roadworthiness

The recommendations of various professional associations claimed until 2008 that patients should not participate actively or passively in road traffic for 24 hours [47–49] after sedation for gastrointestinal endoscopy. However, due to a lack of evidence, this time-frame appears to be too broadly defined, especially with the use of ultra-short acting substances, such as propofol or remifentanil.

A whole series of studies by Korttilla et al. [360–362] dating back to the 1970s already investigated psychomotor function after sedation with various drugs. These showed that even when benzodiazepines were used at higher doses (diazepam 0.45 mg/kg body weight), psychomotor functions were restored after 10 hours [361]. Only when meperidine 75 mg i.m. was used, psychomotor functions were impaired for up to 12 hours. In this case the recommendation not to drive for 24 hours seems justifiable – but meperidine 75 mg i.m. is no longer routinely used in endoscopy [360].

The normalization of psychomotor functions on the day of the exam is primarily dependent on the half-time of the used substance(s), whereby short acting substances have an advantage (see appendix; Table 10, page 93–95; assessed literature quality results 2008).

A study by Riphaus et al. [10] of 98 patients compared sedation with propofol versus midazolam/meperidine for gastroscopy and colonoscopy. No impairment of psychomotor function (tested using a driving simulator) was seen 2 hours after sedation with propofol, as compared to midazolam/meperidine. These results were confirmed in a similar study by Horiuchi et al. [363]. However, a very low mean dose of propofol was used (around 40 mg) in this study, which does not adequately reflect clinical reality in Germany [7, 62].

In another study by Horiuchi et al. [364], 92% of 400 patients drove themselves home after low-dose propofol sedation (dose mostly < 50 mg in Asian patients) for gastroscopy without causing a traffic accident. Roadworthiness appears to recover quickly with the use of short-acting hypnotics (e.g., propofol), depending on their respective half-lives. Nevertheless, based on the available studies by Riphaus et al. [10] in 98 probands and Horiuchi et al. [365] in 48 probands (very small numbers of cases), the use of public transportation (even without an escort) may be considered, at the most. So far, internationally, no group has addressed the issue of operating a motorized vehicle/bicycle in large field studies. Such studies are required in the future.

As a result of the lack of evidence, regarding roadworthiness after propofol sedation and in consideration or patient safety aspects, the guideline group has adapted the guideline by following the recommendations of the most recent evidence- and consensus-based ESGE-guideline of non-anesthesiologist administration of propofol for GI endoscopy [24].
5.4. Documentation

5.4.1. General considerations
Structured documentation is part of a quality process and may help to improve compliance with sedation guidelines [366]. Documentation is an essential part of patient care should be done in all phases of the intervention (it may also provide a record of correct administration of sedation in the event of medicolegal investigations).

This includes

► Preinterventional evaluation of the patient
► Informed consent
► Monitoring during the intervention
► Patient recovery
► Patient discharge

Ideally, a standardized documentation form should be used because this improves documentation compliance [366].

5.4.2. Inability to work

A general or precise recommendation cannot be given on how long a patient is unfit for work after the use of sedatives and analgesics for gastrointestinal endoscopy. As a general guide, an interval of 24 hours is recommended [47 – 49]. However, this interval is not based on any evidence. For persons with a working place of hazardous nature (e.g. crane operators) a longer absence from work (e.g. 48 hours) is recommended after sedation.

5.5. Benchmarking

A "benchmark" in the transferred sense means competitive comparison of the orientation parameter (characteristic) or all comparative parameters for relative evaluation of a product, service, or organization unit. The most important benchmark for sedation during gastrointestinal endoscopy should be complication rates that are as low as possible. A nationwide survey of all endoscopic examinations and associated complications with and without sedation is desirable. The complications mentioned above should be centrally recorded and evaluated, so that subsequent procedures can be optimized. Some projects of this kind have already been launched (e.g. study of the German Association of Gastroenterologists in Private Practice, complication registry of Helios-hospitals in Germany etc.).
Conflict of interest: Scientific support (Capnography device) from Oridion Medical, Israel.

TW: Speakers honoraria from Falk Foundation, Germany.

References

7 Riphaus A, Geist F, Wehrmann T. Endoscopic sedation and monitoring practice in Germany: re-evaluation from the first nationwide survey 3 years after the implementation of an evidence and consent based national guideline. Z Gastroenterol 2013; 51: 1082–1088
14 Rex DK, Oveler C, Kinser K et al. Safety of propofol administered by registered nurses with gastroenterologist supervision in 2000 endoscopic cases. Am J Gastroenterol 2002; 97: 1159–1163
19 Dumonceau JM, Riphaus A, Beilenhoff U et al. Update S3-guideline: TW: Speakers honoraria from Falk Foundation, Germany. Scientific support (Capnography device) 2008; 240: 1143–1151
22 Vargo J, Delege MH, Feld AD et al. Multisociety sedation curriculum for gastrointestinal endoscopy. Gastroenterology 2012; 143: e18–e41
30 Statement on the use of sedation and analgesia in the gastrointestinal endoscopy setting. Gastroenterol Nurs 2008; 31: 249–251

Riphaus A et al. Update S3-guideline: “sedation... Z Gastroenterol 2016; 54: 58–95


VanNatta ME, Rex DK. Propofol alone titrated to deep sedation versus propofol in combination with opioids and/or benzodiazepines and titrated to moderate sedation for colonoscopy. Am J Gastroenterol 2006; 101: 2209–2217


Vargo JJ. See one, do one, teach one. Gastrointest Endosc 2008; 67: 419–421


Kulling D, Orlandi M, Iaunen W. Propofol sedation during endoscopic procedures: how much staff and monitoring are necessary? Gastrointest Endosc 2007; 66: 443–449

Vargo JJ. Procedural sedation and obesity: waters left uncharted. Gastrointest Endosc 2009; 70: 980–984

Department of Health and Human Services. Petition denial for request for removal of labeling for Diprivan (propofol); 2010


Ng JM, Kong CF, Nyam D. Patient-controlled sedation with propofol for colonoscopy. Gastrointest Endosc 2001; 54: 8–13


Egan TD, Kern SE, Johnson KB et al. The pharmacokinetics and pharmacodynamics of propofol in a modified cyclodextrin formulation (Captisol) versus propofol in a lipid formulation (Diprivan); an electroencephalographic and hemodynamic study in a porcine model. Anesth Analg Analg Analg 2003; 97: 72–79, table of contents


Macken E, Gevers AM, Hendricks A et al. Midazolam versus diazepam in lipid emulsion as conscious sedation for colonoscopy with or without reseal of sedation with flumazenil. Gastrointest Endosc 1998; 47: 57–61


Cantar D, Baldridge ET. Sedation with meperidin and diazepam for upper gastrointestinal endoscopy precludes the need for topical anaesthesia. Gastrointest Endosc 1986; 32: 339–341


Lam, for outpatient colonoscopy: analgesia, sedation, and safety. Dig Sci 2006; 51: 1946


Bartelsman JF, Sars PR, Tytgat GN. Flumazenil used for reversal of midazolam-induced sedation in outpatient gynecology. Gastroenterol Endosc 1990; 36: 59–512


Robertson DJ, Jacobs DP, Mackenzen TA et al. Clinical trial: a randomized, study comparing meperidine (pethidine) and fentanyl in adult gastrointestinal endoscopy. Aliment Pharmacol Ther 2009; 29: 817–823

Kapila A, Glass PS, Jacobs JR et al. Measured context-sensitive half-times of remifentanil and alfentanil. Anesthesiology 1995; 83: 968–975


Riphaus A et al. Update S3-guideline: *sedation... Z Gastroenterol 2016; 54: 58–95
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.
Riphaus A et al. Update S3-guideline: sedation... Z Gastroenterol 2016; 54: 58–95
340 Jaca IJ, Desai D, Barkin JS. Paroxysmal supraventricular tachycardia after administration of glucagon during upper endoscopy. Gastrointest Endosc 2002; 56: 304
344 Reanimation – Empfehlungen für die Wiederbelebung: Mit 14 Tabelle.
enn: Dt. Ärzte-Verl; 2011; 5 Aufl
360 Korttila K, Linnaola M. Psychomotor skills related to driving after intramuscular administration of diazepam and meperidine. Anesthesiology 1975; 42: 685 – 691

Riphaus A et al. Update S3-guideline: “sedation... Z Gastroenterol 2016; 54: 58–95