Updated S3 Guideline “Sedation for Gastrointestinal Endoscopy” of the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS)

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Key words
endoscopy, analgesics, sedatives, anesthesia, monitoring, surveillance, adjuvant drug

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* Both authors contributed equally to the preparation of the manuscript
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1 Information on the Guideline

1.1 Publisher

1.1.1 Lead Professional Society

German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS)

1.2 Scope and Purpose

Since the introduction of the first S3 guideline on sedation in gastrointestinal endoscopy in 2008, the use of sedation in gastroenterological endoscopies, in particular of propofol, has become established. It can now be regarded as the standard in gastroenterological practice. In several surveys, also for Germany, a proportion of more than 80% sedated examinations has been demonstrated.

1.2.1 Key Points

A key point is the differentiated indication: the necessity of sedation in gastroenterological endoscopy is not obligatory for all procedures but depends on the type of examination, the duration of the examination, the complexity and invasiveness of the examination, and patient characteristics. However, sedation contributes significantly to the comfort of the examination for both the patient and the endoscopist. It often creates the prerequisite for a successful and low-risk examination, especially in the case of complex therapeutic interventions. The experts considered the review and updating of the guideline to be particularly important to guarantee a successful and low-risk examination.

1.3 Goal Orientation of the Guideline

The goal of the guideline is its easy application in the practice of internal medicine, surgery, gastroenterology, anesthesiology, intensive care, and endoscopy/imaging. In addition, the guideline is intended to provide a road map for common decisions.

The target patient group is adult patients who require sedation for gastrointestinal endoscopy.

1.4 Care Areas

Outpatient and inpatient care, internal medicine, surgery, gastroenterology, anesthesiology, intensive care, and endoscopy/imaging.

1.5 User Target Group/Addressees

The guideline is aimed at the following professional groups involved in diagnosis and therapy: gastroenterologists, surgeons, anesthetists, intensive care specialists, general and visceral surgeons, and endoscopists, as well as patient representatives, patients, and relatives, and serves as information for internists and service providers (health insurance companies and pension insurance companies).

1.6 Composition of the Guideline Group: Stakeholder Participation

The guideline was developed by the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS), which commissioned Prof. Till Wehrmann, Wiesbaden, and Prof. Andrea Riphaus, Frankfurt, as coordinators. PD Dr. Petra Lynen Jansen and Pia Lorenz, DGVS office, Berlin, were methodologically responsible. Prof. Kopp, Work Group for Scientific Medical Professional Societies e.V. (AWMF), Marburg, provided methodological advice and moderated the consensus conference as a neutral guideline expert. Mr. Torsten Karge, CGS Usergroup, Berlin, was available for the guideline portal and provided technical support for the consensus conference.

The guideline project was advertised in the Journal of Gastroenterology and published on the AWMF website, so that other professional societies/representatives could register for participation. The relevant professional societies and patient groups were contacted and asked to nominate their representatives.

1.7 Representatives of the Guideline Group: Participating Professional Societies

- German Society for Endoscopy Assisting Personnel (Deutsche Gesellschaft für Endoskopie-Assistenzpersonal, DEGEA) U. Beilenhoff (Ulm)
- German Society for Anesthesia and Intensive Care Medicine (Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin...
1.8 Representatives of the Guideline Group: Participation of Patients

S. In der Smitten (Berlin) of the German Crohn’s Disease/Ulcerative Colitis Association (Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung, DCCV)

In addition to the steering group (Table 1), five working groups (WGs) were formed, each headed by a leader (Table 2). In addition to gastroenterologists, internists, surgeons, anesthesiologists, intensive care physicians, endoscopists, and patient representatives participated in the working groups.

2 Methodologic Procedure

2.1 Evidence Synthesis

2.1.1 Fundamentals of the Methodology

2.1.1.1 Scheme of Evidence Rating

For recommendations reviewed in this update for which no new relevant literature was found, the evidence levels of the associated studies were retained. If there was new relevant literature, it was assessed and added to the guideline report in the appendix. The literature review was conducted according to the Oxford Centre for Evidence-Based Medicine 2011 evidence classification (Table 4). The details of the search, selection, and evaluation of the evidence are presented in the guideline report.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Steering Committee.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Site</td>
</tr>
<tr>
<td>A. Riphaus</td>
<td>Frankfurt</td>
</tr>
<tr>
<td>T. Wehrmann</td>
<td>Wiesbaden</td>
</tr>
<tr>
<td>A. J. Eckardt</td>
<td>Wiesbaden</td>
</tr>
<tr>
<td>P. Klare</td>
<td>Hausham</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Members of the Guideline Group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>WG 1: Indications/goals/known risks/patients/quality goals</td>
<td>U. Rosien, Hamburg (DGVS)</td>
</tr>
<tr>
<td>WC-head</td>
<td>S. In der Smitten, Berlin (DCCV)</td>
</tr>
<tr>
<td>WG-members</td>
<td>F. Wappler, Köln (DGAI)</td>
</tr>
<tr>
<td>WG 2: Pharmacology</td>
<td>P. H. Tonner, Leer (Ostfriesland) (DGA)</td>
</tr>
<tr>
<td>WC-head</td>
<td>M. Jung, Frankfurt am Main (DGVS)</td>
</tr>
<tr>
<td>WG-members</td>
<td>D. Schilling, Mannheim (DGVS)</td>
</tr>
<tr>
<td>WG 3: Structure quality</td>
<td>T. Wehrmann, Wiesbaden (DGVS)</td>
</tr>
<tr>
<td>WC-head</td>
<td>H. Allescher, Garmisch-Partenkirchen (DGE-BV)</td>
</tr>
<tr>
<td>WG-members</td>
<td>A. Behrens, Berlin (DGVS)</td>
</tr>
<tr>
<td>WG 4: Process quality</td>
<td>S. von Delius, Rosenheim (DGVS)</td>
</tr>
<tr>
<td>WC-head</td>
<td>U. Beilenhoff, Ulm (DEGEA)</td>
</tr>
<tr>
<td>WG-members</td>
<td>H. Bitter, München (GRPG)</td>
</tr>
<tr>
<td>WG 5: Result quality</td>
<td>P. Heidemann, Schwerin (DGVS, Vertreterin niedergelassenen Ärzte/Ärzte)</td>
</tr>
<tr>
<td>WC-head</td>
<td>A. Riphaus, Frankfurt (DGVS)</td>
</tr>
<tr>
<td>WG-members</td>
<td>A. Schaible, Heidelberg (DGAV/CAES)</td>
</tr>
<tr>
<td>Coordinator</td>
<td>A. J. Eckardt, Wiesbaden (DGVS)</td>
</tr>
<tr>
<td>Coordinator</td>
<td>P. Klare, Hausham (DGVS)</td>
</tr>
<tr>
<td>Coordinator</td>
<td>A. Riphaus, Frankfurt (DGVS)</td>
</tr>
<tr>
<td>Coordinator</td>
<td>T. Wehrmann, Wiesbaden (DGVS)</td>
</tr>
<tr>
<td>Coordinator</td>
<td>I. Kopp, Marburg (AWMF)</td>
</tr>
<tr>
<td>Coordinator</td>
<td>P. Lorenz, Berlin (DGVS)</td>
</tr>
</tbody>
</table>
2.1.1.2 Scheme of the Recommendation Grading

When converting the strength of evidence into the recommendation strength, the recommendation grade could be upgraded or downgraded compared to the evidence grade. Reasons for this could be, for example, the lack of consistency of the study results, the relevance of the endpoints and effect sizes, the benefit–risk ratio, patient preference, or feasibility. Grading of the recommendation was also done using the wording “we recommend”, “we suggest”, or “may be considered” (Table 3; German: “soll”, “sollte”, or “kann”). The consensus strength was determined according to Table 3.

2.1.1.3 Statements

Statements are presentations or explanations of specific facts or issues without an immediate call for action. They are adopted in a formal consensus process, as in the case of recommendations, and can be based either on study results or on expert opinions.

2.1.1.4 Expert Consensus

Recommendations for which no systematic literature search was conducted or for which no literature was available after extensive research are referred to as expert consensus. The recommendation grading results exclusively from the wording used (we recommend/we suggest/may be considered) according to the grading in Table 3.

2.2 External Review and Adoption

2.2.1 Adoption by the Boards of the Issuing Professional Societies/Organizations

The complete guideline was reviewed and agreed upon by the executive boards of all participating professional societies and was available as a consultation version for the professional public for four weeks from January 13 to February 12, 2023, for comments on the DGVS website and at the AWMF. Comments were solicited via the DGVS Newsletter. The proposed changes are presented in the guideline report.

2.2.2 Editorial Independence and Funding of the Guideline

The preparation of the guideline was editorially independent. The DGVS financed the use of the guideline portal and the online consensus conference. There was no financial involvement by third parties. Mandate holders and experts worked exclusively on a voluntary basis.

2.2.3 Disclosing and Handling of Conflicts of Interest

In accordance with the AWMF rules for dealing with conflicts of interest, all participants submitted their declarations on the corresponding AWMF form (Form 2018). Conflicts of interest were screened by the guideline coordinators and Prof. Kopp (AWMF). Initially, they were screened for thematic relevance to the guideline and then categorized according to the AWMF criteria as low, moderate, or high with respect to the individual recommendation. The management proposal was discussed, consented to, and implemented at the beginning of the consensus conference with all participating experts.

Paid lecturing/or training and paid authorship/co-authorship were categorized as low conflicts of interest and had no consequences in terms of voting.

The following conflicts of interest were rated as moderate:

- Consultant or expert activity or paid participation in a scientific advisory board of a company in the healthcare industry (e. g., pharmaceutical industry or medical device industry), a commercially oriented contract institute, or an insurance company
- Participation in a scientific advisory board (advisory board)
- Research projects/conduction of clinical studies: financial contributions (third-party funds) for research projects or direct financing of institution employees by a company of the healthcare industry, a commercially oriented contract institute, or an insurance company

The following company was identified as a potential conflict of interest: Medtronic (on the topic of capnography monitoring). In addition, the company E&L medical GmbH was up for discussion as a potential conflict of interest, as this company distributes software for reporting endoscopic procedures. However, since the company itself is not involved in any way in the issue, the evaluators see no or only a minor relevant conflict of interest.

There were no conflicts of interest for Prof. Dr. Andrea Riphaus and Prof. Dr. Till Wehrmann when the 2008 guideline was prepared. In the 2014 update (published in January 2015), Prof. Dr. Andrea Riphaus and Prof. Dr. Till Wehrmann had a relevant conflict of interest regarding the vote on capnography monitoring, as they had received support from Covidien in 2011 (loan of equipment for a study). However, since this event occurred now 10 years ago, it is no longer assessed as a relevant conflict of interest for the current guideline.

Owner interests (patent, copyright, ownership of business shares, stocks, and funds with participation of healthcare companies) were rated as high conflicts of interest. High conflicts of interest related to the guideline were not identified.
As a result, one expert was identified as having a moderate conflict of interest. Moderate conflicts of interest resulted in abstention from voting. In addition, the interdisciplinary, representative composition of the guideline group, as well as the structured consensus finding under neutral moderation, were assessed as protective factors against bias.

### Table 4 Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence [1].

<table>
<thead>
<tr>
<th>Question</th>
<th>Step 1 (Level 1*)</th>
<th>Step 2 (Level 2*)</th>
<th>Step 3 (Level 3*)</th>
<th>Step 4 (Level 4*)</th>
<th>Step 5 (Level 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How common is the problem?</td>
<td>Local and current random sample surveys (or censuses)</td>
<td>Systematic review of surveys that allow matching to local circumstances**</td>
<td>Local non-random sample**</td>
<td>Case-series**</td>
<td>n/a</td>
</tr>
<tr>
<td>Is this diagnostic or monitoring test accurate? (Diagnosis)</td>
<td>Systematic review of cross sectional studies with consistently applied reference standard and blinding</td>
<td>Individual cross sectional studies with consistently applied reference standard and blinding</td>
<td>Non-consecutive studies, or studies without consistently applied reference standards**</td>
<td>Case-control studies, or poor or non-independent reference standard**</td>
<td>Mecha-nism-based reasoning</td>
</tr>
<tr>
<td>What will happen if we do not add a therapy? (Prognosis)</td>
<td>Systematic review of inception cohort studies</td>
<td>Inception cohort studies</td>
<td>Cohort study or control arm of randomized trial*</td>
<td>Case-series or case-control studies, or poor quality prognostic cohort study**</td>
<td>n/a</td>
</tr>
<tr>
<td>Does this intervention help? (Treatment Benefits)</td>
<td>Systematic review of randomized trials or n-of-1 trials</td>
<td>Randomized trial or observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study**</td>
<td>Case-series, case-control studies, or historically controlled studies**</td>
<td>Mecha-nism-based reasoning</td>
</tr>
<tr>
<td>What are the COMMON harms? (Treatment Harms)</td>
<td>Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect</td>
<td>Individual randomized trial or (exceptionally) observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**</td>
<td>Case-series, case-control, or historically controlled studies**</td>
<td>Mecha-nism-based reasoning</td>
</tr>
<tr>
<td>What are the RARE harms? (Treatment Harms)</td>
<td>Systematic review of randomized trials or n-of-1 trial</td>
<td>Randomized trial or (exceptionally) observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study**</td>
<td>Case-series, case-control, or historically controlled studies**</td>
<td>Mecha-nism-based reasoning</td>
</tr>
<tr>
<td>Is this (early detection) test worthwhile? (Screening)</td>
<td>Systematic review of randomized trials</td>
<td>Randomized trial</td>
<td>Non-randomized controlled cohort/follow-up study**</td>
<td>Case-series, case-control, or historically controlled studies**</td>
<td>Mecha-nism-based reasoning</td>
</tr>
</tbody>
</table>

As a result, one expert was identified as having a moderate conflict of interest. Moderate conflicts of interest resulted in abstention from voting. In addition, the interdisciplinary, representative composition of the guideline group, as well as the structured consensus finding under neutral moderation, were assessed as protective factors against bias.

### Table 5 Classification of Consensus Strength.

<table>
<thead>
<tr>
<th>Consensus</th>
<th>% Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong consensus</td>
<td>≥ 95</td>
</tr>
<tr>
<td>Consensus</td>
<td>≥ 75–95</td>
</tr>
<tr>
<td>Majority agree</td>
<td>≥ 50–75</td>
</tr>
<tr>
<td>No consensus</td>
<td>&lt; 50</td>
</tr>
</tbody>
</table>
Overview of all recommendations where it was necessary to abstain because of conflicts of interest

<table>
<thead>
<tr>
<th>Name</th>
<th>Abstentions in WG/Recommendation</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Delius, Stefan</td>
<td>WG 3: Recommendation 3.4.2</td>
<td>Medtronic (on capnography monitoring)</td>
</tr>
</tbody>
</table>

The declarations of interest of all experts are presented in the guideline report.

Participants of the Consensus Conference

Guideline Experts: Hans-Dieter Allescher (DGE-BV), Angelika Behrens (DGVS), Ulrike Beilenhoff (DEGEA), Horst Bitter (GRPG), Alexander J. Eckardt (DGVS), Peggy Heidemann (DGVS), Susanne In der Smitten (DCCV), Michael Jung (DGVS), Peter Klare (DGVS), Andrea Riphaus (DGVS), Ulrich Rosien (DGVS), Anja Schaible (CAES), Dieter Schilling (DGVS), Hans Seifert (DGVS), Peter H. Tonner (DGAI), Torsten Voigtländer (DGVS), Stefan von Delius (DGVS), Frank Wappler (DGAI), and Till Wehrmann (DGVS).

Organization and Methodology: Ina Kopp (AWMF), Torsten Karge (CGS-Usergroup), and Pia Lorenz (DGVS).

The influence of conflicts of interest was further reduced by the formal two-stage consensus building and by the creation of the interdisciplinary working groups.

2.3 Distribution and Implementation

2.3.1 Concept of Distribution and Implementation

The guideline is published in the Journal of Gastroenterology and on the homepages of the DGVS (www.dgvs.de) and the AWMF (www.awmf.de).

2.3.2 Validity Period and Updating Procedure

The validity of the guideline is five years (April 30, 2027). The revision will be initiated by the guideline officers of the DGVS. The steering group will review the need for updating the guideline on an annual basis. For further information, please contact the DGVS office (leitlinien@dgvs.de).

3 Editorial Note

3.1 Gender-Neutral Wording

For the sole purpose of better readability, the gender-specific spelling has been omitted. All personal designations in this document are therefore to be understood as gender neutral.

3.2 Participatory Decision Making

All recommendations of the guideline are to be understood as recommendations that are made and implemented as a participatory decision-making process between physician and patient and, if applicable, the patient’s relatives.

4 Special Note

Medicine is subject to a continuous development process, so that all information, in particular on diagnostic and therapeutic procedures, can only correspond to the state of knowledge at the time of the printing of the guideline. The greatest possible care has been taken regarding the recommendations on therapy and the selection and dosage of drugs. Nevertheless, users are urged to consult the manufacturers’ package inserts and expert information for verification and, in case of doubt, to consult a specialist. In the general interest, any discrepancies should be reported to the DGVS. The users themselves remain responsible for any diagnostic and therapeutic application, medication, and dosage. In this guideline, registered trademarks (protected trade names) are not specially marked. It can therefore not be concluded from the absence of a corresponding reference that it is a free trade name. The work is protected by copyright in all its parts. Any use outside the provisions of copyright law without the written consent of DGVS is prohibited and punishable by law. No part of the work may be reproduced in any form without written permission. This applies to duplications, translations, microfilming, and the storage, use, and exploitation in electronic systems, intranets, and the internet.

1 Guideline – Indications/Goals/Known Risks/Patients/Quality Goals

1.1 Recommendation on Sedation Choices

<table>
<thead>
<tr>
<th>Recommendation 1.1</th>
<th>2022 (modified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1a) We recommend that every patient should be offered sedation before endoscopy.</td>
<td></td>
</tr>
<tr>
<td>Evidence level 5, recommendation grade A, strong consensus</td>
<td></td>
</tr>
<tr>
<td>1.1b) We recommend that patients should be informed about the advantages and disadvantages of an examination with and without sedation.</td>
<td></td>
</tr>
<tr>
<td>Evidence level 5, recommendation grade A, strong consensus</td>
<td></td>
</tr>
<tr>
<td>1.1. c) We recommend that, in principle, simple endoscopic examinations may be performed without sedation.</td>
<td></td>
</tr>
<tr>
<td>Evidence level 5, recommendation grade A, strong consensus</td>
<td></td>
</tr>
</tbody>
</table>

Background

Every patient has the right to an endoscopy that is as painless and stress free as possible. Therefore, it does not seem ethically justifiable to withhold sedation from patients as a matter of principle [2]. Endoscopic examinations can be unpleasant, so sedation is desired or recommended. In particular, involuntary movement by the patient should be avoided during difficult prolonged endoscopic interventions (e.g., ERCP, difficult resections, or drainage procedures). Therefore, sedation should principally be offered to every patient. Differentiated information for patients about sedation options and implementation increases examination acceptance and awareness [3, 4]. After being appropriately informed about sedation, the individual patient’s wishes should, if possible, be taken into consideration.
Simple examinations are defined as diagnostic endoscopies or interventions that are simple, brief, and not painful. A randomized controlled trial [5] and two prospective cohort studies [6, 7] substantiate this statement using colonoscopy as an example. The consent to an unsedated colonoscopy was as high as 88%. In contrast, in another study, only 20% of respondents agreed to colonoscopies without sedation. Male gender, higher education, and lower anxiety were positive predictors for patients to want colonoscopies without sedation [8].

1.2 Recommendation on Indications for Sedation

<table>
<thead>
<tr>
<th>Recommendation 1.2</th>
<th>2022 (modified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend that the following aspects should be considered when deciding for or against a sedation procedure and/or analgesia:</td>
<td></td>
</tr>
<tr>
<td>▪ Patient characteristics (risk profile, comorbidities, preferences)</td>
<td></td>
</tr>
<tr>
<td>▪ Type of endoscopic intervention (indication, duration, invasiveness)</td>
<td></td>
</tr>
<tr>
<td>▪ Structural prerequisites</td>
<td></td>
</tr>
<tr>
<td>Evidence level 5, recommendation grade A, strong consensus</td>
<td></td>
</tr>
</tbody>
</table>

1.3 Recommendation on Examination Quality

<table>
<thead>
<tr>
<th>Statement 1.3a)</th>
<th>2021 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is not possible to make a statement on the effect of the complication rate (because of the endoscopic procedure) if sedation is not used.</td>
<td></td>
</tr>
<tr>
<td>Evidence level 5, strong consensus</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation 1.3b)</th>
<th>2021 (unchanged)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation may be considered for gastroscopy and colonoscopy with the aim of increasing the diagnostic value.</td>
<td></td>
</tr>
<tr>
<td>Evidence level 2b, recommendation grade 0, strong consensus</td>
<td></td>
</tr>
</tbody>
</table>

Background

A large Italian cohort study including more than 12,000 patients showed that sedation can increase the diagnostic value: sedated patients had a higher polyp detection rate than nonsedated patients. Also, the cecum (meaning a complete colonoscopy) was reached more frequently in this study [9]. The latter could be confirmed in other large cohort studies where sedation increased the probability of a complete colonoscopy by almost a factor of two [10].

The need for sedation in gastroenterological interventions is not obligatory in all endoscopic procedures and ultimately depends on the type, duration, complexity, and invasiveness of the examination, as well as on the patient’s wish. Sedation contributes significantly to the comfort of the examination for both the patient and the examiner. It is the prerequisite for successful and low-risk examinations, especially in the case of complex therapeutic procedures.

Previous unpleasant examinations, anxiety, and the patient’s ability to understand should be considered. In addition, there are often – culturally determined – major differences in handling sedation during gastrointestinal endoscopy. For example, in the United States and the United Kingdom, patients are sedated in up to 88% [11] of endoscopic examinations. In contrast, the sedation frequency in Germany and Switzerland in the 1990s was significantly lower at approximately 9% [12], but is clearly increasing with the complexity of the examination. However, survey results also show a significant increase in sedation frequency for endoscopic procedures in Germany of around 90% [13, 14]. This is presumably due on the one hand to an increased frequency of interventional examinations and on the other hand because of patient wishes (e.g., for colon carcinoma screening).

However, there are almost no studies that evaluate the safety of diagnostic and therapeutic endoscopy with or without sedation. An American study failed to meet the comparative objective because of a lack of patient acceptance (high desire for sedation) [5].

The result of a German study showed that colonoscopy can be performed without sedation in more than 90% of cases with a low complication rate [6]. However, in general, patients wish to be sedated [6, 15, 16]. This does not seem to have a lasting effect on the complication risk during endoscopy.

For example, a prospective study by Dillon et al. [17] involving 136 children undergoing colonoscopy under general anesthesia demonstrated that the perforation rate was no higher than in adults under sedation. A meta-analysis examined the perforation rate in adults and found no increased rate under propofol sedation [18]. Thus, the claim that there are fewer colonoscopy perforations if pain is maintained cannot be confirmed.

1.4 Recommendation on Risk Assessment

1.4.1 General Considerations

Sedating and analgesic-acting drugs can induce overlapping and, sometimes, not clearly distinguishable states, ranging from minimal sedation (anxiolysis) to general anesthesia.

Sedation and/or analgesia procedures by physicians who are not anesthesiologists should not reach a planned level of sedation in which life-sustaining reflexes are impaired or abolished.

Planned general anesthesia (with loss of consciousness/protective reflexes) is reserved exclusively for anesthesiologists (exceptions exist in intensive care).

If, in individual cases, a state is reached in which life-sustaining reflexes are impaired or switched off (general anesthesia) and if the procedure is to be continued, an anesthesiologist must be consulted.
Despite the fluent, not always safely controllable, sedation-level transitions, different degrees of (analgo-) sedation can be distinguished.

The degree (depth) of sedation can be determined and classified by a validated scale. While the modified Richmond Agitation-Sedation Score scale (RASS scale) [19] is usually used in European anesthesia, in gastroenterology/endoscopy the classification of the different sedation stages is mainly done according to the American Society of Anesthesiologists [20] (Table 7).

### Recommendation 1.4 2022 (modified)

We recommend that the sedation type and depth, as well as the drug used, should be selected according to the type of intervention, as well as the patient’s ASA grade and individual risk profile. There are special requirements with respect to the facilities, equipment, and qualified personnel. If the prerequisites defined under “structure quality” cannot be met, we recommend that sedation should be avoided after considering the risk benefit, as well as the patient’s wish. If sedation is indicated and/or patients want to be sedated, we recommend they should be referred to a facility that meets these requirements.

**Evidence level 5, recommendation grade A, strong consensus**

### Background

The American Society of Anesthesiologists and the American Society of Gastroenterologists [20, 21] recommend carrying out a risk assessment of any cardiovascular and respiratory problems that could occur during endoscopy before the examination begins. Additionally, a physical examination should be performed that, aside from vital signs, includes auscultation of the heart and lungs. A detailed history should include the following questions about:

- Diseases of the cardiovascular and respiratory system
- Stridor, snoring, sleep apnea syndrome
- Kidney function disorders, liver diseases
- Diabetes mellitus, obesity
- Neurologic/muscular disorders
- Age
- Previous operations which are relevant for the endoscopic access
- Complications on previous occasions when sedatives/analgesics, regional and/or general anesthesia were administered
- Drug allergies, current medication, and possible drug interactions [22]
- Tobacco, alcohol, drug consumption
- Most recent meal: when and what was eaten

In a prospective study at several hospitals in the Melbourne region, risk factors and risk assessment were confirmed by ASA classification [23].

Endoscopic examinations in patients with liver cirrhosis are safely possible under adequate surveillance. The increased sedation risk is determined by the often associated (cardiopulmonary) comorbidity.

---

**Table 6** Modified Richmond Agitation-Sedation Score [19].

<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 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>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>Movement or eye opening when patient is addressed (but no eye contact)</td>
</tr>
<tr>
<td>3</td>
<td>Moderate sedation</td>
<td>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 or physically stimulated</td>
</tr>
</tbody>
</table>

**Table 7** Stages of Sedation, Modified from the American Society of Anesthesiologists [20].

<table>
<thead>
<tr>
<th>Reaction when being addressed</th>
<th>Minimal (anxiolysis)</th>
<th>Moderate</th>
<th>Deep</th>
<th>Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<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>
<td>Patient cannot be woken, not even in response to pain stimuli</td>
<td></td>
</tr>
<tr>
<td>Spontaneous breathing</td>
<td>Not influenced</td>
<td>Adequate</td>
<td>Respiratory function may be inadequate; patients may require assistance in maintaining a patent airway</td>
<td>Inadequate, ITN or larynx mask necessary</td>
</tr>
</tbody>
</table>

---

Leitlinie

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Under sedation, obesity (BMI greater 30 kg/m²) is a risk factor for hypoxemia and higher age for hypotension. However, threshold values are not defined [24–28].

Previous operations (e.g., ERCP after gastrectomy or bypass OP) can increase the examination duration and, thus, the need for sedation [29].

The ASA classification [30] (Table 8) and the structure quality are the bases for the existing guidelines [20, 31–33]. Patients with ASA grade III or higher (Table 8) have an increased risk of complications during sedation or the endoscopic intervention.

The upgrade of the abovementioned statement to a recommendation grade A, with an evidence level of 5, is due to a 2b evidence level for ASA grade and comorbidity, as well as to patient safety considerations.

### 1.5 Recommendation on Anesthesia/Endotracheal Intubation

<table>
<thead>
<tr>
<th>Recommendation 1.5</th>
<th>2022 (modified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend considering the consultation of an anesthesiologist for patients with a high-risk profile. This includes patients with a 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 &lt; 3 cm; Mallampati grade 3 or 4; or a restricted hyoid-to-chin distance &lt; 6 cm).</td>
<td></td>
</tr>
</tbody>
</table>

**Evidence level 5, recommendation grade A, consensus**

### Background

A routine endoscopy under sedation seems to be safely feasible in patients with, at most, mild concomitant disease (ASA I or II) [34–36]. The most frequent adverse events are hypoxemia and hypotension. Only by properly evaluating the sedation/anesthesia risk and weighing the intervention risk can the need/type/depth of sedation be adequately planned prior to the examination. The risk profile also includes pathologic/anatomic features that may lead to respiratory problems and that would complicate any mechanical breathing support or ventilation that may be needed. In addition, existing guidelines provide further guidance on assessing the increased risk of respiratory disability in patients with pre-existing problems during anesthesia or sedation [20, 31–33].

These are:

1. Patients with stridor, snoring, and 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 macroglossia, 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 (< 6 cm for adults), neck tumors, disease or trauma of the cervical spine, tracheal alterations, or 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, persons with alcohol abuse, drug abuse, or patients on long-term and extensive medication, as well as patients with a high ASA grade and/or persons who are not able to cooperate, who are also expected to have higher requirements for sedation
Data are controversial on the significance of obstructive sleep apnea (OSA). Liou et al. found a higher rate of hypoxemia under sedation in individuals at increased risk for OSA when using the Berlin Questionnaire (BQ; the BQ targets OSA and differentially asks about snoring behavior and daytime sleepiness) [37]. In contrast, Andrade et al. did not observe an increased rate of cardiopulmonary complications in patients with known OSA, and Mudambi et al. did not observe an increased rate of hospital or intensive care admissions or emergency department presentations [38, 39]. However, the studies do not distinguish between obstructive sleep apnea and obstructive sleep apnea syndrome with sequelae, which might be more critical to evaluate.

Patients with high-risk profiles and ERCP benefit from examination under intubation anesthesia [40]. However, involving or consulting an anesthesiologist in case of an increased risk profile, expected long intervention duration, or increased risk of a relevant acute complication (e.g., aspiration risk in interventions in the proximal esophagus) does not inevitably lead to an indication for intubation anesthesia [41–44].

### Recommendation 1.6 Recommendation on Protective Endotracheal Intubation

<table>
<thead>
<tr>
<th>Recommendation 1.6</th>
<th>2022 (modified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep sedation leads to impairment of protective reflexes (swallowing reflex and coughing reflex). This increases the risk of aspiration. Thus, in special situations in emergency endoscopy with increased aspiration risk (e.g., severe upper gastrointestinal bleeding) under sedation, we recommend considering an indication for endotracheal intubation. Whether prophylactic intubation is associated with increased risk of pneumonic infiltrate has so far not been conclusively determined.</td>
<td></td>
</tr>
</tbody>
</table>

**Background**

It is a basic fact that deep sedation leads to impairment of the protective reflexes. For this reason, if an additional aspiration risk is present (e.g., during emergency endoscopy for upper gastrointestinal bleeding), tracheal intubation seems sensible to avoid aspiration. However, because there are no high-quality studies that prove that the advantages of this procedure outweigh the disadvantages, it is not possible to issue a general recommendation.

A retrospective case-control study by Koch et al. [45] studied a total of 62 patients, 42 of whom underwent prophylactic endotracheal intubation before the start of endoscopy for variceal hemorrhage. Subsequently, they found pneumonic infiltrates in 17% of the intubated patients. This was not the case in the non-intubated patients. In addition, overall mortality was higher in the group that underwent prophylactic intubation (21% vs. 5%).

In another retrospective case-control study by Rudolph et al. [46] including 220 patients, no significant difference was seen in the frequency of pneumonic infiltrates and overall mortality between the intubated and non-intubated groups. However, deaths caused by aspiration were higher among patients who did not undergo prophylactic intubation (2% vs. 0%).

Because of a lack of clarity in such retrospective analyses about how patients were allocated to the groups and, thus, a possible bias (severely ill patients are more likely to undergo intubation), these studies are only of limited value.

In a population-based cohort study, Bielawski et al. analyzed retrospective data of 3 million ambulatory colonoscopies in the Ontario area [47]. They found an association of anesthesiologist-assisted examinations and aspiration pneumonia. Data on intended or achieved sedation depth and rate of primary intubation examinations are missing. Again, the retrospective approach does not allow for an evaluation of bias in the sedation choice influenced by concomitant diseases.

### 1.7 Recommendation on Patient Positioning

<table>
<thead>
<tr>
<th>Recommendation 1.7</th>
<th>2022 (modified)</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend ensuring that sedated patients are positioned correctly to avoid position-related damage and aspiration, as well as ensuring that body temperature management be adapted to the duration of the examination.</td>
<td></td>
</tr>
</tbody>
</table>

**Evidence level 5, recommendation grade A, strong consensus**

### Background

Positional damage during gastrointestinal endoscopy under sedation/anesthesia should always be avoided. There is no direct evidence of positional damage in endoscopy. The recommendation is, therefore, based on the joint recommendation of the Professional Association of German Anesthesiologists and the Professional Association of Surgeons [48] and Update BDA from 2016.

Patients may move involuntarily, especially with shallow sedation. Appropriate fall prevention must be employed by securing patients appropriately (e.g., lunge protection and safety harnesses).

For correct positioning during the use of HF-surgery, please refer to the S2k guideline on quality requirements in endoscopy.

Positional damage is usually caused by pressure and traction at anatomically exposed sites or by overstretching as a result of prolonged nonphysiological positions. The most frequently affected are brachial plexus, N. ulnaris, and N. fibularis [49].

Positional injuries are most likely to occur during procedures in the abdominal and lateral position or when transferring the patient from the examination table to the bed. The use of appropriate positioning aids is recommended. Particularly during long procedures (e.g., endoscopic submucosal dissection, retroperitoneal intervention, etc.), care should be taken to ensure correct positioning. If necessary, this should include occasional repositioning and relief of stressed regions or joints, analogous to the procedure for surgical operations.

Suitable measures must be taken to prevent patients from suffering hypothermia and their eyes from drying out. To avoid eye damage in an abdominal position, care must be taken to ensure positioning to avoid lower eye compression [48].
2.1 Acceptance by the Patient and the Endoscopist

2.1.1 Patient Acceptance/Satisfaction

We recommend that sedation should be offered because it increases the patients’ comfort and, hence, their acceptance of the endoscopic intervention. Ideally, sedation should not result in memory of unpleasant sensations, but at the same time, the duration of action should be short.

Evidence level 1b, recommendation grade A, strong consensus

Background

The performance of analgesia and sedation for endoscopy is dependent on several factors. The procedure is performed differently in larger clinics than in small hospitals or private practices. Regional differences, safety requirements, and reimbursement also play a role. More than 98% of colonoscopies in the United States and more than 90% in Canada are performed under sedation [15, 50]. Large discrepancies exist in Europe. In Italy, sedation is standard practice. In contrast, in Germany 87% of colonoscopies and 74% of esophagogastroduodenoscopies are performed with sedation [13, 51]. However, in Spain, less than 20% patients are sedated during colonoscopy [52]. A recent Greek survey found that 83.3% of patients are sedated during endoscopy [53].

Only 12% of the endoscopists in the United States would agree to have their own colonoscopy done without sedation. The other half would prefer propofol sedation [15].

Adequate analgesia and sedation can influence the quality of the examination and the satisfaction of both the patient and the endoscopist [54]. Patients primarily wish to be completely pain free, followed by the desire to wake up as soon as possible [55]. In a study by Abraham et al. [56], it was shown that gastroscopies under sedation resulted in less frequent repeat examinations and were associated with increased patient acceptance. The increase in patient acceptance with sedation for endoscopic procedures has also been demonstrated by other studies [57–64]. A large meta-analysis showed greater patient satisfaction under sedation [65]. Patient acceptance is also greater for colonoscopies under sedation with propofol [66].

However, when benzodiazepines are used during upper endoscopy (gastroscopy), patient discomfort may occur (especially vomiting and retching reflex), which may not be noticed by the endoscopist. In a study by Walmsley et al. [67], endoscopists did not notice such discomfort occurring in 12% of patients. Even in the case of moderate sedation with midazolam, patients can sense pain [5], which may not necessarily be noticed by the endoscopist. However, patients frequently do not recall these complaints as a result of the amnestic properties of midazolam.

The variables influencing patient satisfaction were investigated in a study of 456 patients who underwent gastroscopies, colonoscopies, or a combination of both [68]. The multivariate analysis showed that especially long procedures and young patients (<50 years) were factors associated with great dissatisfaction. Therefore, they require increased vigilance regarding sedation. It was demonstrated on 600 patients who had colonoscopies that propofol led to greater postprocedural satisfaction than midazolam [69]. A smaller study on 72 patients who underwent endoscopic submucosal dissections showed that satisfaction of patients sedated with propofol could be increased by premedication with 0.02 mg/kg midazolam [70]. A meta-analysis demonstrated that the sedation depth of patients undergoing colonoscopies has no effect on patient satisfaction. However, more complications arose under deeper sedation compared to mild sedation [71].

2.1.2 Endoscopist Satisfaction

Sedation increases the technical feasibility and the chance that the examination can be completed, and, thus, improves examiner satisfaction (especially in interventional endoscopy).

Evidence level 1b, strong consensus

Sedation can improve technical success and more complete exams, and therefore, it can increase the endoscopist’s satisfaction (especially during interventions) [72, 73]. Similarly, a combination of benzodiazepines with opioids can improve examiner satisfaction. A study of 107 patients compared midazolam combined with placebo and midazolam combined with meperidine for EGD [74]. Endoscopist satisfaction was significantly better with the combination regimen (P < 0.001), whereas little difference was seen in patient acceptance. Sedation with benzodiazepines leads to sufficient sedation in 85% of cases and adequate examination conditions in 71%. However, patient satisfaction is even higher with propofol mono- or combination therapy [65].

Deep sedation may be needed to ensure that examinations can be done safely without unwanted and uncontrollable involuntary patient movement, especially for longer and more complex interventions [68, 75]. Propofol is superior to midazolam in regard to endoscopist satisfaction, particularly during interventional endoscopies [76]. Better examination conditions may be responsible for the trend of increasing propofol use. However, increasing sedation depth, 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 and ▶ Table 9, page 38). One reason for the observed deaths during or after endoscopies could be excessive dosing of the administered medications [77, 78]. A single-center study, which involved 2 audits within 2 years, including more than 14,000 patients in England, showed that the implementation
of a sedation guideline for endoscopy in some cases markedly reduced dosages of sedatives and analgesics. However, the outcome (e.g., mortality) did not change significantly. At the same time, there was an increase in incomplete examinations as a result of reduced patient compliance [78]. Another study including 585 patients undergoing colonoscopies found no effect of the sedation depth (moderate vs. deep) on the examination quality regarding adenoma or polyp detection [79].

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 [80]. An Italian survey showed that propofol was administered by anesthesiologists in 66% of cases [51]. In Greece, about 70% of endoscopists do not work with anesthesiologists [53].

A retrospective analysis of more than 230,000 patients determined sedation and analgesia to be quality indicators for endoscopy [10]. They were directly linked with the success rate of a complete exam. These results are also supported by an Italian survey [81]. In Germany, the drugs most often used for sedation during endoscopy are propofol (97%) and midazolam (69%). A combination of these drugs is used in 43% of cases [14]. However, a recent survey [14] demonstrated that propofol is now being used more often than benzodiazepines. In terms of endoscopist satisfaction and quality of examination outcome, continuous administration, e.g., of propofol and remifentanil, appears to be superior to intermittent administration, although patient satisfaction was higher with intermittent sedation [82].

### 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. Propofol’s exact pharmacodynamic mechanisms are still not completely understood. Propofol is extremely lipophilic and develops its effect within 30–45 seconds. As 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 [83]. After short-term continuous application for 30–60 minutes, patients will take 5–10 minutes to wake up. The quick onset of action with a short effect duration makes propofol a suitable sedative for gastrointestinal endoscopy [72, 84–91]. The effect of propofol is individually different 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 using propofol monotherapy are no more prone to pain sensation than those treated with a standard sedation regimen [66]. This is likely explained by the fact that patients cannot recall painful sensations.

### Table 9 Comparison of Vital Signs During Sedation with Propofol Versus Midazolam/Meperidine for ERCP.

<table>
<thead>
<tr>
<th>Author</th>
<th>Vital sign</th>
<th>Propofol</th>
<th>Midazolam/meperidine</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vargo JJ [58]</td>
<td>$\text{SpO}_2 &lt; 90%$</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 [121]</td>
<td>$\text{SpO}_2 &lt; 90%$</td>
<td>7/75 (9.0%)</td>
<td>8/75 (11%)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>Mean decrease in $\text{SpO}_2$</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>Wehrmann T [115]</td>
<td>$\text{SpO}_2 &lt; 90%$</td>
<td>8/98 (8.2%)</td>
<td>11/99 (11%)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>Mean decrease in $\text{SpO}_2$</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>Krugliak P [120]</td>
<td>N</td>
<td>14</td>
<td>15</td>
<td>ns</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 [66]</td>
<td>N</td>
<td>40</td>
<td>40</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>Decrease $\text{SpO}_2$ (%)</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 in 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).
that might have occurred during the procedure. Even a single bolus dose can take a patient right through several levels of sedation (Table 6, 7) 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 must be able to rapidly control apnea (see section 4: process quality). Administration of propofol for endoscopies requires a high degree of clinical expertise and attention to the patient. In Italy, propofol is administered by an anesthesiologist in two-thirds of all cases, in Greece in even more than 64 % of patients [51, 95].

The downsides to propofol are pain during the injection, allergic reactions, and hyperlipidemia. Besides possible hypoxia from respiratory depression, hypotension and bradycardia may occur [96] (see also Table 9, section 2.2.3.1). In isolated cases (intensive care settings), 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 potential for severe septic complications [97, 98]. With such improper handling (e. g., splitting of ampules), a series of infections have been described. A recent Direct Healthcare Professional Communication (DHPC) by the German Federal Institute for Drugs and Medical Devices (BfArM) in May 2023 states that propofol-containing drugs are only approved for single use in individual patients and must be taken from their container under aseptic conditions. The so-called propofol infusion syndrome (PRIS) may occur as a complication, even after short-term application (symptoms include rhabdomyolysis, cardiac arrhythmias, CK elevation, and high mortality rate) [99, 100]. However, so far, no such case has been reported during sedation for gastrointestinal endoscopy. Allergy to chicken protein, soy protein, or sulfite do not seem to be relevant because of the refining process of propofol solutions [101, 102]. However, they are still listed in the product information and should be observed. In some cases, newer propofol formulas are available [103, 104].

The use of propofol generally does not result in higher complication rates than the use of other sedation strategies, such as regimens based on benzodiazepines. An early meta-analysis showed that sedation using propofol during colonoscopies reduced the number of complications [105]. The dosage of propofol can be reduced when used in combination with other sedatives/analgesics [106, 107]. A meta-analysis of 20 studies showed that propofol was superior to other sedatives in regard to recovery or patient transfer times and resulted in higher patient satisfaction rates. However, no differences were observed regarding complications or technical success [66]. In another meta-analysis, which analyzed 36 studies with 3918 patients who were sedated for endoscopy, propofol led to a shorter recovery time and higher patient satisfaction in comparison to midazolam [65].

A meta-analysis of 22 studies with 1798 patients found that patients receiving propofol for sedation recovered faster and could be discharged sooner, with better sedation and patient cooperation and no differences in adverse events [108]. Similar results were shown in a recent meta-analysis of colonoscopies [109]. In a large multicenter study (ProSed 2) of 368,206 endoscopies, a low number of complications were found (severe complications: 0.01 %, deaths: 0.005 %, mild complications: 0.03 %). Combining propofol with other sedatives allows a significant reduction in the dose used but without a reduction in cardiopulmonary complications [110]. A recent meta-analysis of 22 studies involving 2250 patients also found no benefits of combining propofol with other sedatives other than a reduction in dose [111].

### 2.2.1.2 Techniques of Propofol Administration

Propofol is initially administered as a bolus to induce sedation. To maintain sedation, it is then either given as repeated bolus or 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 personalization sedation” (CAPS). Intermittent bolus administration and administration by infusion pump are standard procedures, while the other methods are still experimental, at least regarding 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-morbidity of the patient (e. g., 40 mg at <70 kg body weight or 60 mg at ≥70 kg body weight). Thereafter, repeated bolus of, for example, 20 mg according to patient needs are given to maintain the desired sedation depth [112]. If necessary, an additional benzodiazepine and/or opioid can be added for induction (see chapter 2.3, Combination Therapy). Intermittent bolus administration has been used in almost all published studies on propofol sedation efficacy during endoscopic examinations/treatments in comparison with other drugs (e. g., midazolam). In endoscopy, it is therefore currently the best-documented and most common mode of administration.

#### 2.2.1.2.2 Continuous Propofol Administration Using Infusion Pump Systems

Also, for this mode of administration, a bolus of propofol adjusted to body weight and, if necessary, age and co-morbidity 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 sedation depth and the patient’s individual 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, and age).

Perfusor administration of propofol has been extensively documented in anesthesia and is considered the standard of care for total intravenous anesthesia. However, only a little of the published data are available for its use in endoscopy. In a randomized comparison between perfusor application and intermittent bolus administration in interventionendoscopy, no relevant difference was found for sedation efficacy or side effects [113]. However, the authors explicitly emphasized the need for a specialist to adjust the infusion rate of the pump. A study in patients older than
80 years demonstrated that continuous propofol administration tended to cause desaturation in geriatric patients, even though the overall complication rate was not higher in comparison to younger patients [114].

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, 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 this procedure in the future. Again, fewer complications were noted with milder sedation [64].

A 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 [115]. Because of the favorable safety profile of propofol, the American endoscopist Douglas Rex postulated that propofol may be administered by gastroenterologists or gastroenterological nurses [116]. In an analysis (retrospective case series and meta-analysis) 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 the methodological weaknesses of this study (retrospective analysis), these results are of limited value. Other potential morbidity parameters were not analyzed.

In another large 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 documented in 5.5% of patients. In most cases, other parameters, such as hemodynamics, were not analyzed [117]. Detailed data on post-procedural 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 [118]. In 2005, the AGA sent a petition to the Food and Drug Administration (FDA) to extend the privileges of propofol administration by anesthesiologists to also include non-anesthesiologists. However, this petition was finally denied in 2010 [119].

In 2010, a recommendation on sedation with propofol by non-anesthesiologists was published by three European professional societies, the European Society of Gastrointestinal Endoscopy (ESGE), the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA), and the European Society of Anesthesiology (ESA). Following internal discussions, support for this recommendation was withdrawn in 2015 by the ESA [120]. An updated version was published in 2015 by the ESGE and the ESGENA [33]. The current recommendations state that for most endoscopic procedures, sedation with propofol by non-anesthesiologic personnel versus traditional sedation (with comparable side effects) provides better sedation, more patient cooperation, higher patient satisfaction, shorter time to sedation, shortened postprocedural recovery times, and better post-sedation recovery scores. For advanced endoscopy procedures, NAPS is comparably safe, but with lower patient and investigator satisfaction. Significant changes compared to the previous version of the recommendation were made regarding monitoring. Capnography is recommended in special situations such as high-risk patients, deep sedation, and long procedures. Propofol should be administered as a monotherapy and as an intermittent bolus or via an infusion pump (including TCI or PCS). Patients with an ASA classification ≥3, a Mallampati score ≥3, or special risks should be sedated by an anesthesiologist. Recent studies have provided further evidence for the safety of NAPS also for special patient populations [121–125].

### Recommendation 2.4

<table>
<thead>
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<th>2022 (unchanged)</th>
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<tr>
<td>We suggest that propofol should be administered as an intermittent bolus application.</td>
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</table>

**Evidence level 1b, recommendation grade B, consensus**

2.2.1.2.4 Patient-Controlled (Analgo-) Sedation (PCS)

Patient-controlled drug administration originated from pain therapy. Today, it is standard in postoperative analgesia. With the help of programmable infusion pumps, patients can self-administer a defined dose of a drug intravenously at the press of a button. To avoid overdoses, a time-delay option is applied for repeat doses (a so-called lockout mechanism) [126]. One downside to this type of dosing is that patients often wait for a painful stimulus to administer the drug. Therefore, often the action of the applied substance occurs after the stimulus has ended [127]. This results in milder sedation but also in insufficient analgesia and lower patient satisfaction [128]. Thus, 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). In these cases, administration of very short-acting drugs via these systems is ideal. A combination of propofol with short-acting opioids (e.g., alfentanil and remifentanil) is often used [129, 130]. In a randomized study in patients undergoing ERCP, a combined regimen of propofol and remifentanil led to more cases of respiratory depression and nausea than the combination of propofol and alfentanil [130]. All the other studied parameters, such as administered 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 [129].

In a randomized study, patient satisfaction was similar with the use of a PCS system (propofol plus alfentanil) as compared to midazolam and meperidine [131] and also in two additional random-
ized studies as compared to diazepam and meperidine (called pethidine in Germany) [132, 133]. In two other studies, patient satisfaction with PCS was even higher than for midazolam alone [134]. However, in another randomized study, a higher pain score was reported for PCS than for midazolam [131]. Fewer adverse events (oxygen desaturation or drop in blood pressure) were observed with PCS using propofol in comparison to diazepam [132, 133]. In two of these studies, 97% and 78% of the patients who were sedated using PCS for colonoscopy said, if necessary, they would be willing to repeat this type of sedation [135, 136]. 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. A randomized, double-blind comparison between remifentanil and meperidine for colonoscopy showed neither a difference in patient or endoscopist satisfaction nor in terms of procedure duration or discharge time from the recovery room [137].

In a Swiss PCS study, 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 [127]. However, among those patients who took part, a significantly lower propofol dose was used during colonoscopy when PCS was employed compared to intermittent bolus administration by a nurse (NAPS) [127].

A recent large single-center study showed that PCS can be used safely in younger and low-risk patients and is associated with fewer cardio-respiratory adverse events [138]. In patients undergoing ERCP, PCS was better than sedation with midazolam and comparable to sedation by anesthesia staff [139]. A meta-analysis of PCS for colonoscopy found that PCS was similarly effective compared to traditional intravenous sedation [140]. However, there were advantages regarding recovery time, oxygen saturation, and incidence of hypotension.

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 [141]. The computer system calculates the individual pump infusion rate needed to maintain a preset blood drug concentration. It uses algorithms that take various patient parameters into account (e.g., age, sex, height, weight, and sedation depth). The infusion rate is adjusted during sedation after the initial dose required to reach the desired blood concentration has been calculated.

The potential advantage of the TCI method compared to continuous infusion (with fixed dose and infusion rate) is the avoidance of drug accumulation (the infusion rate is constantly adjusted). However, the current commercially available infusion pump systems calculate the dosage based on a pharmacokinetic model, which allows a deviation of 20% from the true plasma drug concentration [142]. Nevertheless, TCI provides a more gentle initiation and a more exact titration of the sedation depth, as well as a shorter wake-up period as compared to established bolus injection and infusions based on kilograms of body weight [143].

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. This was maintained during the procedure by an anesthesiologist. 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 seen, and one case was observed where ventilation with a mask became necessary [144].

Colonoscopies were performed in 16 patients using a TCI system in which the infusion rate was controlled by EEG (by determining the bispectral index, BIS). The goal was to reach a median propofol concentration of 2.3 μg/ml [145]. A BIS level of 80 was predominantly observed (corresponding to a mild to moderate sedation depth).

Further studies investigated the combined use of TCI and PCS, 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) [145–148]. In a study by Stonell et al. [148], which compared the TCI/PCS system to repetitive bolus propofol administration by an anesthesiologist during colonoscopy (n = 40), no significant differences were found in sedation efficacy or complication rates. However, the total propofol dose tended to be lower in the TCI group than in the bolus group (233 vs. 288 mg, P = 0.05).

A randomized, controlled, double-blind study on the use of TCI for gastroscopy and colonoscopy demonstrated very high patient and examiner satisfaction with TCI compared with standard sedation with fentanyl and midazolam [149]. A total of 94.3% of patients reported wanting TCI sedation again for a future examination, compared to only 71.4% of patients who received traditional sedation. Depending on the level of the target effect-site concentration chosen, dysphagia occurs under sedation [150]. It is more predictable under TCI because of the calculated concentrations than under non-concentration-controlled sedation. Measurement of BIS used in addition to TCI may help to adjust target concentration [151]. A study of anesthesia personnel in training showed that sedation quality and safety improved when TCI was used compared with manually administered sedation [152]. Further recent studies in different patient populations also support the safe use of TCI [153–157].

2.2.1.2.6 Computer-Assisted Personalized Sedation (CAPS)

The computer-assisted personalized sedation (CAPS) method extends TCI propofol dosing by the addition of various monitoring parameters. These include 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). Thus, sedation is implemented and monitored entirely by computer. A commercially available system from Ethicon only allows the regulation of moderate sedation depths; deep sedation and anesthesia are not yet provided. The system has been available in the United States since 2013 for pa-
2.2.2 Benzodiazepines

Benzodiazepines induce anxiolysis, amnesia, and sedation. They have both anticonvulsive and muscle-relaxing effects. Respiratory depression and hypotension are also observed under benzodiazepines. They act by binding to GABA receptors. Various benzodiazepines can have different pharmacologic characteristics (e.g., a stronger sedating effect or a stronger anxiolytic effect) [163].

2.2.2.1 Diazepam

In the early days, diazepam was the only available sedative for endoscopies but is now rarely used in the Western world for these examinations. This can be attributed to its relatively long half-life compared to more recent short-acting benzodiazepines such as midazolam [164–166]. Diazepam has a markedly longer elimination half-life compared to midazolam (30–100 hours vs. 1.5–3 hours, respectively). The main side effects of diazepam are respiratory depression [167], coughing, and dyspnea. Phlebitis may occur at the injection site, especially if water-soluble forms are used [168]. 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 for a long time was the most used sedative for endoscopy [169]. Its sedation potency is 1.5–3.5 times greater than that of diazepam [170]. The substance is effective after 1–3 minutes and reaches its maximum effect after 3–4 minutes, although the effect duration is between 15 and 80 minutes [171]. This is dependent on cofactors such as obesity, advanced age, and liver or kidney disease. It has dose-dependent hypnotic, anxiolytic, amnestic, and anticonvulsive properties like other benzodiazepines. The main pharmacologic actions are mediated by the activation of GABA receptors. All effects that are mediated by GABA receptors can be reversed by the specific antagonist flumazenil. When given in repeated or continuous doses, midazolam can have cumulative effects. Midazolam is mainly metabolized via CYP3A4 [172]. The side effect profile is equivalent to diazepam, but phlebitis occurs less commonly [173]. As is also sometimes the case with other benzodiazepines, midazolam administration can, in rare cases, lead to paradoxical reactions characterized by aggressiveness, hostility, and agitation. This phenomenon has been described in about 5% of patients receiving midazolam by short-lasting oral administration [174]. A study by Christe et al. [175] of older patients who were sedated with midazolam (mean age 84 ± 7 years) for esophagogastroduodenoscopy showed that confusion occurred in 14% of these patients, even on the next day. Benzodiazepine administration is regarded as an independent risk factor for the occurrence of delirious states [176].

For gastroscopies, midazolam is usually given as a bolus of 30–80 μg/kg body weight [84, 85, 175, 177]. For colonoscopies, an initial bolus between 30 and 50 μg/kg is generally given. Subsequently, lower dose bolii are given until the desired sedation depth is reached [134, 177, 178]. The use of lower doses is recommended for patients older than 60 years [133, 175, 178–180]. Midazolam’s duration of action is dependent on the length of its application because it tends to accumulate (context-sensitive half-life). Midazolam also increases the potency of other sedatives and hypnotics [163]. If sedation is the patient’s preference, it is generally better to administer midazolam before the start of the examination rather than on an as-needed basis during the procedure [181, 182]. However, a meta-analysis of the Cochrane Database on preprocedural administration of midazolam found no clear evidence of beneficial effects [183].

2.2.2.3 Antagonistic Effect of Flumazenil on Midazolam

The effect of midazolam can be inhibited by using the benzodiazepine-specific antagonist flumazenil [184, 185]. A study by Mora et al. [186] 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 [187]. Flumazenil’s half-life 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 to observe and treat a possible medication rebound.

In a study by Andrews et al. [188], 50 patients who underwent gastroscopy with midazolam sedation received either flumazenil or placebo directly after the examination and again 30 minutes later. Those who received flumazenil showed markedly improved memory, psychomotor function, and coordination after only 5 minutes (p < 0.001). However, 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. [189] 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 [190]. However, so far, no other benefits have been reported for either the patient or the endoscopist. Care should also be taken with patients taking carbamazepine, high doses of tricyclic antidepressants, or those suffering from chronic benzodiazepine abuse, as seizures or withdrawal symptoms may occur. Therefore, the routine use of flumazenil cannot be recommended. In patients in whom the use of flumazenil should nevertheless become necessary, an appropriately longer monitoring period should be observed.

Overall, the use of antagonists such as flumazenil seems to be rare. In a study period of 5 years, flumazenil and/or naloxone were used in only 0.03 % of cases. Reasons were a drop in oxygen saturation, respiratory changes, hypotension, and bradycardia. Compared to a matched control group, antagonists were used more frequently in the elderly, females, higher ASA class, and higher Mallampati index [191].

2.2.2.4 Remimazolam

One of the new developments in endoscopic sedation is the benzodiazepine remimazolam, which is currently in the final phase of approval. Due to the special metabolism of remimazolam, the recovery phase is significantly shorter than for midazolam (7.2 min to 15.7 min) [192]. Remimazolam acts comparably to midazolam at the GABA receptor. However, unlike midazolam, it is not metabolized like remifentanil, and it is degraded to inactive metabolites via tissue esterases. A phase IIa dose-finding study demonstrated dose-dependent, rapid, well-controlled, and safe sedation for patients undergoing gastroscopy [193]. A phase III study evaluated the use of remimazolam in 461 patients undergoing outpatient colonoscopy. With a comparable incidence of adverse events, patients receiving remimazolam had a more favorable neuropsychiatric recovery profile [194]. A protocol for a meta-analysis of existing studies on remimazolam was recently published [195].

2.2.3 Propofol Versus Midazolam

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<th>Recommendation 2.5</th>
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<tr>
<td>Based on the data on action profile and complications, we suggest that propofol be preferred over midazolam.</td>
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**Evidence level 2b, recommendation grade B, strong consensus**

Data on efficacy and complications suggest that propofol should be preferred to midazolam during sedation for gastrointestinal endoscopy. Individual adjustments must be made according to the patient’s situation and the type of exam, as well as to the personnel, equipment, and structural requirements mentioned in this guideline.

Patients, as well as endoscopists, judge sedation with propofol as good or better than sedation with midazolam [87, 88, 132, 196, 197]. Therefore, in recent years, propofol has gained importance as a sedative for gastrointestinal endoscopy. Some have termed this a paradigm shift in endoscopy, if nothing else, because of explicit requests for propofol sedation by some patients [72].

Randomized studies suggest that propofol is preferable for EGD, colonoscopy, and ERCP [72, 84–91, 197–201]. The advantages of propofol sedation compared to benzodiazepines are a shorter time of onset [87], significantly better patient cooperation (especially in interventional endoscopy such as ERCP) [198, 202], and a shorter recovery time [200], including recovery of psychomotor function [86]. In patients undergoing ESD, a comparison of propofol versus midazolam showed markedly better endoscopist-satisfaction with the exam conditions in the propofol group [203].

Propofol facilitates the performance of colonoscopy [204], and moderate sedation (“conscious sedation”) is usually sufficient [205].

The in-depth analysis shows no influence of propofol on patient satisfaction for upper GI-endoscopy [84, 85, 197, 206] but an advantage for propofol during colonoscopies [86, 87, 196].

A comparative meta-analysis of five publications including 552 patients showed that endoscopist satisfaction was higher for propofol than for midazolam. Patient satisfaction and transfer criteria did not differ. However, hypotension occurred more often under propofol than midazolam [207].

A recently published double-blind study on outpatient colonoscopies showed clear advantages of propofol compared to a midazolam bolus or titrated midazolam regarding examination duration and induction time, as well as recovery and transfer time [208].

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 midazolam and meperidine [72]. However, in the propofol group, one case of aspiration pneumonia occurred and three patients required endotracheal intubation [72]. Endoscopist satisfaction was higher in the propofol group and examination times were significantly shorter. Apnea was a frequent complication with potentially severe consequences.

Propofol also has advantages over midazolam for more complex procedures, such as endoscopic submucosal dissection [209]. Body movements occurred less frequently in patients sedated with propofol than with midazolam [210]. Apart from hypotonias, which occurred more frequently under propofol, side effects were comparable in both groups. A comparative study of 90 patients showed that propofol is also preferable to midazolam in patients with liver disease (such as liver cirrhosis) [211].

2.2.3.1 Cardiorespiratory Complications

Comparative data on complications from 12 randomized studies were compiled in a meta-analysis by Qadeer et al. [105] that describes 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 endoscopic interventions (EGD and ERCP), no significant difference was seen. A more recent meta-analysis included 20 studies and found higher complication rates with propofol but no increase in complication rates [66].

When propofol is used for ERCP, there is in some cases a significantly higher risk of arterial hypotension compared to midazolam/meperidine [197–199, 212, 213]. There is 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 [214] 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 was reported (1.4 %), leading to discontinuation of the intervention. Short-term mask ventilation was necessary in 40 (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 higher propofol doses were independent risk factors for cardiorespiratory complications [214]. In a comparative study of i. v. propofol monosedation versus i. v. propofol combined with oral midazolam in patients undergoing ERCP, fewer episodes of oxygen desaturation, lower propofol doses required, and less anxiety levels of the patients prior to the procedure were noted in the propofol/midazolam combination group [215].

In a large multicenter study of 177 944 patients in ASA classes I and II who underwent esophagogastroduodenoscopies or colonoscopies, 64.4 % of patients received propofol alone and 22.4 % a combination of propofol and midazolam. Sedation was provided by endoscopy personnel in 56.5 %. No severe adverse events occurred, and milder adverse events were more common in patients receiving midazolam and an opioid [216]. In contrast, an analysis of 73 029 procedures recorded 39 life-threatening events, such as cardiorespiratory arrest or significant hypoxia. Patients in all ASA classes were included. The authors note that there was an increase in complications, particularly in patients sedated with propofol. This was mainly attributed to patients with comorbidities, as well as a tendency toward deeper sedations [217]. However, a meta-analysis on the incidence of the cardiorespiratory side effects of propofol found no significant differences compared to traditional sedatives such as midazolam [218].

2.2.3.2 Amnesia

2.2.3.3 Diazepam Versus Midazolam

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<td>If benzodiazepines are to be used for sedation in justified individual cases, we recommend that midazolam should be preferred over diazepam because of its shorter half-life.</td>
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Evidence level 2b, recommendation grade A, consensus

Amnesia following the use of midazolam has been well studied [219] and has been shown to be significant. If amnesia is not desired, midazolam should not be used. An alternative benzodiazepine is diazepam [165, 166]. The longer half-life of diazepam has not been reported as a disadvantage compared to midazolam [166, 170, 220]. However, in some studies, patient comfort was lower after diazepam than after midazolam. Of all sedation concepts, midazolam has the highest potency of amnesia as a side effect. Examples of justified use of benzodiazepines can be found in [107, 215].

2.2.4 Other Drugs as Monotherapeutics

2.2.4.1 Introduction

Other drugs are either sedating/hypnotic or analgesically active substances that do not fall under the usual substance classes. These include opioids and ketamine (as monotherapeutics), inhalation anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), and neuroleptanalgesics. There are only a few older studies on these substances, which show, at a moderate level of evidence, that these drugs are basically 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 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 and airtight laryngeal mask) is not the usual practice.
5. Based on the current data, there is not enough evidence for the routine use of NSAIDs for endoscopic interventions.

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<th>Recommendation 2.7</th>
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<td>We suggest that opioids, ketamines, inhalation anesthetics, and neuroleptics should not be used as monotherapeutics for sedation in endoscopy.</td>
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Evidence level 5, recommendation grade B, strong consensus

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 for the patients to breathe spontaneously or to ventilate the patient, should this prove necessary. The effects on blood pressure and heart rate are mild, usually causing a drop in these parameters because of the central inhibition of the sympathetic nervous system. Smooth muscle spasms of the bile duct and pancreas and constipation can also occur. Nausea and vomiting under fentanyl are comparable to other opioids. Although fentanyl is usually used for general anesthesia (often in combination with other drugs) or for chronic pain (usually transdermal), 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 [221, 222]. A study comparing fentanyl and meperidine during endoscopic procedures showed shorter examination times when fentanyl was used. A more rapid patient recovery was reached with its use. However, meperidine showed a better analgesic effect in postprocedural pain scores [223]. In contrast, in 180 patients who received deeper sedation for analgesia, the fentanyl group showed a better postprocedural pain score than remifentanil [224].

2.2.4.2.2 Remifentanil

2.2.4.2.2.1 General Considerations

Data on the routine use of remifentanil, a highly potent synthetically synthesized opioid with an extremely short half-life (2–3 min), are scarce. Remifentanil is predominantly used in combination with midazolam or propofol to reduce the dose applied. Within a few minutes after intravenous injection, remifentanil is hydrolytically cleaved in blood and tissue by nonspecific esterases, regardless of liver and kidney function. There is no accumulation even after prolonged continuous use [225]. As with other opioids, the use of remifentanil can lead to respiratory depression. Muscle rigidity, especially of the respiratory muscles, is also observed. These side effects occur primarily with bolus administrations. Therefore, the substance should be applied only as a continuous infusion in spontaneously breathing patients. Use is restricted to a site that is fully equipped to monitor and support respiratory and cardiovascular functions (according to the product information).

In a randomized study by Akcaboy et al. [226], 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. After bolus administration, the duration of the examination was longer, and the oxygen saturation 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-blind 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 similar in both groups. In addition, no differences were observed regarding procedure duration and the required times for discharge of the patients from the recovery area [137]. 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 [227]. Comparing remifentanil alone and pethidine with midazolam in colonoscopies, similar adverse event frequency was found with shorter recovery time and better intraprocedural communication with patients [228]. Another study also found adequate analgesia, faster recovery, and greater investigator satisfaction with remifentanil alone compared with remifentanil and midazolam, as well as pethidine and midazolam [229].

Using the up-and-down method, a pharmacokinetic model for dosing remifentanil with propofol was designed [230]. With the goal of suppressing gag reflexes upon insertion of the endoscope into the pharynx in 50% to 90% of cases, a target concentration of 0.05 mg*kg⁻¹*min⁻¹ without TCI for remifentanil combined with a propofol bolus of 1 mg/kg or a target concentration of 2 ng/ml (equivalent to approximately 0.1 mg*kg⁻¹*min⁻¹ without TCI) for remifentanil combined with a propofol bolus of 0.75 mg/kg was found. Remifentanil target concentrations are reached approximately 5 minutes after the start of the infusion [230].

The very good controllability, as well as the fast recovery times under remifentanil, make these substances a promising analgesic in combination with a well-controllable sedative in gastrointestinal endoscopic procedures.

2.2.4.2.3 Sufentanil

Sufentanil has a spectrum of activity favorable for analgo-sedation with potent analgesia and less respiratory depression compared with other opioids [231]. Greater hemodynamic stability and a shorter context-sensitive half-life have been described compared to the other opioids [232]. Sufentanil appears superior to fentanyl as an analgesic for procedural sedation because of lower risk of accumulation, greater therapeutic range, and spectrum of action. Due to its stronger sedative properties, sufentanil can be used in combination with sedatives and as a monotherapeutic. Compared with the partial opioid agonist nalbuphine, sufentanil produces equally good analgesia in colonoscopy patients [233]. However, respiratory depression occurred more frequently. Overall, the data on sufentanil for procedural sedation are still too limited to make an assessment.

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 “monoanesthetic” for short diagnostic and therapeutic interventions in children and for special situations in adults. After intrave-
Wehrmann T, Riphaus A et al. Updated S3 Guideline
and an effect duration of about 10 min) and a rapid onset of action
of ketamine. It causes a so-called dissociative anesthesia without cardiorespiratory
depression [235]. The analgesic effect starts at sub-hypnotic
mechanical irritation of the heart itself. Moderate hyperventilation is observed after keta-
melodic reactions can be reduced by also giving midazolam [235, 237]. In Germany, in addition to racemic ketamine, the levora-
tory isomer S+-ketamine is also commercially available. S+-keta-
mine is approximately two times more potent than ketamine and
is said to have fewer side effects [237, 238]. However, the litera-
ture on this subject so far is inconclusive.

For the reasons given above, ketamine is not recommended as a
routine monotherapy for endoscopic examinations.

Most studies on the use of ketamine relate to its use in combi-
nation therapies (mainly with midazolam) for endoscopic inter-
ventions in children [239, 240]. It was shown that adequate seda-
tion can be achieved without cardiorespiratory complications. Al-
though 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. [241] 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 under-
go another similar procedure. A randomized study by Ong et al. [242], which compared ketamine combination sedation (keta-
mine plus midazolam, pentazocine, and propofol) with propofol
monosedation for ERCP, demonstrated, especially in younger pa-
tients, a better patient tolerance of the combination sedation.
However, patient satisfaction was similar in both groups. In addi-
tion, hypoxia occurred more frequently when the combination
therapy was used.

A recent study in colonoscopy patients showed better hemo-
dynamic stability and fewer respiratory complications in the keta-
mine/propofol group than the propofol group with similar patient
and endoscopist satisfaction [243]. Further studies also demon-
strated advantages of a combination of ketamines with other sedatives/analgesics [244–246].

2.2.4.3.2 Etomidate
In recent years, the use of etomidate for sedation during endo-
scopic procedures has been increasingly studied. Like propofol and
the benzodiazepines, the imidazole derivative etomidate is an aga-
nist at the GABA receptor. It has a short onset and half-life comparable
to propofol. Hypotension is less pronounced after bolus injec-
tion than after propofol [247]. Due to suppression of the adrenal
cortex via inhibition of 11β-hydroxylase with a drop in serum corti-
sol, etomidate is unsuitable for prolonged sedation without ade-
quate cortisol substitution. Clinically relevant inhibition of cortisol
synthesis may also occur after bolus administration of etomidate
(e.g., for intubation) especially in patients with comorbidities. For
this reason, the administration of etomidate should be critically
considered in the context of sedation for endoscopy [248–251].

A meta-analysis comparing sedation with propofol and etomi-
date found no differences in sedative effects, cardiovascular side ef-
teffects, and recovery time [252]. In contrast to propofol, etomidate
caused fewer respiratory complications and injection pain, but pa-
tients had more frequent myoclonias. In a study comparing etomi-
date with midazolam, myoclonias were observed in 12.1 % of pa-
tients [253]. Patient satisfaction was higher with midazolam. Better
hemodynamic stability was observed with a combination of etomi-
date and midazolam than with propofol and midazolam [253].

Due to the still relatively poor data situation and the potential
side effects such as myoclonia and suppression of the adrenal cor-
tex, especially in patients with comorbidities, no recommendation
for etomidate in gastrointestinal endoscopy can be made at present.

2.2.4.3.3 Dexmedetomidine
Dexmedetomidine is a specific α2-adrenoceptor agonist charac-
terized by sedative and low analgesic properties. Unlike other se-
datives/hypnotics, dexmedetomidine does not cause respiratory
depression. The substance has been approved in Germany since
2011 for sedation of adult patients in the intensive care unit up to a
sedation level of RASS –3. Since the publication of the pre-
vious version of this guideline, it has also been approved for the
sedation of adult, non-intubated patients before and/or during
diagnostic or surgical procedures (source: product information
preparation Dextra, as of January 2020).

When rapidly administered intravenously, α2 agonists such as
dexmedetomidine exhibit a typical hemodynamic profile. Initially,
there is an increase in blood pressure followed by a mild hypotensive
phase [254]. Therefore, because of the pronounced hemodynamic
effects, dexmedetomidine should not be administered as a rapid in-
tavenous infusion or even as a bolus [255]. Alpha 2 agonists should
not be used in patients with bradycardic arrhythmias or in patients
who are dependent on adequate mean pressure [256]. In case of
volume deficiency, pronounced hypotensive phases may occur. Ac-
cordingly, the volume status should be assessed and compensated
before administration of α2 agonists. The drug should only be admi-
nistered by experienced users, and continuous monitoring must be
midazolam was published by Nishizawa et al. [257]. Dexmedetomidine achieved deeper sedation on the Ramsay scale and therefore appears particularly suitable for ERCP and ESD. In 2015, a number of studies on the use of dexmedetomidine for sedation found in recovery time.

The use of dexmedetomidine may be considered for endoscopic procedures.

Evidence level 1b, recommendation grade 0, strong consensus

2.2.4.4 Inhalation Anesthetics as Monotherapeutics

2.2.4.4.1 Nitrous Oxide (Laughing Gas)

Nitrous oxide (laughing gas) may be considered for analgesia and sedation during colonoscopy only if the structural requirements are met.

Evidence level 1b, recommendation grade 0, strong consensus

2.2.4.4.1.1 General Considerations

Nitrous oxide (N₂O), the so-called “laughing gas,” is a stable, slow-reacting, colorless, and odorless gas. It has strongly analgesic and mildly narcotic properties. Nitrous oxide has a rapid onset of action and a short recovery time. Mixed with oxygen, it is normally used to initiate or maintain anesthesia. In Germany, a fixed mixture of 50% nitrous oxide and 50% oxygen has been commercially available since 2008 (Livopan; in Great Britain available as Entonox since 1965, in other countries available as Emono or Meo-pa). Nitrous oxide is a gas at room temperature and must only be applied using suitable inhalation and anesthesia equipment. It has a mild sedative and a strong analgesic effect. Although normally, the circulation is only slightly affected, 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 metabolisms can be affected [260]. 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 considered (see statement of the BDA and the German Society for Anesthesiology and Intensive Care Medicine; DGAII) [261].

In a meta-analysis 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 [262]. There were no differences with regards to pain during exams that avoided analgesics but also no differences regarding colonoscopies with intravenous sedation. The use of nitrous oxide led to a more rapid discharge, as compared to intravenous sedation. A Cochrane meta-analysis analyzed the use of nitrous oxide during colonoscopy [263]. A total of 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 [263]. 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 leads 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 i.v. sedation when both were applied on demand [264, 265]. Few new studies indicate that nitrous oxide’s sedation quality is comparable to an i.v. sedation [266–268].

The data situation still appears to be too weak to allow a clear assessment of the significance of nitrous oxide for the performance of endoscopy. It should be noted, however, that occupational safety regulations must be observed when using nitrous oxide.

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 [269–271]. By combining different substances, dose reductions can lead to more rapid recovery after the procedure [87, 196, 272, 273]. Although combination therapy causes hypotension and oxygen desaturation more frequently than monotherapies [274–276], the occurrence of accidental overdosing is reduced [112, 116] (see also section 2.3.3). In recent years, combinations of sedatives with i.v.-applied lidocaine have also been described [277–280].

Because of the synergistic effects of propofol, midazolam, and opioids, the dosage of propofol can generally be reduced when combining these substances (mainly shown in studies of general anesthesia), and side effects can therefore be reduced [281, 282]. In addition, the combination appears to provide improved
2.3.2 Specific Combinations

2.3.2.1 Combination of Benzodiazepine Plus Opioids

A study by Milligan et al. [272], 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. [294], which 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 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 time, or procedure time [295]. The combination of midazolam and fentanyl, however, had a similar analgesic effect but a shorter recovery time than midazolam plus meperidine [296].

2.3.2.2 Combination of Propofol Plus Opioids

In a randomized, controlled study by Van Natta et al. [106], 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). A large study of 222 patients undergoing complex endoscopic procedures demonstrated no difference in vital signs between the study groups, and there was no significant difference in patient satisfaction [297]. The combination of propofol and opioid showed no difference in safety between propofol and standard sedation. In addition, Lee’s study showed that the use of propofol was associated with significantly increased patient satisfaction.

2.3.2.3 Combination of Sedative Plus Propofol

A total of 64 patients underwent two long (> 30 min) consecutive endoscopic examinations and initially received propofol and then a combination of midazolam and propofol. The advantage of combined sedation was that a significantly lower dose of propofol (~59 %) was required. However, the postinterventional recovery time was twice as long for the combination regimen (4 vs. 8 min) [298]. 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 [273]. However, the combination regimen was also associated with a longer recovery time (25 ± 8 min vs. 19 ± 7 min, respectively, P < 0.05). Another study showed a similar effect of dose reduction and a shorter postinterventional recovery time with the use of a combination of propofol with midazolam as compared to propofol monotherapy (13.0–14.7 versus 18.1 min, P < 0.01, respectively) [106].

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<tr>
<th>Recommendation 2.10</th>
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<tr>
<td>We suggest that a combination of propofol and midazolam should not be used.</td>
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<td>Evidence level 1b, recommendation grade B, consensus</td>
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2.3.2.4 Combination of Sedatives Plus Spasmolytics

A prospective, double-blind, placebo-controlled study by Mui et al. [299] investigated the use of the spasmolytic hyoscine N-butyllbromide (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. Since the focus of this guideline is sedation and not spasmolysis, no firm recommendation is given.
2.4.2 High-Risk Patients

**Recommendation 2.11**

<table>
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<tr>
<td>Patients with a higher ASA grade and/or older patients are at a higher risk of sedation-related side effects (cardio-respiratory depression). We suggest that the dose of the sedative/analgesic used should be adjusted/reduced accordingly.</td>
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</table>

**Evidence level 2b, recommendation grade B, strong consensus**

2.4.3 Substance Type

In accordance with the modified recommendations of the American Society of Gastroenterology for elderly patients undergoing gastrointestinal endoscopy [307], fewer substances should be administered more slowly and at a lower cumulative dose [307, 308]. In many cases, midazolam and/or opioids are used to sedate elderly patients. Since there is an increased risk of hypoxemia with the use of benzodiazepines in elderly patients, patients with obesity, and anemic patients, a reduction in dose seems advisable [309]. Postintervention hypoxemia risk is also increased, especially in elderly patients [213].

Since propofol has a limited therapeutic range, it can lead to more cardiorespiratory complications in older high-risk patients than in younger patients [92, 310]. 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 [311–313]. If special care is taken in sedating elderly patients, it has been shown that propofol can be safely used in this patient group [213, 310, 313]. In a study of elderly patients receiving propofol for endoscopic examination, it was shown that patients over 70 years of age required lower doses of propofol than patients under 70 years of age. The incidence of major and minor complications was the same in both patient groups [313]. Based on 27,000 patients, it was demonstrated that under sedation with propofol, there was a drop in oxygen saturation in 2.3% of patients, even though 2 L of oxygen were administered during the procedure. In elderly patients over 70 years of age, it was even more than 5% [117]. In these patients, hemodynamic parameters were only recorded in a few cases, so it can only be guessed whether further complications would occur. There was also no monitoring of ventilation, so hypoventilation and hypercapnia can also only be speculated on. Continuous administration of propofol in patients over 80 years of age led to a clear tendency of increased decreases in oxygen saturation, even though they were not more complications overall compared to younger patients [114]. A cohort study by Vargo et al. [300] 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 an increasing ASA grade who were undergoing colonoscopy.

In a randomized study by Riphau et al. [314], 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 [315]. Because of its shorter duration of action, better controllability, and fewer complications regarding hepatic encephalopathy in cirrhotic patients, propofol should be preferred over benzodiazepines and/or opioids in such cases [314–318].

### 2.4.4 Obesity

Data on the effect of obesity on sedation for endoscopy are still limited. Morbid obesity can result in several 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 [319]. In another study, a multivariate analysis of 799 patients identified a direct association between BMI and sedation problems in patients who were sedated with propofol [320]. An analysis of 799 patients identified BMI and higher ASA classification as predictors for respiratory and cardiac complications [321]. A multivariate analysis identified ASA class III or greater and an elevated BMI as independent risk factors for mechanical, respiratory support [322].

### 2.4.5 Elderly Patients

As in obese patients, data on sedation for endoscopy in geriatric patients is sparse. Generally, aging leads to a reduction in organ function. Impaired hepatic or renal function are of particular importance for the metabolism and elimination of sedatives and analgesics [323]. In addition, as a result of existing comorbidities, polypharmacy is common in the elderly. This can lead to drug interactions with the substances used for sedation. One study showed that patients older than 70 years required less propofol than those younger than 70 years [313]. In patients older than 90 years of age, only minimal doses of propofol are required to reach adequate examination conditions [324]. Furthermore, patients older than 80 years have a higher risk of oxygen desaturation [114]. A study in more than 10,000 patients showed a general increase in the rate of complications with age [325]. A German study of patients older than 80 years showed only a slightly increased risk when mild sedation was used [213]. Required doses for adequate sedation were 10–20% lower in high-risk patients than in those with an ASA classification of I and II [310]. Meticulous monitoring is therefore required in high-risk, elderly patients. Also, several recent studies showed that sedation can be safely performed in the elderly if careful attention is paid to sedative/analgesic dosing and adequate monitoring [156, 326–330]. Post-procedural pneumonias can occur more often in sedated patients [27].

### Recommendation 2.13

Propofol may be considered for sedation in elderly patients.

**Evidence level 1b, recommendation grade A, strong consensus**

### 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 [322, 331–334]. A study of propofol sedation for endosonography included patients of all ASA classes. It found no correlation between ASA class and risk of complications. However, sedation was performed by an anesthesiologist [72]. It should be considered that patients with multiple comorbidities and high-risk patients have special staffing requirements (see chapter 3.3).

A meta-analysis on the sedation of patients with liver cirrhosis showed that propofol has similar side effects and a shorter recovery and discharge time than midazolam (296). Another meta-analysis came to the same conclusion that the frequency of side effects under midazolam and propofol is similar [335]. However, the efficacy of the propofol sedation was significantly better. Therefore, propofol sedation should be preferred in patients with liver cirrhosis. Patients undergoing variceal ligation experienced more frequent desaturations (23.2% vs. 7.7%), bradycardia (22.5% vs. 17.2%), and hepatic encephalopathy (6.6% vs. 0.6%) in the midazolam group compared to patients who were not sedated with midazolam, respectively [336].

### Recommendation 2.14

We recommend that specific antagonists for benzodiazepines and opioids should be immediately available in the endoscopy suite.

**Adapted from the ASGE, 2008**

**Evidence level 5, recommendation grade A, strong consensus**

### Recommendation 2.15

Offering music to the patient may be considered to reduce the dose of the sedative used.

**Evidence level 1b, recommendation grade A, strong consensus**

Several studies found a positive effect of music regarding the reduction in sedative and analgesic doses. These results were also confirmed by meta-analyses.
A recent randomized controlled trial also found the benefit of music during colonoscopies. In the music group, patients had less pain, were more satisfied, and the examination was easier to perform. In addition, the need for midazolam and pethidine was less than in the control group [337]. The anxiety level was also favorably influenced by music during endoscopy. In 180 patients, no difference in anxiety level was found depending on age or type of examination. However, music significantly reduced anxiety [338]. In contrast, a study of 307 patients showed that music had no effect on pain perception during endoscopic procedures [339].

A meta-analysis by Rudin et al. [312] evaluated six randomized controlled studies with a total of 641 patients. In three studies, endoscopy was done with music alone. This reduced the patients’ anxiety levels in comparison to the control group by 8.6% (P = 0.004). In the remaining three studies, patients received 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 for sedatives by 15% (P = 0.055). Another meta-analysis of eight 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 time, 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 [340]. A third meta-analysis of eight studies included 712 patients. No difference was found regarding various endpoints regardless of whether music was used or not. However, overall satisfaction scores were significantly higher in the music group [341]. In a recent study of patients undergoing colonoscopy, an EMG of the facial musculature was used to objectify stress levels. It was found that patients who listened to music during the procedure had significantly lower stress levels than the control group [342]. While patient satisfaction showed no differences, endoscopists were significantly more satisfied with the course of colonoscopy.

Overall, the data suggest that music during an endoscopic procedure may lead to a shorter examination time with possible reduction in sedative doses. Since the use of music entails little effort and does not lead to relevant side effects, its use can be recommended in patients who wish to have it.

**Acupuncture/Hypnosis**

Although there has been increasing interest in alternative medicine in recent years, data on the use of acupuncture during endoscopic procedures are still scarce. While there is evidence of a reduced need for sedatives/analgesics in patients with acupuncture [342], other results show no effect on sedation [343]. Further studies must be done before the value of acupuncture for sedation in endoscopic gastrointestinal procedures can be assessed. The same is true for hypnosis.

### 3 Guideline – Structure Quality

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 societies [21, 81, 117, 344–373], as well as the current S2k guideline, “Quality-Requirements for Gastrointestinal Endoscopy” (AWMF register no. 021–022).

#### 3.1 Personal Requirements

The endoscopic examination and/or treatment and the sedation procedure are distinct medical procedures. If physicians perform the diagnostic or therapeutic intervention and, at the same time, also carry out the sedation, they take full responsibility not only for the intervention but also for the sedation and/or analgesia. This includes monitoring and, if required, restoration of vital functions.

Special theoretical and practical knowledge on sedation and/or analgesia is necessary not just for physicians, but also for supporting nurses and other assisting staff. A physician cannot perform the invasive intervention and at the same time monitor the sedation and/or analgesia procedures.

Therefore, all personnel involved in sedation and monitoring should be familiar and trained with the sedation technique used, as well as its monitoring and complication management (see point 3.3.1).

Whether, in individual cases, physicians performing the sedation can be substituted by qualified, specially trained, nonphysician personnel must be decided on a case-by-case basis by physicians who perform the diagnostic or therapeutic intervention. These physicians take responsibility, and they must perform an on-site assessment with consideration of the structure of the working place, the patient’s 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 is sufficiently qualified and capable of carrying out their tasks appropriately.

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

<table>
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<tr>
<td>We recommend that physicians who are responsible for the sedation should be experienced in intensive care medicine. They should be trained and proficient in the use of sedatives and analgesics. This involves knowledge, recognition, and treatment of expected side effects including cardiopulmonary resuscitation, maintaining upper airway patency, intubation, and assisted ventilation.</td>
<td>Evidence level 5, recommendation grade A, strong consensus</td>
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As in the guidelines of other professional societies [21, 311, 361–372, 374–380], personal prerequisites for carrying out analgeo-sedation include knowing how to deal with an emergency situation (including correcting circulation problems) and being proficient in endotracheal intubation.

This has not changed, even in the new versions of various international guidelines [373, 381–384].
3.2 Education and Training Courses

<table>
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<tr>
<td>As part of quality assurance, we recommend physicians and nonphysician assisting personnel should participate in specifically designed sedation training. The knowledge of the nonphysician personnel should be certified.</td>
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</table>

Evidence level 5, recommendation grade A, strong consensus

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 using simulators, improve physicians’ confidence in handling emergency situations [385, 386].

A much broader training program for nonphysician assisting personnel (nurses) was the subject of several studies using propofol [94, 334]. The DGVS has developed a structured curriculum for a joint one-day team training for physicians and nurses [387]. For training of qualified, nonphysician assisting personnel (nurses or physician’s assistants) a 3-day curriculum is offered by the DEGEA and accredited by the DGVs [387]. In addition, since 2012, a training curriculum of the ESGE and ESGENA exists [388], which was developed in accordance with the German recommendations. All curricula rely on the use of simulator-based training.

Recently, there have been positive recommendations from numerous international guidelines on this subject [373, 381–384, 389, 390]. High safety in the use of NAPS by trained teams has also been documented in mostly retrospective studies [391–393]. For sedation with midazolam plus opiates (moderate sedation), a reduction in the number of hypoxias by trained compared with untrained endoscopists was reported [386].

<table>
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<tr>
<th>Recommendation 3.3</th>
<th>2022 (modified)</th>
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<tr>
<td>We recommend that the qualification of physicians and nonphysician assisting personnel who are involved in sedation, monitoring, and follow-up should be ensured by periodical participation in structured education curricula. In addition to theoretical knowledge, these curricula should transmit practical competencies including complication management (e.g., simulation training). Note: It is generally preferable for the whole endoscopy team (physicians and nonphysician assisting personnel) to do the training together.</td>
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Evidence level 2, recommendation grade A, strong consensus

3.3 Personnel Requirements

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<thead>
<tr>
<th>Recommendation 3.4</th>
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<td>For every endoscopy under sedation, we recommend that one person is solely responsible for the performance, monitoring, and documentation of the sedation. This person should have verifiable specific training and be experienced in the monitoring of patients who have received medication (sedatives, hypnotics, and/or analgesics). In all cases, if an increased patient risk (e.g., ASA class ≥ III and procedural special risk factors for cardiopulmonary events), anatomical peculiarities of the airways, or severe neurologic diseases are expected, we recommend that a second physician (qualified in resuscitation and intensive care) be present whose only task is the sedation and the monitoring of the patient.</td>
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</table>

Evidence level 5, recommendation grade A, consensus

The guideline of the DGAII [376] states: “Since the examiner is usually unable to watch the patient’s vital signs 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 co-morbidities (ASA class ≥ III) have an increased sedation risk during emergency and long lasting (> 60 min) endoscopies [220, 394–396]. Questions regarding the composition of endoscopy teams or persons involved in endoscopic procedures or interventions 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) [387, 388]. In principle, as a prerequisite of training in sedation and emergency management, assistants should have formal training in a medical profession (nurses, physician’s assistants, etc.).

The recommendation also corresponds to most of the current international guidelines [373, 381–384, 390]. In a new ASGE guideline, which focuses on this topic (“Staffing requirements”) [397], a differentiated procedure between the performance of unsedated endoscopies (not the subject of the current guideline), the administration of moderate sedation (by benzodiazepines and other substances excluding propofol), and of deep sedation (with propofol) is recommended. The sole focus of the sedating person on the sedation procedure (“sole task”) is only required for deep sedation with propofol. Furthermore, the German “Pro-Sed” studies [34, 398] indicate that for low-risk patients and interventions, a “sole task” approach, also for propofol, is not mandatory. However, definite proof, based on hard endpoints, has not yet been provided for this strategy. Based on “primacy of patient safety”, the previous recommendation remains valid. The ASA classification (as an excellent factor) proves difficult to classify the risk of patients who should have a second physician present, as the definition of this group is very diverse. For example, uncompensated heart failure or severe COPD is certainly an indication for physician-guided sedation rather than NAPS sedation, but poorly controlled diabetes mellitus or chronic, rate-controlled atrial fibrillation are mostly not. However, most of the guideline group voted in favor of maintaining the 2014 recommendation.

A recent retrospective Scandinavian study [392] showed that for ASA I-II patients, complex endoscopic examinations (ERCP, EUS, balloon enteroscopies, and also those with high procedural risk) are also safely possible in a “NAPS setting”. The evidence of a single retrospective study is currently not sufficient to change the recommendation.

### 3.4 Monitoring During and After the Endoscopic Procedure

**Recommendation 3.5**

We recommend that monitoring measures should be based on the patient’s health status, the invasiveness of the endoscopic procedure to be performed, and the type of sedation/analgesia used.

**Evidence level 5, recommendation grade A, strong consensus**

Several prospective complication registers [220, 394–396] showed an increased complication rate in patients ASA class III and higher, both for interventional endoscopy and emergency examinations. In a single-center, prospective-case series of patients undergoing interventional endoscopies (majority upper GI tract hemostasis and ERCP) [214], an increased morbidity and mortality was found, and patients with higher ASA class and those who underwent emergency interventions were at highest risk. This is also confirmed in recent German publications [34, 398]. The recommendation is in consensus with all international guidelines dealing with this topic [373, 381–384, 390].

**Recommendation 3.6**

We recommend that sedation should be initiated by an appropriately qualified physician (see Recommendation 3.1).

**Evidence level 5, recommendation grade A, strong consensus**

The delegation of medical services, such as the delegation of monitoring to assistants, requires the presence of a physician who is personally responsible for delegating this activity.

In Germany, the indication for sedation and the choice of special medication must be made by a physician who is qualified to do so (a requirement of pharmaceutical law).

**Recommendation 3.7**

Subsequent monitoring and continuation by an experienced person with appropriate training (physician, nurse/physician assistant) may be considered.

**Evidence level 1, recommendation grade 0, strong consensus**

The safety of NAPS sedation has been documented in numerous international, mostly prospective, studies [34, 125, 398–406].

The previous Recommendation 3.3.3.1c is redundant to Recommendation 3.4 (previously 3.3.2.1) and was left in the previous guideline versions of 2008 and 2014 to emphasize the importance of this passage (“the sedating person is solely responsible for the administration, monitoring, and documentation of sedation”) under the primacy of patient safety. Because of redundancy, this recommendation has now been deleted. The adoption of the resolution was only by simple majority (no consensus reached) because, to many members of the guideline group, this statement is still important. However, there are modifications of this recommendation in the literature.

The European guideline is more open regarding the requirement that no relevant restriction of the activities of the person monitoring the sedation is allowed [362] and this applies equally to the ASGE guideline [367]. It is stated that short activities, which can be interrupted at any time without danger, can be additionally assumed by this person [362, 367]. A possible example would be the handing of biopsy forceps, e.g., for taking Helicobacter samples during gastroscopy. A precise definition of these “short interruptible tasks” [367] is not given. However, the German guideline group remained stringent in this regard because of the legal requirements underlying the expert opinion from 2006 on the ability to delegate intravenous sedation in endoscopy by Prof. Dr. Dr. A. Ehlers (see DGVS homepage at www.dgvs.de).
Under appropriate conditions, NAPS is safe and efficient [334, 407–409] in patients with ASA classification I–III (Table 8). NAPS should not be performed in ASA IV patients [334, 407–409]. NAPS should be performed by an appropriately trained person supervising only this task. To date, only one prospective case series exists in diagnostic OED and colonoscopy. In 27,000 patients, it showed that even when supervised by the assisting endoscopy nurse (“2-person procedure”), NAPS appears to be safe [117]. However, randomized studies on this issue are not available to date, and most of the studies on NAPS (> 95%) were conducted in a “3-person setting”. The fact that in Germany, as shown in a survey by A. Behrens et al. [410], a “third person” is only involved in a maximum of 50% of cases makes it irrelevant for the guideline recommendation (which must primarily be based on published evidence and safety of use). Directly comparative, randomized studies on the frequency of complications in procedures using a “2-person vs. 3-person procedure” in the context of sedation during GI endoscopy are lacking to date. A first study implementing such a setting has only recently been completed (“Pro-Sed 3” study), but the results have not yet been published in full.

Postinterventional monitoring is necessary to detect any sedation sequelae. The duration of the postinterventional monitoring phase depends on the expected risk [270]. The duration of action and the half-life of the substance used should be considered.

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, if appropriate, with the use of a pulse oximeter. Patients can be released from the monitoring area when their vital signs are stable and they are alert [376]. 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.

Since follow-up should also include follow-up of problems not caused by sedation (e.g., perforation, nausea, etc.), a change in the wording of the 2014 recommendation (although without any evidence) seemed appropriate. Almost all international guidelines recommend patient monitoring independent of whether the focus is on sedation or not [373, 381–384, 390]. In sedated patients, detection of even non-sedation-related problems (e.g., perforation or other technical complications) may be delayed.

Monitoring persons must always be present in the recovery area or have the recovery unit in view (telemetric monitoring via cameras, etc. is not recommended).

However, they may, for example, use the telephone or file reports (i.e., perform tasks that can immediately be terminated). For safety reasons, patients who are awake should remain in the monitoring area until they are discharged. This prevents patients from leaving the area on their own while still under the influence of the sedation (see verdict of the German Supreme Court [Bundesgerichtshof], reference no. VI ZR 265/02).

This recommendation corresponds to all recommendations of other professional societies [373, 381–384, 390].

### 3.5 Facility and Equipment Requirements

**Recommendation 3.11 2022 (modified)**

We recommend that sedation should only be carried out in an environment adequately equipped to monitor and support respiratory and cardiovascular function. There should be an additional, separate recovery area.

This recovery area should also allow the monitoring of vital signs and treatment of cardio-pulmonary complications and should be supervised by persons qualified for this purpose.

**Evidence level 5, recommendation grade A, consensus**
The person in charge of the clinical monitoring checks breathing by observation, palpation of thorax, and abdominal wall movement and possibly by auscultation 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 societies, pulse oximetry is required for monitoring during all examinations [5, 361, 372]. For sedated and high-risk patients, continuous blood pressure and ECG monitoring are also demanded.

In addition to clinical monitoring, pulse oximetry is now a prerequisite for sedation (especially after the introduction of the quality assurance agreement for colonoscopy in accordance with § 135 SGB V). Here, oxygen saturation and heart rate are measured continuously. In Switzerland, according to a survey from 2012, 100% of all endoscopies with propofol sedation were monitored by pulse oximetry [411]. Similar studies from other countries, as well as from Germany [13, 14, 50, 51], show comparable figures with a monitoring rate of 96% to 97%. Sedation with propofol also requires monitoring of blood pressure. Monitoring devices in which oxygen saturation, heart rate, and automatic blood pressure measurements are displayed on a monitor mounted directly next to the endoscopy monitor are best because the examiner can view everything at once. Documentation of the measurement parameters is also preferable. In Germany, the frequency of blood pressure monitoring almost doubled within 3 years after implementation of the first national care guideline in 2008 [14].

Almost all current international guidelines support this recommendation [373, 381–384]. In some guidelines, the assessment of the patient’s level of consciousness (e.g., using the MOAA/S score) is additionally required [382, 384]. In the opinion of the guideline group, there is no hard evidence for this. The partial tac-ticle measures on the patient, which are necessary to determine the MOAS/S score, interfere with the course of endoscopic procedures. This is especially true for those of short duration. If anything, such measures may only be useful for longer-lasting procedures. Since the recommendation essentially refers to technical monitoring, it does not make sense to include the above-mentioned aspect. The fact that the consciousness of the sedated patient must be monitored is already included in the recommendations of WG II. Whether the MOAA/S score system makes sense here appears at least debatable.

### 3.5.1 Extended Monitoring

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<thead>
<tr>
<th>Recommendation 3.12</th>
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<tr>
<td>We recommend that mandatory monitoring during endoscopy should include pulse oximetry and blood pressure measurement.</td>
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<td>Evidence level 5, recommendation grade A, strong consensus</td>
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<th>Recommendation 3.13</th>
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<td>Capnography may be used for early detection of apnea. The additional use of capnography may be considered for multi-morbid or highly obese patients who have a high procedural risk for cardiopulmonary complications.</td>
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<td>Evidence level 1, recommendation grade 0, strong consensus</td>
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Capnography records the concentration of CO₂ in the breath. Breathing activity can be graphically displayed. By observing the continuous display of the expiratory CO₂ concentration on a monitor, apnea can be detected earlier than with pulse oximetry. The time difference of detection between these methods lies in the range of up to 1 minute [412–417]. Measurement of the absolute CO₂ tissue concentration (e.g., using transcutaneous measurement) or in the exhaled air is less important as compared to capnometric measurements in patients receiving general anesthesia (the focus should be on continuous capnographic monitoring).

Three recent international guidelines recommend the use of capnography in high-risk patients, deep sedation, and long-duration procedures, without a clear, definitive recommendation (“recommended”) [373, 381, 383]. A Cochrane analysis evaluated the effect of capnography on the performance of painful procedures in an emergency unit (no endoscopic examinations). Three randomized controlled studies were found, but a reduction in complications could not be shown [418].

Regarding the use of capnography in endoscopic examinations/interventions, a retrospective analysis of billing data from 258,000 patients was presented by Joplink et al. [419]. The setting of capnography alone, pulse oximetry alone, or the combination of both monitoring methods was analyzed. Retrospective analysis showed that the use of capnography (alone or in combination) significantly reduced the need for pharmacological interventions. The number of recorded deaths was also lower with the use of capnography but did not reach significance (odds ratio 0.18, P = 0.16) [419].

Regarding a possible cost–benefit analysis, a literature-based study was conducted in the United States. It showed that a reduction in side effects could be expected in 27.2% of cases with deep sedation and in 15% of cases with moderate sedation. Thus, it was determined (for the United States setting) that the use of capnography was cost effective [420].

In a meta-analysis of the literature of randomized controlled trials regarding the achievement of a lower hypoxemia rate by the use of capnography, nine studies were evaluated [421]. It was shown that the simple hypoxemia frequency (pO₂ < 90%) was significantly decreased, with an odds ratio of 0.61, as was the occurrence of severe hypoxemia (pO₂ < 85%), with an odds ratio of 0.53. However, the frequency of need for assisted ventilation or increased oxygen delivery was not different with the use of capnography compared with standard monitoring [421].

In addition, several randomized controlled trials can be found in the current literature:
In a single-center study by Slagelse et al. involving 540 patients sedated with NAPS, the number of adverse events (especially hypoxemia) with or without the use of capnography (in addition to standard monitoring) was evaluated. The number and duration of hypoxemia episodes were reduced by 40% (mild hypoxemia, pO₂ < 90%) and 21% (severe hypoxemia, pO₂ < 85%) by capnography (however, both effects were not significant). Overall, the study demonstrates only a very limited clinical benefit of capnography [422].

The results were somewhat more favorable in an RCT by Friedrich-Rust et al. in two centers on 533 patients undergoing colonoscopy under NAPS or MAC sedation with or without additional capnography. Hypoxemia (pO₂ < 90%) was observed in only 18% of patients monitored with capnography but in 32% under standard monitoring (significant effect). Additional risk factors for the occurrence of hypoxemia were age, BMI, the presence of sleep apnea syndrome, and the use of anesthesia-guided sedation (MAC) [423].

In contrast, another RCT performed at a single center in 452 patients undergoing gastroscopy or colonoscopy (ASA class I and II), the hypoxia rate was not significantly different without or with capnography (54% vs. 50% of patients, respectively) [424].

In two further RCT from the Frankfurt working group on capnography during PEG insertion, the frequency of hypoxemia was significantly reduced in 150 patients (odds ratio 0.29 for hypoxia < 90% and odds ratio 0.35 for severe hypoxia < 85%) [425]. In another 147 patients, the significance of a parameter calculated from capnography, the so-called integrated pulmonary index (IPI), was evaluated. Here, no relevant advantage of this method over the standard evaluation of capnography was shown [426].

In two prospective uncontrolled studies, capnography was considered useful in severely obese patients (BMI 46.4) [427] or when used during ERCP (N = 11 patients) [428].

Another study compared capnography via conventional determination of CO₂ concentration from nasal respiratory flow to a newer method, which determines CO₂ content via a special mouthpiece, thus orally. In 104 patients who underwent gastroscopy (ASA I and II patients), a more accurate detection of CO₂ concentration was shown with oral capnography (100% accuracy) versus nasal capnography (47% accuracy) [429].

All published studies (not only those included in the meta-analysis) showed a significant reduction in the number of observed hypoxemias with the additional use of capnography (see above). Evidence of a significant reduction in robust endpoints, such as mortality or permanent damage, or even a reduction in the frequency of endotracheal intubations, was not reported. Therefore, only a “may be considered” recommendation seems possible. Especially the use of capnography, in addition to standard monitoring, in multi-morbid or severely obese patients and complex procedures may well be useful.

Statement 3.14 2022 (unchanged)

A benefit of EEG monitoring with respect to relevant parameters in gastrointestinal endoscopy has not been demonstrated.

Evidence level 1b, strong consensus

The electric activity of the human brain correlates with the level of alertness and cerebral perfusion. Therefore, measurement of the electrical activity of the brain via EEG can be useful during general anesthesia or deep sedation. Bispectral (BIS) monitoring is used to evaluate sedation depth in intensive care medicine and in surgical patients.

An anesthesiology group investigated the correlation of sleep depth under propofol sedation using the BIS index and a complementary topographic EEG in patients sedated with propofol during endoscopy. Changes in the different brain regions between the natural sleep depth and under propofol sedation were shown [430].

A German working group evaluated the correlation between the clinical assessment of consciousness and various EEG parameters during frontotemporal EEG using a Neuroline 720 device from Ambu during gastroenterological and bronchoscopic examinations under propofol sedation. A total of 171 patients (ASA I and II) were evaluated. Only a weak correlation between the clinically determined level of consciousness and the EEG parameters, in particular the BIS index, was found. Therefore, due to the numerous artifacts, it was concluded, especially for the BIS monitoring, that the application of this method during endoscopy is not meaningful [431].

Most of the many other studies [432–441], however, showed no significant reduction in the required propofol dose in mostly interventional endoscopies. The use of BIS monitoring also did not lead to a reduction in surrogate patient safety parameters (hypoxemia and RR drop) [436]. In addition, some studies reported an inadequate or too slowly correlated assessment of the patient’s sedation depth in comparison to clinical observation of sedation depth and evaluation using BIS monitoring [438].

A meta-analysis on BIS monitoring included 12 studies, 6 of which were judged to be of poor quality [442]. Overall, the evidence quality from all studies was considered “low”. As a result, there was no significant effect of BIS monitoring on the duration of endoscopic examination, on the duration of awakening after sedation, and ultimately on clinically relevant adverse events. Only hypoxemia frequency and the number of blood pressure drops were significantly reduced. Overall, it was concluded that the validity of the existing studies is very limited [442].

In a randomized controlled trial of 115 patients undergoing colonoscopy under propofol sedation, there was only a moderate correlation between clinical assessment of sedation depth (MOAA/s) and BIS score [443].

In a randomized trial on the use of BIS monitoring in gastric ESD procedures in 90 patients, the need for interventions (e.g., chin-lift maneuver or increasing oxygen delivery) was required in 47.8% of patients without compared to 30% of patients with BIS monitoring [444]. However, again, no difference was found in the incidence of sedation-assisted complications. The conclusion was that BIS monitoring is not clinically relevant [444].

Another randomized study investigated BIS monitoring in 280 patients undergoing screening colonoscopies. The only finding was that the required propofol dose was higher in the group receiving BIS monitoring. Overall, BIS monitoring was again not considered helpful for clinical use [445]. In contrast, a randomized study of 50 patients undergoing outpatient colonoscopy conduct-
ed in 2019 found that the required propofol dose was lower under BIS monitoring. In addition, cognitive status was evaluated before and after sedation in both groups (MMSE, Triage test, and clock pointer test), with a more favorable outcome under BIS monitoring [446].

In a comparative study [447] with another EEG-monitoring method, which detects acoustic-evoked potentials, BIS monitoring was superior (on the assessment of sedation depth under propofol).

In a randomized controlled trial by Wehrmann et al. [199], a significant reduction in the required propofol dose during ERCP was demonstrated when using another alternative EEG-monitoring procedure, the Narcotrend system. However, this was not demonstrated using the same Narcotrend procedure in a more recent randomized study investigating the control of propofol sedation during ERCP [448]. However, a lower rate of hypoxemia and drop in blood pressure was found under Narcotrend monitoring.

In summary, no significant relevant advantages for the use of EEG monitoring in gastrointestinal endoscopy could be documented when considering current and older studies. Therefore, the use of such procedures can still not be recommended.

3.5.2 Addendum: Newer Monitoring Procedures (Without Recommendation)

Two studies employed bio-impedance monitoring to assess respiratory minute volume (RMV). This method involves placing three adhesive electrodes on the sternum, the xiphoid, and the right axillary line of the patient. By analyzing the wall movement of the chest, the respiratory minute volume is estimated [449]. An initial randomized study of 51 patients undergoing upper gastrointestinal endoscopies showed a better assessment of patients’ respiratory function using this method to determine respiratory minute volume than using respiratory rate alone [449].

In a second study of 73 patients undergoing upper gastrointestinal interventions, a decrease in minute volume was observed in 15.3% of patients undergoing standard monitoring compared to only 7.2% of patients studied with the new RVM monitoring (bio-impedance technique) (a decrease in minute volume <40% from baseline was considered relevant). This effect was even more pronounced in the 10% of patients in whom the anesthesiologist determined respiratory minute volume in advance as clinically meaningful [450].

In one study, photoplethysmography was used to detect respiratory rate (the Nelcor system, which is attached to the finger). A feasibility study on 26 patients described no increased sensitivity using this monitoring method for the detection of apnea episodes [451].

In another study, by Parisian anesthesiologists, a photoplethysmography method was used for blood pressure monitoring. In this feasibility study of 20 patients undergoing gastroscopy and colonoscopy, a decrease in mean arterial pressure to <65 mmHg was demonstrated in 91% of patients undergoing standard monitoring but only in 30% of patients additionally examined with the photoplethysmographic method [452].

Another study describes the use of acoustic monitoring to detect respiratory activity compared to capnography [453]. Here, a sensor is attached to the neck of the patient. Forty-nine patients undergoing MAC sedation during gastroscopy with ESD were evaluated. A higher technical failure rate was found for capnography (40%) compared with the acoustic monitor (22%), and vital signs were not different in the two groups [453].

In another feasibility study in 12 patients by the Cleveland Group, exhaled air temperature was measured and evaluated to determine respiratory rate. This initial evaluation found the device to be practicable. The so-called “Linsham Respiratory Monitor” is incorporated into a face mask, through which an endoscope can also be orally inserted [454].

However, all the newer abovementioned methods have so far only been evaluated in feasibility studies. A definite assessment of their clinical value is not possible at present, and therefore, no recommendations can be made.

4 Guideline – Informed Consent/Prerequisites for Performance of Sedation/Preservation of Vital Functions/Clinical Monitoring/ Emergency Management

4.1 Informed Consent

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<th>Recommendation 4.1</th>
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<tr>
<td>When patients are given information about the endoscopy, we recommend that they should also be told about sedation side effects, especially anterograde amnesia, and the possibility of restricted psychomotor capability after the sedation.</td>
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Evidence level 5, recommendation grade A, strong consensus

4.1.1 General and Legal Aspects

The law on medical interventions, the physician’s duty to inform, and patient information are very complex. According to constant jurisdiction of the German Federal Supreme Court, every medical intervention constitutes a personal injury offense according to paragraph 223 ff. StGB, 823 I BGB (German Civil Code). A medical intervention includes not only the performance of diagnostic procedures but also therapeutic measures such as surgery or drug administration [455]. The consent (“informed consent”) that is necessary for these procedures is only valid if the patients have been given sufficient information and are able to exercise their right to self-determination. If patients are not competent to give their consent (e.g., children and severely mentally retarded persons), the physician must inform their representative (guardian, agent for healthcare matters, or other responsible persons) [456]. To be able to give their consent, patients must also understand the implications of the intervention. Aside from the legal aspects, a well-performed informed consent process increases patient satisfaction [457]. Patients should receive information even if they have already undergone a similar endoscopic intervention and they feel sufficiently informed. Many patients are not good judges of their own level of information and understanding. Moreover, in-
Wehrmann T, Riphaus A et al. Updated S3 Guideline

4.1.2 Informing Person

Recommendation 4.2 2022 (unchanged)

We recommend that a competent and experienced physician should inform patients about the procedure in a form they can understand.

Evidence level 5, recommendation grade A, strong consensus

Background

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. The physician must make sure that the patient has this understanding. Delegation (e.g., to a nurse) is impermissible by law in Germany.

4.1.3 Informed Consent Procedure

Statement 4.3 2022 (modified)

The foundation of the consent procedure should be a discussion between the physician and patient. The content and range of the discussion should be documented. The patients should receive copies of the information and consent that they signed (according to paragraph 630e BGB (German Civil Code)).

Evidence level 5, strong consensus

Recommendation 4.4 2022 (modified)

We recommend that information should be provided in a timely manner so that the patient can make a well-founded decision about consent (according to paragraph 630e BGB (German Civil Code)).

Evidence level 5, recommendation grade A, strong consensus

Background

The discussion must be patient centered, i.e., dependent on the patient’s comprehension and scope of information needs. In addition, standardized patient information sheets can be used, but they only support the transfer of information and documentation and are no substitute for the personal patient information session. Under civil law, the physician has the burden of proof that the patient was properly informed [455]. Therefore, written documentation is essential. A waiver should not be offered to the patient and certainly not suggested. If, however, patients refuse to be informed of their own accord, the waiver must be documented and signed by the patient [456]. The importance of the patient’s right to self-determination also requires that the declaration of consent is offered in a timely manner [458] to ensure that patients can decide without time pressure. The correct timing of informed consent depends on the circumstances of the individual case. Even in emergencies, responsive patients should be informed as soon as time permits before giving consent [458]. In principle, the information should be provided to the patients as early as possible. It is recommended that informed consent be performed together with the information about the endoscopic procedure.

4.1.4 Content of the Patient Information Interview

Recommendation 4.5 2022 (unchanged)

We recommend that the discussion should include information on the preparation for sedation, various sedation methods, and their possible complications. It should also include informing patients that it is possible to perform the intervention without sedation.

Evidence level 5, recommendation grade A, strong consensus

Background

In almost all types of endoscopic interventions, adverse effects of sedation are responsible for at least 50% of complications [459]. Complications of sedation (aspiration, arterial hypotension, bradycardia, apnea, etc.) are therefore typical complications and must be discussed in detail with the patient. 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 the patient’s level of anxiety/fear into account when setting the sedation dose. These three factors have been shown to predict the patients’ cooperation during the intervention and their satisfaction afterward [460–462]. Overall, the tendency should be to offer sedation to younger and more anxious patients, as well as to women [5, 8, 55, 460]. During long examinations and difficult interventions (e.g., ERCP or a difficult polypectomy), sedation is necessary to avoid unwanted involuntary patient movement [165, 463]. This too should be explained to the patient. If the patient is injured after refusing to consent to a necessary examination on the basis of factually incorrect and/or unobjective information, the physician may be responsible [464]. Sedation can be refused if either the patient has a very high ASA risk class [465, 466] or if the hospital and personnel are not adequately equipped to perform sedation according to the required standards. The physician must then explain to the patient why sedation is impossible.

Whether patients should be informed of the possibility of dying because of the intervention is debated. In two verdicts of the Regional Appeal Court Stuttgart, Germany [464, 467], and one of the Regional Appeal Court Zweibrücken, Germany [468], the courts demanded that patients be gently informed before colonoscopy of the possibility of dying as a result of perforation. In another case, it was decided that patients must be informed that they could die because of an ERCP. In the case of very urgent or emergent procedures, the extent of information may be adjusted to the situation.
4.1.5 Safety Information (Behavior After Sedation)

**Recommendation 4.6**

We recommend that patients should be informed about what is safe to do and not to do after sedation and discharge from outpatient care. They should be given an information leaflet.

*Evidence level 5, recommendation grade A, strong consensus*

**Background**

Postprocedural conduct (management of discharge, see point 5.2): patients undergoing endoscopy as an outpatient procedure should be told that they need to bring someone who will accompany them home safely. All patients who are sedated must be told that they must not actively participate in road traffic, operate complicated machinery, drink alcohol, or make important or legally binding decisions. Due to the propofol’s half-life, a period of rest and abstinence from the above-mentioned activities on the day of the procedure is sufficient for monosedation. When other drugs are used, also in combination with propofol, this period may be longer (e.g., 24 hours when using midazolam). Patients should always be given a telephone number to contact the physician or hospital if they feel unwell or have complications or bleeding after the endoscopy [456]. Information on the do’s and don’ts for the period after the examination should be given to the patient in written form and in person [456]. For critical procedures or patients with severe comorbidities, targeted questioning by a nurse via telephone calls the next day was more effective than a written reminder [469].

4.2 Requirements for Carrying Out Sedations

**Recommendation 4.7**

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

*Evidence level 2b, strong consensus*

**Background**

Peripheral venous access is a fundamental requirement for the administration of sedatives. A comparative study by Smith et al. [470] investigated the functionality of a butterfly versus indwelling catheter 1 hour after endoscopy, a time when most benzodiazepines and opioids have not even reached their half-life. Only 44% of the butterflies but 98% of the indwelling catheters were still functional.

4.3 Protection of Vital Functions

**Recommendation 4.8**

We recommend that sedated patients should prophylactically receive oxygen via a nasal cannula.

*Evidence level 2b, recommendation grade A, strong consensus*

**Background**

Incidents caused by sedation are usually cardiopulmonary events [459]. They make up about half of all complications in endoscopy and, depending on the patient’s risk level, can also occur during gastroscopy without sedation [471]. Earlier publications reported a 5% incidence of cardiopulmonary events with benzodiazepine use [220], and recent studies with propofol report an incidence of 0.1% [394]. Older patients, in particular, are at risk of hypoxia under sedation [127, 178]. Prophylactic oxygen administration via a nasal cannula can significantly reduce the frequency of hypoxic events [472–477]. However, there are also indications that prophylactic oxygen administration can delay the early detection of hypoxic events using pulse oximetry [270, 465]. Despite this fact, the guideline authors consider the “safety-buffer” effect of prophylactic oxygen administration to be more important than its possible disadvantage of delayed hypoxemia detection.

Recent studies have investigated the use of nasal high flow during sedation for gastrointestinal endoscopy [478]. Nasal-high-flow therapy uses special large lumen nasal cannulae that allow a high gas flow of up to 60 liters per minute with variable oxygen content. This results in a low positive pressure in the airways. Data for use in gastrointestinal endoscopy is sparse, so its use outside of studies is not reasonable. The same applies for nasally applied PEEP (especially in patients with obstructive sleep apnea and/or significant obesity). So far, only feasibility studies are available. A randomized German study (Th. Rösch et al. at the University Hospital Hamburg-Eppendorf) will start soon [479].

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 impulse pitch level. Thus, if the tone frequency becomes lower or the digitally visible oxygen saturation drops continuously, countermeasures must be taken. Initially, this means asking patients in a loud voice and stimulating them to breathe deeper. If patients fail to develop spontaneous breathing with these measures, ventilatory support must be performed using a bag mask. Finally, if necessary, the airways should be secured instrumentally (e.g., endotracheal intubation). If the patient was sedated with benzodiazepines, the antagonist flumazenil may be given in addition intravenously (naloxone is used as an antagonist for opioids). 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 to cause excessive activation of the sympathetic autoregulative nervous system in unsedated patients [480], thus increasing the probability of cardiovascular events. Heartrate variability is enhanced further by sedation [481]. However, cardiopulmonary events can also be observed in unsedated patients during gastroscopy [482, 483].

4.4.2.2 Tachyarrhythmias

There are only a few reports of supraventricular or ventricular tachyarrhythmias during endoscopic procedures [484–487]. In emergencies, antiarrhythmics and a defibrillator should be kept at hand [488, 489].

4.4.2.3 Bradyarrhythmias

Occasionally, bradycardia occurs, especially during colonoscopy with or without sedation. The incidence is reported to be 0.5 % [490]. However, drug intervention was only necessary in one-third of the patients. The intervention consists of administering 0.5 mg atropine intravenously. This can be repeated if necessary up to a dose of 3 mg, and/or adrenaline (2–10 µg/min) can be given intravenously. In life-threatening situations, cardiopulmonary resuscitation should be done [491].

4.4.3 Arterial Hypotension

The incidence of arterial hypotension during colonoscopy varies between 0.3 % [490] and 3 %–19 % [480] depending on the definition. In the case of arterial hypotension, volume resuscitation with crystalloid infusion should be done. If hypotension persists, vasoactive substances should be given. Prophylactic infusion during all colonoscopies is not recommended [492], but it may be a good choice in older dehydrated patients. Prophylactic intravenous administration of crystalloid fluids can also be useful for long procedures carried out under propofol sedation because of its pronounced blood-pressure-reducing properties.

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 [493]. ST depression can be significantly reduced by oxygen supplementation during endoscopy [473]. There is one published report of a case of myocardial infarction during colonoscopy [303].

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 [459]. Localized pain at the injection site, especially in small-caliber peripheral veins, is a more common phenomenon after propofol administration. This type of “injection pain” can be largely avoided by intravenous injection of a local anesthetic before propofol application or by its injection on an “as-needed” basis [494–497].

5 Guideline – 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>2022 (unchanged)</th>
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<tbody>
<tr>
<td>We recommend that there should be a written and easily understandable procedure plan for performing sedation and/or analgesia, for monitoring the patient after sedation, for the criteria for discharge to the outpatient or general inpatient area, and for the management of any complications. The respective responsibilities should be clearly defined.</td>
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<td>Evidence level 5, recommendation grade A, strong consensus</td>
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5.2 Discharge Criteria

5.2.1 Patient Instructions

<table>
<thead>
<tr>
<th>Recommendation 5.2</th>
<th>2022 (modified)</th>
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<tbody>
<tr>
<td>We recommend that patients should be accompanied when they are being discharged. They should also receive written instructions, including a 24-hour emergency telephone number in case of examination-related complications (sedation or intervention).</td>
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<td>Evidence level 5, recommendation grade A, consensus</td>
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5.2.2 Minimum Criteria for Discharge

<table>
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<th>Recommendation 5.3</th>
<th>2022 (unchanged)</th>
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<tr>
<td>The use of minimal discharge criteria after sedation and/or analgesia from the recovery area is wise. We recommend the use of a standardized discharge checklist.</td>
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<td>Evidence level 5, recommendation grade A, strong consensus</td>
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Various scoring systems to assess postsurgical recovery have been used after sedation for endoscopy. The most popular systems are the modified Aldrete score (for early or phase I recovery) and the postanesthetic discharge scoring system (PADSS, for intermediate or phase II recovery) [500, 501]. Despite limitations of the PADSS, inherent to its focus on surgical procedures (e.g., one of the five criteria in this system is “surgical bleeding”), safe discharge after gastrointestinal endoscopy was reported in a relatively small prospective study [502]. A checklist (Table 10) is recommended that assesses the ability of the patient to be discharged from the outpatient area (modified according to Ead et al. [498]). At a minimum, criteria proposed by the German Society of Anesthesiology should be met [20]. Commonly used tests to evaluate psychomotor functions are the coherent response to questions, the ability to stand on one foot, and the ability to walk in a straight line for 5 m without instability.

The use of the modified Aldrete score [503] only allows statements about patients’ vital signs but not about their psychomotor performance. The latter may be considerably impaired even when a maximum score is reached [504]. 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 and meperidine), patients have a prolonged phase of amnesia and impaired reflexes and judgement.

Patients undergoing colonoscopy, who are sedated with a frequently employed combination of midazolam plus an opiate, show impairment of reaction time, fine motor skills, and perception for at least 30 minutes after the procedure. Study data show that the remaining aftereffects of midazolam impair various psychomotor functions for at least 1 hour after administration [504, 505]. In these cases, midazolam seems to be the main reason for the persistent impairment of psychomotor function after sedation [506]. A study by Thapar et al. [506] comparing the effect of midazolam and meperidine, patients have a prolonged phase of amnesia and impaired reflexes and judgement.

5.3 “Street Fitness”

5.3.1 Roadworthiness

Even after reaching the required discharge criteria, psychomotor function can still be significantly impaired. Therefore, the time to active and passive participation in road traffic should be determined individually depending on the drugs used and the individual patient’s risk profile at the time of discharge.

We recommend that upon discharge, patients should refrain from driving, operating heavy machinery, or engaging in legally binding decisions for at least 12 hours if sedation with propofol alone was administered.

Evidence level 1b, recommendation grade A, strong consensus

5.2.3. Use of Scoring Systems for Discharge

We recommend that scoring systems (e.g., the Aldrete score) should not be the sole basis for deciding whether patients can be discharged because they do not evaluate psychomotor function.

Evidence level 1b, recommendation grade A, strong consensus

Evidence level 1b, recommendation grade A, strong consensus

Evidence level 1b, recommendation grade A, strong consensus
Overall, after the use of short-acting hypnotics (e.g., propofol) as a monosubstance, roadworthiness seems to be restored quickly considering the drug’s half-life. Nevertheless, on the basis of the results obtained in the present prospective study by Riphaus et al. [86] of 98 subjects and also by Horiuchi et al. [514] with a sample size of 48 subjects (and thus a very small number of cases), the use of public transportation (even without an escort) may be considered, at the most. For driving a motor vehicle/bicycle, further large, prospective field studies are needed, which have not yet been presented by any working group worldwide.

In accordance with the low evidence of the currently available data on roadworthiness after propofol sedation and the primary consideration of patient safety, the guideline group has once again adopted the recommendations of the current evidence- and consensus-based guideline of the European Society of Gastrointestinal Endoscopy (ESGE) on propofol sedation by non-anesthesiologists [362] (see Recommendation 5.8 and 5.9).

This is also in the light of a study by Brechmann et al. [515] in which, with the aid of a multi-dimensional questionnaire, 82 patients completed a questionnaire 1 hour before and after, as well as 1 week after, propofol monosedation. It was shown that a clear euphoric effect was detectable in 36 of these patients (44 %). Thus, it is not only a sedating effect that may have an impact on driving capability.

First, data from Riphaus et al. [516] suggest that gender differences influence recovery time after propofol monosedation during colonoscopy. The aim of this study was to investigate whether and to what extent gender differences in recovery time can be detected using EEG monitoring to maintain a constant sedation level. As a result, women woke up significantly faster than men, with time to eye opening of 7.3 ± 3.7 versus 8.4 ± 3.4 min (P = 0.005) and time to full orientation of 9.1 ± 3.9 versus 10.4 ± 13.7 min (P = 0.008), respectively. Propofol dosage was not significantly different, with a trend toward more propofol per kg body weight in women (3.98 ± 1.81 mg versus 3.72 ± 1.75 mg, P = 0.232, respectively). The results are best explained by gender-related differences in the pharmacokinetics and pharmacodynamics of opioids, muscle relaxants, and intravenous anesthetics. The faster recovery time may be related to a possible lower plasma concentration of propofol in women, as well as to differences in the concentration of glucuronidated degradation products in women and men. Also, CYP2B6 (a propofol degradation enzyme belonging to the cytochrome P450 enzymes responsible for oxidative metabolism of drugs) concentration was 1.9 times higher in the liver of women than in men [517].

Thus, the influence of gender should be considered when propofol is used as sedation for gastrointestinal endoscopy. This includes appropriate dosing for females and caution regarding possible overdose in male patients.

Based on the most recent data, focusing solely on the half-life of the drug used does not appear to be sufficient for determining wake-up time and subsequent “street fitness”. Further data regarding gender-sensitive pharmacokinetics and dynamics are necessary to allow personalized medicine to ensure the greatest possible patient safety in sedation during gastrointestinal endoscopy.

### Background

Until 2008, the recommendations of various professional societies stated that patients should not participate actively or passively in road traffic for 24 hours [376, 377, 508] 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 Kortilla et al. [509–511] 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 [510]. Psychomotor functions were impaired for up to 12 hours only when meperidine 75 mg i. m. was used. 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 [509].

Normalization of psychomotor function on the day of the examination is primarily dependent on the half-life of the substance used, whereby short-acting substances have an advantage. In a prospective study by Riphaus et al. [86] involving 98 patients sedated during gastroscopy and colonoscopy using either propofol or midazolam/pethidine, there was no impairment of psychomotor abilities two hours after sedation with propofol compared with midazolam/pethidine (using a driving simulator).

These results were confirmed for propofol in a similar study by Horiuchi et al. [512]. However, a very low medium propofol dose (around 40 mg) was used, which is not routinely employed for propofol sedation in Germany [13, 14].

In another study by Horiuchi et al. [513], 92 % of 400 patients drove themselves home after low-dose propofol sedation (dose usually < 50 mg in Asian patients) for gastroscopy without causing traffic accidents.

A current study by Sato et al. [125] investigated the safety and efficacy of propofol sedation administered by assistants at a mean dosage of 105 mg during outpatient gastroscopy and colonoscopy in a total of 117,661 ASA I and II patients. A questionnaire-based postintervention evaluation (2 weeks after the examination) included questions about whether patients “drove themselves home or to the office after the medical checkup?” and “had an accident shortly after the medical checkup?” It was found that many of at least 66,250 people were able to drive themselves home or to work after the procedure without being involved in a traffic accident. Which mode of transport they used was not specified in the study. Likewise, due to the query by questionnaire instead of, for example, a telephone follow-up, any serious accidents that made it impossible for the patient to answer the questionnaire were not recorded.
5.4 Documentation

**Recommendation 5.10** 2022 (unchanged)

We recommend that the patient file or the documentation form should contain time-dependent documentation of the vital signs (heart rate, blood pressure, and oxygen saturation), the drugs used including name and dose, as well as the administration of intravenous fluids, and the flow rate of oxygen. Complications and their management should be documented as well.

*Evidence level 5, recommendation grade A, strong consensus*

5.4.1 General Considerations

Structured documentation is part of a quality process and may help to improve compliance with sedation guidelines [518]. Documentation is an essential part of patient care and should be done in all phases of the intervention (it may also provide a record of correct sedation administration and monitoring in the event of legal issues).

This includes:
- Pre-interventional evaluation of the patient
- Informed consent
- Monitoring during the intervention
- Patient recovery
- Patient discharge

Ideally, a standardized form should be used to improve documentation [518].

5.4.2 Inability to Work

**Recommendation 5.11** 2022 (unchanged)

We recommend that the duration of the inability to work should be assessed individually, specific to the workplace, taking into account the effect profile of the used drugs.

*Evidence level 5, recommendation grade A, strong consensus*

5.5 Benchmarking

**Recommendation 5.12** 2022 (modified)

We recommend that all complications that occur during endoscopy with or without sedation should be documented. These include, in particular:
- Blood pressure changes requiring intervention
- Cardiac arrhythmia requiring intervention
- Hypoxemia
- Aspiration
- Mask ventilations
- Unplanned intubations
- Neurological deficits
- Unplanned intensive care monitoring
- Resuscitations
- Deaths

*Evidence level 5, recommendation grade A, strong consensus*

**Recommendation 5.13** 2022 (modified)

As part of internal quality management, we recommend that a team meeting should be held regularly (at least every 3 months). Documentation of this team meeting should at least include information on the complications given under 5.12.

*Evidence level 5, recommendation grade A, strong consensus*

**Background**

A “benchmark” is a standard or reference point (metric) for a 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., a study of the German Association of Gastroenterologists in Private Practice, complication registry of Helios-hospitals in Germany, etc.).

**Conflict of Interest**

The overview of the authors’ conflicts of interest are published in the guideline report (german version).
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