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Domitille Renard, Thomas Clavier, Osama Abou-Arab, Gérard Amarenco, Emmanuel Besnier, et al.. Consensus on the Management of Anesthetic Agents During Digestive Motility Measurements and Proposal of a Standardized Protocol for Anesthesia (French Neuro Gastroenterology Group GFNG and Committee of Anesthetic French Experts). *Neurogastroenterology & Motility*, 2025, <10.1111/nmo.70098>. <hal-05128042>

HAL Id: hal-05128042

<https://normandie-univ.hal.science/hal-05128042v1>

Submitted on 23 Jan 2026

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ORIGINAL ARTICLE OPEN ACCESS

Consensus on the Management of Anesthetic Agents During Digestive Motility Measurements and Proposal of a Standardized Protocol for Anesthesia (French Neuro Gastroenterology Group GFNG and Committee of Anesthetic French Experts)

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Received: 29 December 2024 | **Revised:** 4 May 2025 | **Accepted:** 1 June 2025

Keywords: anesthesia protocol | Delphi | digestive motility | experts groups | FLIP | manometry

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ABSTRACT

Introduction: Techniques for measuring digestive motility are becoming increasingly precise and enable therapeutic interventions. However, while most of these interventions require general anesthesia, there is limited data on the impact of anesthetic agents on these measurements, and no standardized anesthesia protocol currently exists to guide such procedures. Our working group carried out two Delphi processes involving experts in neurogastroenterology and anesthesiology to reach a consensus on which drugs affect these measurements and to establish an anesthesia protocol.

Method: Two expert groups were formed, comprising 13 neurogastroenterology experts from the French Neuro-Gastroenterology Group (GFNG) and 15 full- or associate professors in anesthesia and intensive care. The first Delphi process involved the neurogastroenterologists and aimed to identify which anesthetic drugs influenced digestive pressure measurements. The second Delphi process, involving anesthesiologists, sought to develop an anesthesia protocol. Each expert indicated their level of agreement with each statement using a 6-point Likert scale. A statement was endorsed when at least 80% of experts agreed with it. The strength of evidence for each statement was evaluated using the GRADE system.

Results: The Delphi process with neurogastroenterologists was conducted over three rounds and ultimately resulted in 91 amendments. The second Delphi process with anesthesiologists took place over two rounds and included 28 amendments, leading to the development of an anesthesia protocol.

Conclusion: To our knowledge, this work is the first to establish an expert consensus on anesthetic agents that can affect digestive motility measurements and to propose an anesthesia protocol that accounts for the needs of neurogastroenterologists.

1 | Introduction

Investigation of digestive motility has been performed for decades, using either pull-through or stationary manometry techniques, and more recently high-resolution manometry or the Functional Lumen Impedance Planimetry (FLIP) system [1, 2]. Most explorations can be done routinely without the use of any anesthetics to diagnose motility disorders. With the development of new surgical and/or endoscopic therapeutic procedures [3, 4], there is a growing trend to perform motility recordings during general anesthesia to guide surgical or endoscopic procedures. For example, distensibility measurement of the Lower Esophageal Sphincter (LES) can guide the length of surgical myotomy or predict clinical outcomes after endoscopic or surgical procedures in cases of lower esophageal sphincter achalasia [1]. In addition, endoscopic probe placement may require the use of general anesthesia before starting the recording. Anesthetic agents, like opioid analgesics, sedatives, or neuromuscular blockers can be used in these cases. However, while normal pressure values are available in unsedated healthy volunteers (HVs) for these techniques [2, 5], there is also evidence in the literature that some of these agents can impact digestive motility [6]. To our knowledge, no national or international recommendations are available to date to guide clinicians on how to limit the potential bias caused by anesthetic agents during digestive motility measurements performed under general anesthesia. The aim of this project was therefore (1) to establish a national consensus among neurogastroenterologists experts on the use of anesthetic drugs in the context of digestive motility measurements and (2) to develop a protocol for anesthesiologists to limit the impact of anesthetic drugs on digestive motility measurements.

2 | Methods

The French Neuro-Gastroenterology Group (GFNG) initiated a Delphi process to develop consensus statements on the potential impact of different classes of anesthetic drugs on digestive motility and their possible use in the context of digestive motility measurements. The Delphi process is based on principles of evidence-based

medicine, systematic literature reviews, and a voting process. This approach aims to establish consensus for complex medical issues for which evidence from controlled trials is scarce [7].

The first step of the Delphi process was the creation of a working group consisting of two members of the GFNG (CD and GG) and two anesthesiologists (DR and TC) with expertise in neurogastroenterology and the Delphi consensus process, and the selection of an expert panel through the GFNG society. Experts were selected if they were authors or co-authors of at least 20 publications in the field of digestive motility and/or endoscopic management of digestive motility disorders. Thirteen neurogastroenterologists/endoscopists experts mandated by the GFNG agreed to participate in the consensus. Statements to evaluate the current knowledge regarding the potential impact of different classes of anesthetic drugs on digestive motility and their possible use in the context of digestive motility measurements were then drafted to be submitted to the neurogastroenterologists expert panel. A systematic literature review was performed by the working group to identify evidence to support each statement and was shared with each member of the expert panel [6]. This literature review only included studies performed in humans using conventional perfused manometry, high-resolution manometry, electronic barostat, or FLIP system to assess digestive motility. The four members of the working group drafted and finalized 88 statements which were evaluated by neurogastroenterologists/endoscopists experts during the first round of the Delphi. Each expert indicated the degree of agreement for each statement using a 6-point Likert scale (Table 1). When at least 80% of the experts agreed with a statement (agree with minor reservation: A or strongly agree: A+), the statement was endorsed. The strength of evidence for each statement was scored using the GRADE system (Table 2) [8]. Experts were blinded to the voting results of other experts and were able to provide feedback regarding the wording of the statements or any new statement suggestion that could be added to the list. The working group adjusted the final statement list after the first round, which comprised 91 statements in its finalized version. At the initiative of the anesthesiologists' coordinators (DR and TC), 8 statements were also added regarding the management of non-anesthetic drugs

Summary

- Data on the impact of anesthetic drugs on the measurement of gastrointestinal motility are limited.
- Two expert groups comprising neurogastroenterology experts from the French Neuro-Gastroenterology Group and full or associate professors in anesthesia and intensive care convened to identify which drugs may affect these measurements, and propose an anesthesia protocol to minimize the potential impact of the drugs used.
- The methodology involved two separate Delphi processes.

TABLE 1 | Six-point Likert scale.

Point	Description
A+	Agree strongly
A	Agree with minor reservation
A–	Agree with major reservation
D–	Disagree with major reservation
D	Disagree with minor reservation
D+	Disagree strongly

frequently used in practice during general anesthesia. Two other rounds of repeated voting of the statements and voting discussion were then organized until a stable level of consensus voting was reached. After the final voting round, the manuscript was drafted and circulated among the expert panel for final approval.

The second step of the process was the creation of a panel of anesthesia experts. Experts were selected if they were full- or associate professors in anesthesia and intensive care in a teaching hospital, with at least 20 publications in their field (authors or co-authors). Fifteen experts in anesthesia agreed to participate in the consensus. Statements were drafted with the objective of validating an anesthesia protocol, taking into account the impact of different anesthetic agents on endoscopic measurements. The panel of anesthesia experts had access to the literature review conducted by the initial working group. The consensus required two rounds of the Delphi method, with 28 and then 11 amendments. Similar to the experts from the GFNG, each anesthesia expert indicated the degree of agreement for each statement using a 6-point Likert scale (Table 1). When at least 80% of the experts agreed with a statement (agree with minor reservation: A or strongly agree: A+), the statement was endorsed. Experts were blinded to the voting results of other experts and were able to give feedback regarding the wording of the statements or any new statement suggestion that could be added to the list. The working group adjusted the final statement list after the first round, which comprised 28 statements in its finalized version.

After the final voting round, the complete manuscript was drafted and circulated among the panel of experts (GFNG experts and anesthesia experts) for final approval.

TABLE 2 | Grading of recommendation assessment, development, and evaluation system (8).

Code	Quality of evidence	Definition
A	High	Further research is very unlikely to change our confidence in the estimate of effect. <ul style="list-style-type: none"> – Several high-quality studies with consistent results – In special cases: one large, high-quality multicenter trial
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. <ul style="list-style-type: none"> – One high-quality study – Several studies with some limitations
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. <ul style="list-style-type: none"> – One or more studies with severe limitations
D	Very low	Any estimate of effect is very uncertain. <ul style="list-style-type: none"> – Expert opinion – No direct research evidence – One or more studies with very severe limitations

3 | Results

3.1 | GFNG Experts' Delphi Process

Statements endorsed and statements of interest are presented according to the anesthetic drug class (Table 3). The complete list of statements and their respective levels of agreement is provided in (Table S1).

3.1.1 | Opioid Analgesia

1. Opioids impair digestive motility. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 100%, A 0%, A– 0%, D– 0%, D 0%, D+ 0%. **GRADE B**
2. Opioids impair digestive motility through peripheral μ receptor. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 100%, A 0%, A– 0%, D– 0%, D 0%, D+ 0%. **GRADE C**
3. Opioids are likely to impair esophageal motility. **STATEMENT ENDORSED.** Overall agreement 92%: A+ 85%, A 8%, A– 7%, D– 0%, D 0%, D+ 0%. **GRADE B**
4. Opioids are likely to impair gastric motility. **STATEMENT ENDORSED.** Overall agreement 85%: A+ 70%, A 15%, A– 15%, D– 0%, D 0%, D+ 0%. **GRADE C**

TABLE 3 | List of the main GFNG group statements with the corresponding degrees of agreement (endorsed statements are presented in bold).

Drug class	Statement	Percentage of A, A+
Opioids	Opioids impair digestive motility	100.00
	Opioids impair digestive motility through peripheral μ receptor	100.00
	Opioids are likely to impair esophageal motility	92.31
	Opioids are likely to impair gastric motility	84.62
	Opioids are likely to impair small bowel peristaltic motility	84.62
	Opioids inhibit colonic peristaltic motility	92.31
	During a general anesthesia, opioids may impair accuracy of digestive motility measurement	91.70
	During a general anesthesia, opioid free anesthesia should be favored, when possible, not to impair accuracy of digestive motility measurement	76.82
Halogens	Halogens may impair digestive motility	53.84
	During a general anesthesia, halogens free anesthesia may be favored, when possible, not to impair accuracy of digestive motility measurement	38.46
Barbiturics	There is no evidence that barbiturics alter digestive motility	75.00
	During a general anesthesia, the use of barbiturics may be acceptable during digestive motility measurement	38.50
Ketamine	There is no evidence that ketamine alters digestive motility	83.30
	During a general anesthesia, the use of ketamine may be acceptable during digestive motility measurement	83.30
Propofol	Propofol has no or limited impact on gastrointestinal motility	83.30
	During a general anesthesia, propofol might be acceptable to perform digestive motility measurement	83.30
Neuromuscular blocking agents	The impact of curares on sphincters pressure (lower esophageal sphincter or pyloric), when it occurs, is likely to be driven through indirect action on the striated muscle	76.92
	Curares may impact sphincters (lower esophageal sphincter or pyloric) pressure measurement	83.30
	During a general anesthesia, the use of curares might be avoided, when possible, during digestive motility measurement	83.30
Non-anesthetic drugs	Concomitant use of D2 antagonist should be avoided, when possible, during motility digestive measurement	91.70
	Concomitant use of dexamethasone is acceptable during digestive motility measurement	92.31
	Concomitant use of alpha-2 antagonist should be avoided, when possible, during motility digestive measurement	69.23
	Concomitant use of sympathomimetics should be avoided, when possible, during motility digestive measurement	76.92
	Concomitant use of 5-HT3 antagonists should be avoided, when possible, during motility digestive measurement	91.70
	Concomitant use of nefopam is acceptable during digestive motility measurement	53.85
	Concomitant use of paracetamol is acceptable during digestive motility measurement	100.00
Concomitant use of atropine should be avoided, when possible, during motility digestive measurement	84.62	

Abbreviation: GFNG, French Neuro Gastroenterology Group.

5. Opioids are likely to impair small bowel peristaltic motility. **STATEMENT ENDORSED**. Overall agreement 85%: A+ 39%, A 46%, A- 15%, D- 0%, D 0%, D+ 0%. **GRADE C**
6. Opioids inhibit colonic peristaltic motility. **STATEMENT ENDORSED**. Overall agreement 92%: A+ 85%, A 8%, A- 7%, D- 0%, D 0%, D+ 0%. **GRADE D**
7. During a general anesthesia, opioids may impair accuracy of digestive motility measurement. **STATEMENT ENDORSED**. Overall agreement 92%: A+ 59%, A 33%, A- 8%, D- 0%, D 0%, D+ 0%. **GRADE B**
8. During a general anesthesia, opioid free anesthesia should be favored, when possible, not to impair accuracy of digestive motility measurement. **STATEMENT NOT ENDORSED**. Overall agreement 77%: A+ 46%, A 31%, A- 23%, D- 0%, D 0%, D+ 0%. **GRADE B**

The effect of remifentanyl on digestive motility is currently the most studied among opioids analgesia drugs. Most studies assessed its effect on esophageal motility in HVs [9–15]. While low doses of remifentanyl did not affect the LES pressure [9], a decrease in both the inspiratory and expiratory esophagogastric junction pressures was observed after the administration of doses of remifentanyl used in clinical practice [10–12]. These effects were abolished after the administration of methylnaltrexone (μ -opioid receptor antagonist) in one report [10], but not in a second study using very low doses of naloxone (μ -opioid receptor antagonist) [11]. Using high-resolution manometry, more recent studies demonstrated increased integrated relaxation pressure and a decrease in distal latency after remifentanyl administration [13–15]. Similar results were found in HVs after the administration of fentanyl [16, 17], but not with alfentanil [18].

The effect of opioids on gastric and antro-duodenal motility was evaluated in only two studies [19, 20]. A potential effect was shown in these studies, consisting mainly of alterations in the duration and the motility index of the interdigestive motility complex, but further studies are needed to confirm these findings. To date, no specific study has assessed the effect of opioid analgesia on colonic motility in humans.

3.1.2 | Sedative Agents

1. Halogens may impair digestive motility. **STATEMENT NOT ENDORSED**. Overall agreement 54%: A+ 8%, A 46%, A- 39%, D- 7%, D 0%, D+ 0%. **GRADE C**
2. During a general anesthesia, halogen-free anesthesia may be favored, when possible, not to impair the accuracy of digestive motility measurement. **STATEMENT NOT ENDORSED**. Overall agreement 39%: A+ 8%, A 31%, A- 61%, D- 0%, D 0%, D+ 0%. **GRADE C**

The literature regarding the potential effect of inhaled anesthetics on digestive motility remains scarce. The influence of these agents on esophageal motility has been assessed in six reports to date [21–26], with four studies showing a decrease in LES resting pressure and lower esophageal motility following the administration of sevoflurane or enflurane [21–24]. A more recent study

using the FLIP system also identified an effect of sevoflurane administration on esophageal measurements, suggesting a potential misclassification of esophageal spastic disorders [26]. Lastly, one study investigated the effect of sevoflurane administration on colonic motility (motility index, and spontaneous or bisacodyl-induced high amplitude propagating contractions), but no particular effect was found in this sole report [27].

3. There is no evidence that barbiturics alter digestive motility. **STATEMENT NOT ENDORSED**. Overall agreement 75%: A+ 25%, A 50%, A- 8%, D- 7%, D 0%, D+ 0%. **GRADE D**
4. During a general anesthesia, the use of barbiturics may be acceptable during digestive motility measurement. **STATEMENT NOT ENDORSED**. Overall agreement 38%: A+ 15%, A 23%, A- 54%, D- 0%, D 8%, D+ 0%. **GRADE D**

The influence of thiomebutal sodium administration on digestive motility has been evaluated in only one report to date [28]. Results of anorectal manometry did not differ after its administration even if the relaxation of the internal anal sphincter during the rectoanal inhibitory reflex (RAIR) was less pronounced under anesthesia with thiomebutal.

5. There is no evidence that ketamine alters digestive motility. **STATEMENT ENDORSED**. Overall agreement 83%: A+ 42%, A 41%, A- 8%, D- 8%, D 0%, D+ 0%. **GRADE C**
6. During a general anesthesia, the use of ketamine may be acceptable during digestive motility measurement. **STATEMENT ENDORSED**. Overall agreement 83%: A+ 42%, A 41%, A- 8%, D- 8%, D 0%, D+ 0%. **GRADE C**

The effect of ketamine on digestive motility has been assessed in four studies to date. One study investigated sphincter of Oddi motility following ketamine administration, without any sphincter of Oddi motility alteration detected [29]. A second report using colonic manometry results found no difference in total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions between recordings starting 4h or 24h after anesthesia [27]. Lastly, two other studies [30, 31] exhibited contradictory results regarding the relaxation of the internal anal sphincter during RAIR, at the difference of the anal resting pressure which was not modified by ketamine administration.

7. Propofol has no or limited impact on gastrointestinal motility. **STATEMENT ENDORSED**. Overall agreement 83%: A+ 50%, A 33%, A- 0%, D- 8%, D 0%, D+ 9%. **GRADE C**
8. During a general anesthesia, propofol might be acceptable to perform digestive motility measurement. **STATEMENT ENDORSED**. Overall agreement 83%: A+ 42%, A 41%, A- 8%, D- 8%, D 0%, D+ 0%. **GRADE C**

The effect of propofol administration on esophageal motility was prospectively assessed in four studies to date [9, 18, 32, 33]. Two of these conducted on HVs reported no difference in the esogastric pressure gradient or the LES pressure before and after administration of propofol [9, 18]. A significant dose-dependent decrease in LES resting pressure was found in two other studies; however, the esogastric pressure gradient

remained unchanged [32, 33]. Another report showed that propofol administration did not affect gastric tone in HVs [34]. Lastly, three studies found lower anal sphincter resting pressure compared to baseline after the induction of conscious sedation using propofol, but no difference was found in the detection of the RAIR [35–37].

3.1.3 | Neuromuscular-Blocking Agents

1. The impact of curares on sphincters pressure (LES or pyloric), when it occurs, is likely to be driven through indirect action on the striated muscle. **STATEMENT NOT ENDORSED.** Overall agreement 77%: A+ 15%, A 62%, A– 23%, D– 0%, D 0%, D+ 0%. **GRADE C**
2. Curares may impact sphincters (LES or pyloric) pressure measurement. **STATEMENT ENDORSED.** Overall agreement 83%: A+ 42%, A 41%, A– 17%, D– 0%, D 0%, D+ 0%. **GRADE C**
3. During a general anesthesia, the use of curares might be avoided when possible during digestive motility measurement. **STATEMENT ENDORSED.** Overall agreement 83%: A+ 42%, A 41%, A– 17%, D– 0%, D 0%, D+ 0%. **GRADE C**

Four studies investigated the effect of neuromuscular blocking agents on esophageal motility [38–41]. The esogastric pressure gradient following the administration of vecuronium [38], suxamethonium [39] or rocuronium [40, 41] remained unchanged, but this was not the case with pancuronium infusion, with an increase in esogastric pressure gradient resulting from an increase in the LES pressure rather than a decrease in intragastric pressure [38]. Regarding the impact of neuromuscular blocking agents on gastric motility, three studies on HVs showed a rise in intragastric pressure following the administration of suxamethonium, which was attributed to fasciculations of the abdominal muscles [42–44]. Moreover, one retrospective report found that suxamethonium administration was associated with a decreased pyloric distensibility [45].

3.1.4 | Non-Anesthetic Drugs Frequently Used During General Anesthesia

1. Concomitant use of dopamine-2 receptor antagonist should be avoided, when possible, during motility digestive measurement. **STATEMENT ENDORSED.** Overall agreement 92%: A+ 42%, A 50%, A– 0%, D– 8%, D 0%, D+ 0%. **GRADE B**

Large amounts of data are available in the literature regarding the acceleration of gastric emptying time following dopamine-2 receptor antagonist administration [46]. There is also evidence regarding their ability to enhance esophageal motor function and antroduodenal motility [47].

2. Concomitant use of dexamethasone is acceptable during digestive motility measurement. **STATEMENT**

ENDORSED. Overall agreement 92%: A+ 39%, A 53%, A– 8%, D– 0%, D 0%, D+ 0%. **GRADE D**

To our knowledge, no study has investigated the effect of dexamethasone on human digestive motility to date.

3. Concomitant use of sympathomimetics should be avoided, when possible, during motility digestive measurement. **STATEMENT NOT ENDORSED.** Overall agreement 77%: A+ 30%, A 47%, A– 23%, D– 0%, D 0%, D+ 0%. **GRADE C**

Several sympathomimetic agents are available nowadays, and their effects on digestive motility are well described in the literature. Subcutaneous epinephrine administration was associated with decreased LES resting pressure and esogastric gradient pressure in one report [25]. The same findings were reported after administration of salbutamol in one study [48] but not in another report [49]. Beta-adrenoceptor [50] or alpha-adrenoceptor [51, 52] agonists' administration can also impact gastric motility and, in particular, gastric accommodation. The inhibitory effect of beta-adrenoceptors or alpha-adrenoceptors on small bowel motility is also described in the literature [53, 54]. Lastly, the administration of sympathomimetics was associated with impaired colonic motility [55–58].

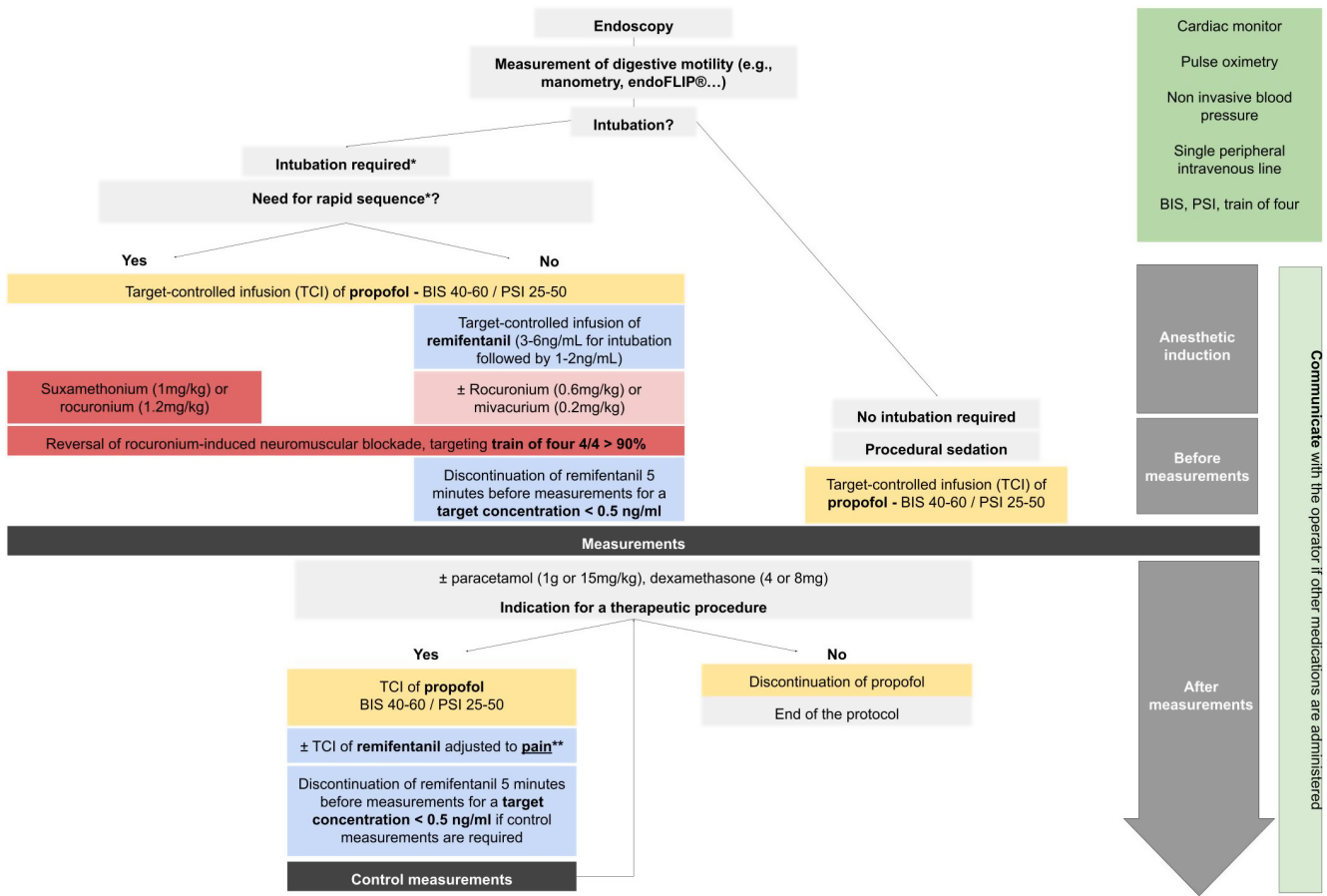
4. Concomitant use of 5-HT3 antagonists should be avoided, when possible, during motility digestive measurement. **STATEMENT ENDORSED.** Overall agreement 92%: A+ 33%, A 59%, A– 0%, D– 8%, D 0%, D+ 0%. **GRADE C**

Three studies investigated in HVs the effect of 5-HT3 antagonists (or 5-HT4 for the mosapride) on esophageal motility with similar results [59–61]. No effect was found on baseline LES pressure, but an increase in contractions amplitude of the body of the esophagus, but not their velocity, was found. Ondansetron induced motility changes in the antrum but had no effect on fundic relaxation promoted by intraduodenal infusion in one report [62]. The administration of 5-HT3 antagonists was also associated with an improvement in gastric accommodation in dyspeptic patients in one report [63]. Lastly, cilansetron increased meal-stimulated and markedly neostigmine-stimulated phasic motility of the sigmoid colon in another study [64]. Administration of 5-HT3 antagonists was associated with slower colonic transit time in another study [65].

5. Concomitant use of paracetamol is acceptable during digestive motility measurement. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 100%, A 0%, A– 0%, D– 0%, D 0%, D+ 0%. **GRADE D**

Only one study investigated the effect of paracetamol administration on antroduodenal motility, and no significant change was observed following its administration [19].

6. Concomitant use of atropine should be avoided, when possible, during motility digestive measurement. **STATEMENT ENDORSED.** Overall agreement 85%: A+ 46%, A 39%, A– 7%, D– 8%, D 0%, D+ 0%. **GRADE B**



Anesthesia protocol for measurements of digestive motility via endoscopy

BIS : bispectral index, PSI : patient monitored state, TCI : target-controlled infusion

*Risk assessment must take into account patient's comorbidities, the procedure, local practices and applicable guidelines

**Depending on the intensity of the painful stimulus or based on the patient's sympathetic response

FIGURE 1 | Anesthesia protocol for measurements of digestive motility via endoscopy.

Several studies demonstrating an effect of atropine administration on esophageal motility [66, 67], gastric motor function [68, 69], and antroduodenal motor activity [70] are available in the literature. There is also evidence that atropine administration can significantly reduce colonic motility [71].

3.2 | Anesthesia Expert's Delphi Process

A diagram of the proposed anesthetic protocol is available (Figure 1).

The complete list of statements and their respective levels of agreement is provided in the Appendix (Table S2).

A few key concepts concerning general anesthesia for the non-anesthetist:

- Preoxygenation is a necessary step before anesthesia induction, aimed at increasing the patient's oxygen reserves [72, 73].

- Induction refers to the switch from conscious state to anesthetized state. Typically, three types of drugs are used: a hypnotic agent (e.g., propofol, etomidate, and ketamine), an opioid (e.g., remifentanyl, sufentanyl, and alfentanil), and a neuromuscular blocking agent if intubation is planned or if required by the surgery (e.g., suxamethonium, rocuronium, atracurium, and cisatracurium) [73, 74]. A summary table of the main anesthesia drugs, developed in a previous study by our team, is available in the Appendix (Table S3) [6]. Between administration of the drugs and intubation, the patient is usually ventilated with a face mask for a few minutes.
- Neuromuscular blockade is monitored using a tool called the train-of-four (TOF), which assesses the degree of muscle relaxation [74].
- For patients at risk of aspiration (e.g., full stomach, gastric emptying disorders, and symptomatic hiatal hernia), a rapid sequence induction (or crush induction) is performed. In this case, mask ventilation is avoided, and intubation is carried out promptly after induction [73, 74]. This induction requires specific drugs with a short delay of action.

- The Bispectral Index (BIS) and the Patient State Index (PSI) are two tools used to monitor the depth of anesthesia based on electroencephalographic analysis [75].

3.2.1 | Preoperative Phase

1. The patient should be monitored with a cardiac monitor, pulse oximetry, and non-invasive blood pressure according to the current recommendations. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 93%, A 7%, A- 0%, D- 0%, D 0%, D+ 0%
2. A single peripheral venous access is sufficient for an endoscopic procedure to measure endo-luminal pressure. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 73%, A 27%, A- 0%, D- 0%, D 0%, D+ 0%

The proposed monitoring is not specific to the procedure studied, and it complies with the recommendations of the French Society of Anesthesia and Intensive Care (SFAR) [76].

3. The depth of hypnosis should be adjusted according to Bispectral Index monitoring or to a Patient State Index. **STATEMENT ENDORSED.** Overall agreement 86%: A+ 53%, A 33%, A- 7%, D- 7%, D 0%, D+ 0%.
4. Bispectral Index target should be between 40 and 60 or Patient State Index target should be between 25 and 50. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 73%, A 20%, A- 7%, D- 0%, D 0%, D+ 0%.

The Bispectral Index (BIS) and the Patient State Index (PSI) are not typically used during routine endoscopies, as the procedures are often short and have low morbidity [77, 78]. The main rationale for monitoring the depth of anesthesia using BIS or PSI in this context is to allow for the administration of the lowest possible dose of hypnotics, thereby limiting their potential impact on pressure measurements. Several meta-analyses have indeed found a reduction in propofol usage between standard anesthesia and BIS-guided anesthesia down to 1.32mg/h/kg [79, 80], a trend that has also been observed with PSI [81]. Using these monitoring tools also presents additional advantages, particularly in terms of safety and efficiency. Adjusting sedation doses helps reduce recovery times (eye opening, extubation, discharge times, etc.) by avoiding over-sedation [80–82] and decreasing patient discomfort or intra-procedural awakenings in cases of under-sedation [75, 83, 84].

3.2.2 | Induction

1. Intubation is indicated for patients undergoing pressure measurements via endoscopy. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 60%, A 40%, A- 0%, D- 0%, D 0%, D+ 0%.

This proposal concerns measurements that need to be performed in the upper gastrointestinal tract. The rationale for intubating patients with upper gastrointestinal motility disorders lies in the high incidence of motility issues in this

population, such as achalasia, gastroparesis, and esophageal dysmotility, which significantly increases the risk of aspiration [85–87]. Aspiration can lead to serious complications, such as aspiration pneumonia, acute respiratory distress syndrome (ARDS), chronic lung diseases, and death [88]. Securing the airway with intubation ensures better protection against inhalation of gastric contents during procedures [87]. Additionally, intubation facilitates easier airway management, especially when the operator is performing precise measurements. Furthermore, if the measurements are followed by therapeutic intervention, the procedure could be lengthy, necessitating prolonged airway control to ensure patient safety throughout the entire operation. Nevertheless, the decision to proceed with intubation should be left to the anesthesiologist's discretion, based on the risk of aspiration. Risks assessment must take into account patient's comorbidities (e.g., gastroparesis, esophageal sphincter dysfunction, and difficult airway access), the procedure (e.g., prolonged procedure), local practices, and applicable guidelines.

2. Pre-oxygenation with FiO₂ 100% for 3 min, aiming for an FeO₂ of at least 90% should be performed according to the current recommendations. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 87%, A 13%, A- 0%, D- 0%, D 0%, D+ 0%.

Parameters of an appropriate pre-oxygenation and intubation conditions are based on the SFAR recommendations [72, 89].

3. For standard induction, propofol target-controlled infusion should be preferred, and adjusted according to the Bispectral Index or to the Patient State Index. **STATEMENT ENDORSED.** Overall agreement 86%: A+ 53%, A 33%, A- 0%, D- 14%, D 0%, D+ 0%.
4. If indicated, the short-acting opioid that should be preferred is remifentanyl target-controlled infusion. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 80%, A 20%, A- 0%, D- 0%, D 0%, D+ 0%.
5. At Induction, the effect-site concentration of remifentanyl target-controlled infusion should be 3–6 ng/mL. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 67%, A 26%, A- 7%, D- 0%, D 0%, D+ 0%.
6. For intubation indicated for patients undergoing pressure measurements via endoscopy, a short-acting neuromuscular blocker (succinylcholine; 1mg/kg or mivacurium; 0,15mg/kg) or one that can be quickly reversed (rocuronium; 0.6mg/kg (standard induction) or 1.2mg/kg (crush induction)) should be used. **STATEMENT ENDORSED.** Overall agreement 80%: A+ 47%, A 33%, A- 13%, D- 7%, D 0%, D+ 0%.
7. Intubation should be performed when:
 - a. propofol and remifentanyl target-controlled infusions are in target zones AND
 - b. the patient is curarized (TOF 0/4 or fasciculations). **STATEMENT ENDORSED.** Overall agreement 80%: A+ 67%, 13%, A- 13%, D- 0%, D 7%, D+ 0%.
8. If crush induction is required (e.g., symptomatic gastroesophageal reflux), the same molecules should be used.

If the crush induction is performed without target-controlled infusions, it should be followed by propofol target-controlled infusions for anesthesia maintenance. **STATEMENT ENDORSED.** Overall agreement 86%: A+ 53%, A 33%, A- 0%, D- 7%, D 7 0%, D+ 0%.

Proposals concerning the molecules to be used come from the expert group's opinion. The rationale is as follows:

- propofol, due to its short duration of action, seems to have the least impact on the measurements, and target-controlled infusion allows for great flexibility [6];
- if intubation is required, the use of an opioid analgesic is almost always required in adults (except for crush induction). Remifentanyl seems to be the most pertinent drug because of its short duration of action, its minimal impact on measurements, and its target-controlled infusion option [6];
- lastly, short-acting or reversible neuromuscular blockers also minimize the impact on the measurements [6], by allowing measurements to be performed on patients who are not under neuromuscular blockade, in line with the needs expressed by neurogastroenterologists in the first Delphi.

For the induction of anesthesia with remifentanyl, target concentrations typically range from 3 to 6 ng/mL. This range allows for effective analgesia while facilitating smooth induction and intubation [90–92].

3.2.3 | After Induction

1. The hypnotic that should be preferred for hypnosis maintenance is propofol target-controlled infusion, adjusted according to the Bispectral Index or to the Patient State Index. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 60%, A 33%, A- 0%, D- 0%, D 7%, D+ 0%.
2. The maintenance opioid that should be preferred (if needed) is remifentanyl target-controlled infusion, with a target effect-site concentration of 1–2 ng/mL. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 53%, A 40%, A- 0%, D- 0%, D 0%, D+ 7%.

Depending on the intensity of the painful stimulus (which can be predicted based on the type of procedure), or based on the patient's sympathetic response (e.g., heart rate and blood pressure), it may be necessary to add an analgesic. Opioids are the most commonly used agents.

Propofol and remifentanyl indeed seem to have the least impact on the measurements [6], with remifentanyl's short duration of action allowing for rapid elimination [93]. The typical target concentrations are based on various studies that highlight effective dosing strategies to achieve optimal analgesia while minimizing side effects. Literature suggests that a target effect-site concentration of around 1–2 ng/mL is often effective for providing analgesia during surgical procedures. Adjustments can be made depending on the duration of the surgery and the patient's individual response [90–92].

3.2.4 | Before Pressure Measurements

1. If remifentanyl was continued after intubation, it should be stopped at least 5 min before pressure measurements. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 73%, A 20%, A- 0%, D- 0%, D 7%, D+ 0%.
2. Pressure measurements could begin if the target-controlled infusion plasma concentration of remifentanyl is below 0.5 ng/mL. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 33%, A 67%, A- 0%, D- 0%, D 0%, D+ 0%.
3. If the patient was paralyzed with rocuronium, sugammadex should be administered 10 min before pressure measurements, with a dosage adjusted to the level of paralysis according to current recommendations (4 mg/kg after re-appearance of at least 1 to 2 PTC responses; 2 mg/kg after spontaneous re-appearance of the 2nd TOF response). **STATEMENT ENDORSED.** Overall agreement 93%: A+ 53%, A 40%, A- 0%, D- 0%, D 7%, D+ 0%.
4. Pressure measurements could begin if the train of four indicates a T4/T1 ratio > 90%. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 67%, A 33%, A- 0%, D- 0%, D 0%, D+ 0%.

These proposals are based on the pharmacokinetics of the different agents [93] and on the SFAR guidelines regarding the use of neuromuscular blockers [94], with the objective of minimizing the impact of anesthetic agents on endoscopic measurements in line with the needs identified by neurogastroenterologists in the first round of Delphi (no opioids, no neuromuscular blocker). The timing and chosen target for remifentanyl is based on its rapid elimination, which allows the target effect to be reached at the moment of measurement close to 0 ng/mL [93].

3.2.5 | After Pressure Measurements

1. After pressure measurements, remifentanyl target-controlled infusion with an effect-site concentration should not be reintroduced except if further procedures are necessary (myotomy, sphincterotomy, etc.). **STATEMENT ENDORSED.** Overall agreement 86%: A+ 73%, A 13%, A- 7%, D- 0%, D 7%, D+ 0%.
2. Post-interventional analgesia should be based on paracetamol (1 g or 15 mg/kg if weight < 60 kg). **STATEMENT ENDORSED.** Overall agreement 86%: A+ 60%, A 27%, A- 13%, D- 0%, D 0%, D+ 0%.
3. Post-interventional analgesia with paracetamol (1 g or 15 mg/kg if weight < 60 kg) should be administered after the measurements are completed. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 80%, A 13%, A- 7%, D- 0%, D 0%, D+ 0%.
4. If further procedures are necessary after the measurements (e.g., interventional procedure), remifentanyl should be adjusted to the pain induced by the procedure. **STATEMENT ENDORSED.** Overall agreement 100%: A+ 87%, A 13%, A- 0%, D- 0%, D 0%, D+ 0%.

Remifentanyl does not need to be continued if no painful procedure follows the measurements, and the dosage should be adjusted according to the pain intensity of the procedure, if performed [90–92]. Although the measurements themselves are not very painful, intubation can be, and ensuring the patient's comfort postoperatively is important. The use of paracetamol, a well-known analgesic with no major side effects when contraindications are respected, seems beneficial and has no significant impact on digestive motility [19, 95].

3.2.6 | Other

1. Dexamethasone should be preferred as the first-line treatment for postoperative nausea and vomiting over ondansetron and droperidol. **STATEMENT ENDORSED.** Overall agreement 80%: A+ 67%, A 13%, A– 13%, D– 7%, D 0%, D+ 0%.
2. Dexamethasone should be administered at a dose of 4 mg to 8 mg if the weight is > 60 kg, and if prevention of postoperative nausea and vomiting is necessary. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 60%, A 33%, A– 0%, D– 7%, D 0%, D+ 0%.

To our knowledge, no study has specifically investigated the potential impact of dexamethasone on human digestive motility. However, this molecule appears to be preferable to 5-HT3 antagonists, which are known to influence motility measurements negatively [60–65]. Moreover, it is recommended as a first-line treatment in the SFAR guidelines for the prevention of postoperative nausea and vomiting (PONV) [96, 97].

3. Central alpha–2 receptors antagonists should be avoided before measurement (clonidine, dexmedetomidine). **STATEMENT ENDORSED.** Overall agreement 93%: A+ 80%, A 13%, A– 0%, D– 7%, D 0%, D+ 0%.

Central alpha–2 receptors antagonists do not present any indication for digestive motility measurements. These molecules seem to have a potential impact on measurements [25, 51, 52, 54–58]. It is therefore logical to avoid them in this protocol.

4. The administration of atropine or sympathetic agonists should be avoided, if possible, before performing pressure measurements. **STATEMENT ENDORSED.** Overall agreement 86%: A+ 60%, A 26%, A– 7%, D– 7%, D 0%, D+ 0%.
5. If the administration of atropine or sympathetic agonists is needed during the procedure (e.g., arterial hypotension unresponsive to volume expansion and sedation modulation, severe symptomatic bradycardia), the endoscopist should be informed. **STATEMENT ENDORSED.** Overall agreement 93%: A+ 93%, A 0%, A– 7%, D– 0%, D 0%, D+ 0%.

As previously stated, atropine and sympathetic agonists seem to have a potential impact on measurements [66–70]. Nevertheless, these drugs are mainly used in emergency situations during general anesthesia when no therapeutic alternatives are available. In this context, it is important for the endoscopist to be

informed of their use to take it into account when interpreting measurements.

6. If the administration of opioids is needed for post-procedural analgesia while there is still an awake pressure measurement, the endoscopist should be informed. **STATEMENT ENDORSED.** Overall agreement 86%: A+ 87%, A 0%, A– 13%, D– 0%, D 0%, D+ 0%.

Some procedures require prolonged post-intervention pressure measurements, sometimes over 24 h. These procedures are not very painful and do not typically justify the postoperative prescription of opioids (unless the patient has been previously treated with this type of molecule). In view of the impact of opioids on digestive motility, the endoscopist should be informed if opioids are administered while measurements are still in progress.

4 | Discussion

Per-procedural motility measurements are increasing worldwide. These include, among others, antireflux surgery, Heller's cardiomyotomy, and peroral endoscopic myotomies (POEM) at the esophageal and/or pyloric levels. However, considering the potential action of anesthetic drugs on gastrointestinal motility, the lack of standardized anesthetic protocols may have dampened measurement accuracy. This may have contributed to limiting the spread of such measurements due to imperfect reproducibility. Using two independent Delphi processes (GFNG and panel of anesthesia experts), this work allowed the creation of a specific standardized anesthesia protocol for endoscopy and/or surgery when measurement of digestive motility is considered. To our knowledge, this is the first protocol of its kind available in the literature, and we hope that its dissemination could help to improve the performance of digestive motility measurements during endoscopy.

Although the literature remains scarce regarding the effects of anesthetic drugs on digestive motility measurements, GFNG experts were able to reach a consensus on this subject, emphasizing that the use of opioids and neuromuscular blocking agents can have an impact on those measurements. Indeed, it was shown in prior reports that the reproducibility of digestive motility measurements can vary among centers. For example, a recent meta-analysis pooled measurements from esogastric junction FLIP in HVs (N = 154 subjects, N = 15 included reports) [98]. Results evidenced significant heterogeneity between studies and the use of sedation was mentioned as a possible bias to explain these findings, as the anesthesia protocol varied across centers. Similar conclusions were reported from studies using pyloric FLIP [45, 99]. Therefore, the use of our standardized anesthesia protocol could help to limit this heterogeneity among centers with regard to the methodology of these measurements.

One limitation of this study is that the standardized anesthesia protocol has been built using anesthetic drugs available in France. Noteworthy, these drugs are commonly used in routine anesthetic care worldwide. Therefore, most of these statements will likely be extended to most other countries, including European countries [100]. This may therefore contribute to the dissemination of the present anesthesia protocol. Of note, the present anesthesia protocol has also taken into consideration

drugs routinely used in the perioperative management. These included for instance dopamine antagonists or agents acting on sympathetic/parasympathetic balance, which were not evaluated in previous reports nor reported in most clinical studies. Taken altogether, the recommendations from this report may help in the future to standardize procedures for per-procedural motility measurements, and therefore increase their accuracy and reproducibility, and further extend their use. Finally, we acknowledge the absence of a comprehensive joint Delphi process. This approach was not ideal for the current project, as few individuals possess dual expertise in both relevant fields. After the anesthesia protocol was drafted, the document circulated among members of the GFNG for final approval of the algorithm.

5 | Conclusion

To our knowledge, this work, through the use of two independent Delphi processes (GFNG and panel of anesthesia experts), is the first to provide expert opinions from neurogastroenterologists on the impact of anesthetic agents on endoscopic measurements, highlighting which agents should be avoided. It also proposes an anesthesia protocol that takes into account the needs of endoscopists, aiming to improve the accuracy of measurements and enhance patient care.

Author Contributions

Drafted consensus questions, drafted literature review sections, set up the voting and summaries access, summarized voting outcomes: D.R., T.C., G.G., and C.D. Participated in voting, reviewed, and corrected content: all members of the consensus. All authors have approved the final version of the article, including the authorship list.

Acknowledgments

Working group: Charlotte Desprez (CD), Guillaume Gourcerol (GG), Domitille Renard (DR), Thomas Clavier (TC). GFNG: Gérard Amarenco, Charlene Brochard, Benoit Coffin, Charlotte Desprez, Guillaume Gourcerol, Jérémie Jacques, Anne-Marie Leroi, Chloé Melchior, François Mion, Sabine Roman, Heithem Soliman, Fabien Wuestenberghs, Frank Zerbib. Anesthesia experts group: Osama Abou-Arab, Emmanuel Besnier, Alice Blet, Matthieu Boisson, Audrey De Jong, Denis Frasca, Marc Garnier, Aurelie Gouel, Arthur James, Yoann Launey, Daphné Michelet, Maxime Nguyen, Emmanuel Rineau, Amélie Rollé, Stéphanie Sigaut.

Conflicts of Interest

A.M.L. is a consultant for Medtronic. F.M. has served as a consultant or speaker for: Laborie, Medtronic, Dr. Falk Pharma, Dr. Schaer, Sanofi Winthrop. G.G. has served as a consultant or speaker for: Enterra Medical, Medtronic, Laborie, Viatrix, Kyowa Kyrin, Biocodex, Lilly. The remaining authors have no conflicts of interest to declare.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

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