Impact of anesthesia drugs on digestive motility measurements in humans: A systematic review

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REVIEW

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Impact of anesthesia drugs on digestive motility measurements in humans: A systematic review

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Abstract

Background and Purpose: Measurement of gastro-intestinal motility is increasingly performed under general anesthesia during endoscopic or surgical procedures. The aim of the present study was to review the impact of different anesthetic agents on digestive motility measurements in humans.

Methods: This systematic review was performed using the Medline-Pubmed and Web of Science databases. All articles published until October 2023 were screened by identification of key words. Studies were reviewed if patients had an assessment of digestive motility using conventional perfused manometry, high-resolution manometry, electronic barostat or functional lumen impedance planimetry with the use of inhaled or intravenous anesthetic anesthetic agents (propofol, ketamine, halogens, nitrous oxide, opioids, and neuromuscular blockades).

Results: Four hundred and eighty-eight unique citations were identified, of which 42 studies met the inclusion criteria and were included in the present review. The impact of anesthetics was mostly studied in patients who underwent esophageal manometry. There was a heterogeneity in both the dose and timing of administration of anesthetics among the studies. Remifentanil analgesia was the most studied anesthetic drug in the literature, showing a decrease in both distal latency and lower esophageal sphincter pressure after its administration, but the impact on Chicago classification was not studied. Inhaled anesthetics administration elicited a decrease in lower esophageal sphincter pressure, but contradictory findings were shown on esophageal motility following propofol or neuromuscular blocking agents administration.

Conclusion: Studies of the impact of anesthetics on digestive motility remain scarce in the literature, although some agents have been reported to profoundly affect gastrointestinal motility.

KEYWORDS
anesthesiabarostat, digestive motility, endoFLIP, manometry

1 | INTRODUCTION

Historically, gastrointestinal motility has been investigated using pull-through or stationary manometry techniques.[1,2] More recent devices have been developed in the last two decades, like high-resolution manometry or the Functional Lumen Impedance Planimetry (FLIP) system, which have evidenced digestive motility disorders that could not have been shown previously.[3,4] In most cases, these motility tests (i.e., esophageal manometry or anorectal manometry) can be routinely performed awake without the use of anesthetics. However, severe stress, young age, or difficulty in positioning the catheter may require the use of general anesthesia. In addition, recent development of transorificial endoscopic surgery has encouraged the use of per-procedural recording to guide the surgical procedure.[3] For example, lower esophageal sphincter (LOS) distensibility measurement performed during an endoscopic and/or surgical procedure may be necessary to diagnose LOS achalasia, guide the length of endoscopic or surgical myotomy length, and accurately predict the clinical outcomes after endoscopic or surgical procedures.[3] Such procedures however require the use of anesthetic agents, including opioid analgesics, sedatives (intravenous or inhaled), and neuromuscular blockers.

Even though normal values are available in unsedated healthy volunteers (HVs) for all of these techniques,[4,5] there is a lack of data regarding the impact of anesthetics on the results of digestive motility tests. In a recent study, our group demonstrated the possible impact of general anesthesia on pyloric measurement using the EndoFLIP® system in patients with gastroparesis.[6] To our knowledge, no national or international recommendations are available regarding the type of anesthesia that can be administered during gastrointestinal motility measurements. Moreover, many centers have no established local protocol, leaving either the endoscopist or anesthetist to decide on the type of administered anesthesia, regardless of its possible impact on the motility measurement. Consequently, the results of most motility studies performed under general anesthesia should be carefully extrapolated to other centers, as the general anesthesia protocol can differ widely between centers and patients.[3] The conditions of these measurements, especially the anesthetic agents used for anesthesia are crucial and should be considered for comparisons within and between studies. To date, no review has been carried out on the potential impact of anesthetics on digestive motility measurements. The aim of the present study was therefore to review the impact of anesthetic agents on digestive motility measurements in humans.

2 | MATERIALS AND METHODS

2.1 | Search strategy

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[7] It was performed without temporal limitation using the Medline-Pubmed, and Web of Science databases. The search was built with the help of a research librarian (EL). Keywords and MeSH terms were determined by two neurogastroenterologists (CD and GG) and two anaesthetists (DR and TC). The search was built as follows using a combination of keywords and mesh terms: ("tone" OR "tonus" OR "motilit*" OR "sphinct*" OR "endoflip" OR "functional lumen impedance planimetry") AND ("gastric" OR ""oesophageal" OR "esophageal" OR "pylorus" OR "duodenal" OR "intestinal" OR "jejunal" OR "ileal" OR "gastrointestinal" OR "colonic" OR "colon" OR "colorectal" OR "rectal") AND ("propofol" OR "ketamine" OR "dexmedetomidine" OR "halogenated" OR "sevoflurane" OR "isoflurane" OR "desflurane" OR "nitrous oxide" OR "sufentanil" OR "fentanyl" OR "remifentanil" OR "alfentanil" OR "curarization" OR "neuromuscular block*" OR "rocuronium" OR "atracurium" OR "cisatracurium" OR "vecuronium" OR "sugammadex" OR "succinylcholine" OR "suxamethonium" OR "lidocaine" OR "volatile anesthetic"). To identify missing papers, bibliographies of all included studies and all relevant systematic reviews were reviewed.

2.2 | Eligibility criteria

All articles published until October 2023 were screened by identification of keywords. Only articles written in English were included in the present review. Experimental studies (randomized and non-randomized controlled trials) and observational studies (cohort-prospective and retrospective) were included. Case reports, case studies, opinions, editorials, commentaries, letters, conference abstracts, and reviews or systematic reviews were excluded. Studies were reviewed if patients underwent an assessment of digestive motility (i.e., lower esophageal sphincter or motility, gastric or pyloric motility, duodenal, jejunal, colonic, and/or anorectal motility) using several measurement modalities of digestive motility, (i.e., by conventional perfused manometry or high-resolution manometry, by electronic barostat or Endo-FLIP®, or Functional Lumen Impedance Planimetry) with the use of inhaled and/or intravenous anesthetic agents (propofol, ketamine, halogens, nitrous oxide, opioids, neuromuscular blockades). Topical and perimedullary administration of local anesthetics were excluded. Articles were included if the study examined the impact of intravenous and/or inhaled anesthetic agents on digestive motility. Inclusion criteria are summarized in Table 1. Two reviewers (CD and DR) independently screened all potential articles based on their titles and abstract. In cases of disagreement, the paper was read and discussed by both reviewers and two others (GG and TC) until a consensus was reached. Following this, independent screening of the full texts of eligible articles was conducted and papers that satisfied all the inclusion criteria were included in this review.

2.3 | Data extraction and analysis

Relevant data were extracted from each study, including study design, target population, digestive motility examination methods,

TABLE 1 Summary of inclusion criteria.

Study design	Included: • Experimental studies: randomized and non-randomized controlled trials • Observational studies: cohorts (prospective and retrospective) Excluded: case reports, case studies, opinions, editorials, commentaries, letters, conference abstracts, and reviews or systematic reviews
Sites of digestive motility assessment	• Lower esophageal sphincter • Esophageal motility • Gastric or pyloric motility • Duodenal, jejunal, motility • Colonic and/or anorectal motility
Modalities of digestive motility measurement	• Conventional perfused manometry • High-resolution manometry • Electronic barostat • Endo-FLIP® • Functional Lumen Impedance Planimetry
Anesthetic agents used	• Sedative agents: propofol, ketamine, halogens, nitrous oxide • Opioids • Neuromuscular blockades
Route of administration	• Inhaled • Intravenous

anesthesia protocol used, measure outcomes, and year of publication. The data were first processed by a neurogastroenterologist (CD) to analyze the measurements taken, and then by an anesthetist (DR) with a closer look at the anesthesia protocols used. Disagreements were resolved through discussion. Data were summarized using a table with entries for the types of examination performed and the types of anesthetic agents used to present the key elements of each study. Descriptive analyses of the included studies were conducted.

3 | RESULTS

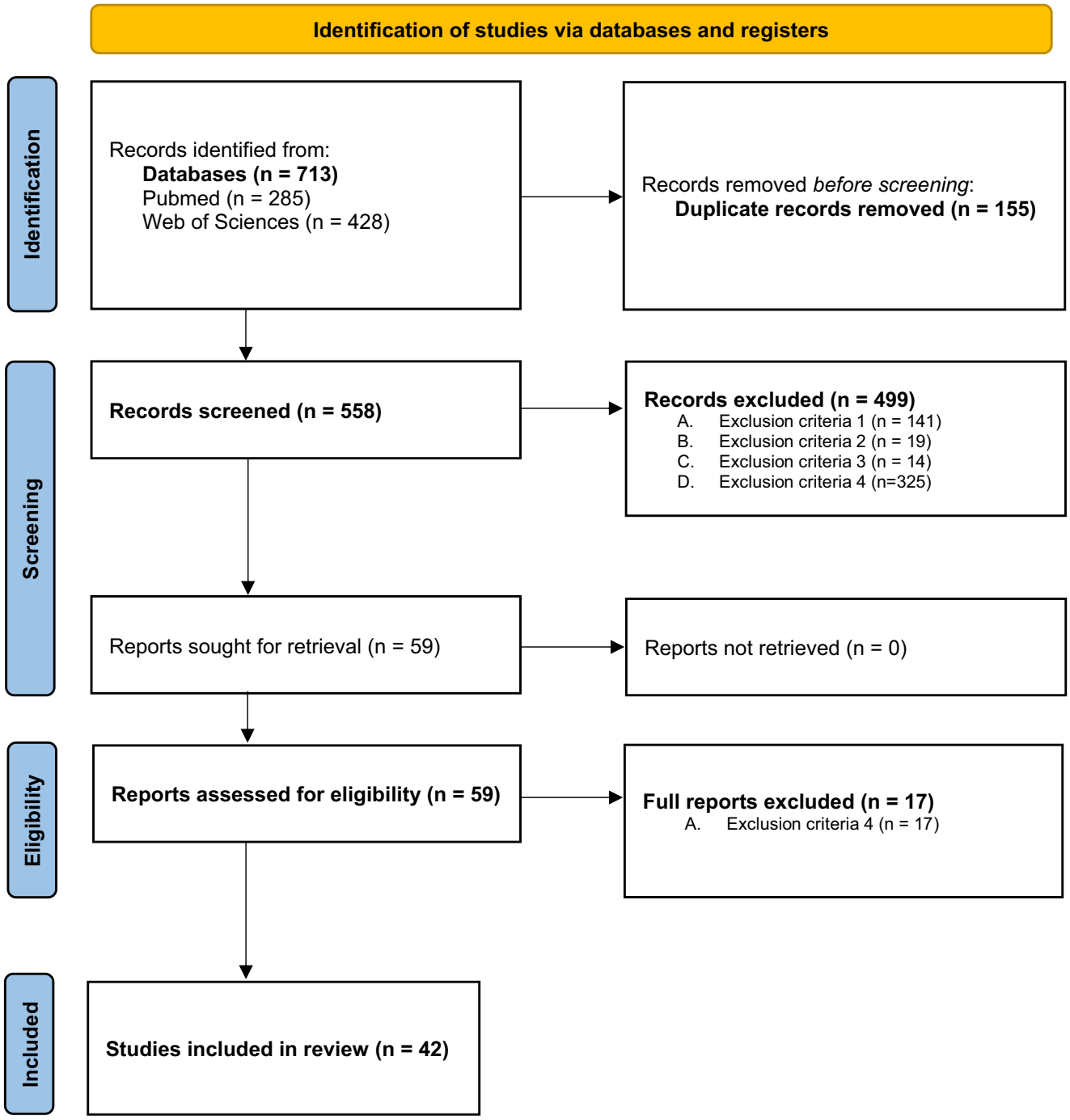
Four hundred and eighty-eight unique citations were identified, of which 42 studies met the inclusion criteria and were included in the present review (Figure 1). The results of the different studies were classified by drug types to facilitate the reading of the manuscript. The characteristics of the different anesthetics used in all studies are summarized in Table 2 and the main findings of the study by drug class can be found in Table 3. The characteristics of the studies included, and their principal findings are presented in Table 4.

3.1 | Part. 1: Opioid analgesia

3.1.1 | Fentanyl and alfentanil

Fentanyl and alfentanil are two intravenous synthetic opioid analgesics which act by agonism of μ-opioid receptors and are metabolized by the liver. Their pharmacokinetics are similar to those of morphine, although they differ in their peak and duration of action.[57] Fentanyl has a distribution half-life of 1.7 min, an elimination half-life of 219 min, and a distribution volume of 4 L/kg. Alfentanil has a distribution half-life of 0.4 min, an elimination half-life of 94 min, and a distribution volume of 0.75 L/kg. Its rapid onset of action is a result of its rapid passage across the blood–brain barrier because of the high amount of non-ionized molecules. Precautions should be taken when administering fentanyl, particularly in cases of impaired hepatic metabolism (e.g., in premature children or the elderly), where there is a risk of respiratory depression, and in obesity.[57]

The impact of alfentanil and fentanyl on digestive physiology was assessed in four studies[8-11] among included studies and three of these studies used high-resolution esophageal manometry. Usual dosages of alfentanil and fentanyl for daily practice were used in these studies (fentanyl: 100–200 μg, alfentanil: 20 $\mu g\,kg^{-1}$). The addition of alfentanil during propofol induction in 17 HVs did not elicit any change in oesogastric pressure gradient (the difference between oesogastric junction OGJ and gastric pressure) compared to placebo in the first study.[8] This study did not assess the potential impact of alfentanil on final diagnosis according to Chicago classification. Another study compared the results of high-resolution manometry after probe placement performed under conscious sedation with fentanyl or performed without sedation on a different day.[9] Both the supine and upright integrated relaxation pressure and the supine distal contractile integral were significantly increased ($p = 0.007$ and $p = 0.004$) after sedation compared to no sedation high-resolution manometry. However, these differences did not affect the Chicago classification version 3.0 results, as a diagnosis of normal esophageal motility was found in all 12 HVs after sedation.[9] Similar results were exhibited in a third study with a retrospective design (83 patients with administration of fentanyl and 91 controls), as the distal



Exclusion criteria

1. Animal studies
2. Articles not written in English
3. Article type: review, comment, case-report
4. Article off topic

FIGURE 1 Flow chart of the study.

contractile integral was higher in patients who underwent fentanyl administration than in controls, without any consequences in the Chicago classification version 3.0 results.[10]

The effect of fentanyl on the antroduodenal motility was evaluated in one prospective study with administration during Phase II of the interdigestive motility complex ($N = 11$ patients).[11] Fentanyl

TABLE 2 Characteristics of the different anesthetics used among studies.

Drug class	Anesthetic agent studied	Mechanisms of action	Characteristics
Opioids	Alfentanil	μ-opioid receptor agonists	Short onset of action, short elimination half-time
	Fentanyl		Short onset of action, long elimination half-time
	Remifentanil		Short onset of action, very short elimination half-time, on/off effect
Hypnotic drugs	Halogens	GABA receptors agonists, NMDA receptors antagonists	Inhaled drugs, for maintenance of anesthesia, eliminated in about 10 min
	Propofol	GABA receptors agonist	Induction or maintenance of anesthesia, short onset of action, short elimination half-time. Hypotensive effects
	Thiopental	GABA receptors agonist	Induction of anesthesia, short onset of action, short elimination half-time. Hypotensive effects
	Ketamine	NMDA receptors antagonist	Induction or maintenance of anesthesia, sedative and analgesic action, short onset of action, short elimination half-time. No hypotensive effects
Neuromuscular Blockades	Suxamethonium	Depolarising agent	Short onset of action. Indicated where there is a risk of inhalation
	Rocuronium	Nondepolarizing agent	Short onset of action or not depending on dose, can be indicated where there is a risk of inhalation
	Others	Nondepolarizing agent	Longer onset of action

Abbreviations: GABA, gamma-aminobutyric acid; NMDA, N-methyl-D-aspartate.

injection induced a burst of propagating activity indistinguishable from Phase III, and a reduction in the duration of the interdigestive motility complex, mainly by reducing the duration of the Phase II. The motility index of Phase II in the antrum remained unchanged after fentanyl administration but increased in the duodenum.

3.1.2 | Remifentanil

Remifentanil is an intravenous synthetic opioid analgesic which also acts by agonism of μ-opioid receptors, but it differs by an ester linkage and is metabolized by nonspecific esterases.[58] It has a distribution half-life of 1–1.5 min, an elimination half-life of about 4 min, and a distribution volume of 0.3 L/kg. It often has better haemodynamic tolerance, less accumulation, and is easier to handle thanks to its on/off effect.[58]

Remifentanil is the most frequently studied opioid analgesia drug found in the neurogastroenterology literature to date, with 10 studies available to our knowledge.[12–19,47,48] However, only seven prospective reports in HVs[12–18] used a prospective design to study its impact on esophageal motility. A first study in 2005 prospectively evaluated the administration of a low dose of remifentanil in 10 HVs (light sedation).[12] No effect of remifentanil was shown on the LOS pressure, nor on the oesogastric pressure gradient in comparison to baseline.[12] These results were not confirmed in a more recent study which used higher doses of remifentanil.[13] Indeed, remifentanil administered in 14 HVs at a target concentration of 5 ng/mL resulted in a mean decrease in LOS pressure of 6.5 mmHg (95% confidence interval −1.7 to −11.2). However, this dose of remifentanil was rather high and is not frequently used in daily practice. Two further prospective studies[14,17] confirmed these findings using usual doses of remifentanil for daily practice (with target concentrations of 3[14] and 4 ng/mL,[17] respectively), as a decrease in both the inspiratory and expiratory OGJ pressures were shown after the administration of remifentanil. In one of these two reports, the administration of methylnaltrexone (μ-opioid receptor antagonist) after remifentanil abolished this effect, with similar results in the placebo group.[14] All these studies did not assess the potential impact of remifentanil on final diagnosis according to Chicago classification.

Three more recent studies also assessed the impact of remifentanil on the different metrics of esophageal motility by using high-resolution esophageal manometry.[15,16,18] A study in 2015 showed that the integrated relaxation pressure was higher after remifentanil infusion, with a dose–response association as different concentrations of remifentanil were tested (1, 2, or 3 ng/mL).[15] A decrease from baseline of the distal latency was also observed, with a dose–response association with remifentanil.[15] No difference was found after the administration of naloxone (a μ-opioid receptor antagonist) in this cross-over study, but the doses of naloxone used were low (bolus injection of 6 μg/kg and a naloxone infusion of 0.1 μg/kg/

TABLE 3 Main findings of the literature review. Results from studies specifically designed to study one or more anesthetic agent(s) are described here.

Drug class	Anesthetic drug studied	Corresponding studies	Number of RCT	Number of studies in HV	Main findings		
					Esophageal motility	Gastric, small bowel motility	Colonic, ano-rectal motility
Opioids	Alfentanil	*N* = 1 study Ahlstrand 2012[8]	1	1	1 study: no change in oesogastric pressure gradient	Not evaluated	Not evaluated
	Fentanyl	*N* = 3 studies Su 2020,[9] Balko 2021,[10] Schurizek 1989[11]	0	2	2 studies: increase in integrated relaxation pressure and distal contractile integral. No impact on Chicago classification v3.0	1 study: reduction in the duration of the interdigestive motility complex	Not evaluated
	Remifentanil	*N* = 8 studies Thorn 2005,[12] Ahlstrand 2011,[13] Savilampi 2013[14]/2015,[15] Cock 2018,[16] Ander 2017,[17] Cajander 2021,[18] Wallden 2008[19]	4	8	Perfused manometry 3 studies: decrease in LOS resting pressure 1 study: no effect on LOS pressure HR manometry 3 studies: Increase in integrated relaxation pressure and decrease in distal latency	No conclusion can be drawn (1 study with methodological bias)	Not evaluated
Hypnotic drugs	Halogens	*N* = 7 studies Sehhati 1980,[20] Mather 1992,[21] Kohjitani 1999[22]/2002,[23] Thorn 2006,[24] Shurizek 1989,[25] Ammoury (2022)[26]	3	6	4 studies: decrease in LOS resting pressure (dose–response effect), but preservation of the oesogastric pressure gradient 1 study: no effect on LOS pressure	No conclusion can be drawn (1 study with methodological bias)	1 study: No effect on total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions
	Propofol	*N* = 9 studies Ahlstrand 2012,[8] Thorn 2005,[12] Ammoury 2012,[26] Turan 2010,[27] de Leon 2011,[28] Hammas 2001,[29] Liu 2009,[30] Tran 2014,[31] Arbizu 2022[32]	4	7	2 studies: no effect on LOS pressure 1 study: decrease in LOS resting pressure (dose–response effect) 1 study: increase in LOS resting pressure (dose–response effect)	1 study: no effect on gastric tone	1 study: No effect on total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions 3 studies: Decrease in anal sphincter resting pressure, no difference in the detection of RAIR
	Thiopental	*N* = 2 studies Frenckner 1979,[33] Shurizek 1989[25]	1	2	Not evaluated	No conclusion can be drawn (1 study with methodological bias)	1 study: Decrease in anal sphincter resting pressure, no difference in the detection of RAIR
	Ketamine	*N* = 4 studies Ammoury 2012,[26] Varadarajulu 2008,[34] Keshtgar 2015,[35] Paskins 1984[36]	1	0	Not evaluated	1 study: no effect on sphincter of Oddi resting pressure nor on the results of sphincter of Oddi dysfunction classification	1 study: No difference in total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions 1 study: No difference in the detection of RAIR 1 study: No difference in anal resting pressure. Less pronounced relaxation of the IAS during RAIR

TABLE 3 (Continued)

Drug class	Anesthetic drug studied	Corresponding studies	Number of RCT	Number of studies in HV	Main findings		
					Esophageal motility	Gastric, small bowel motility	Colonic, ano-rectal motility
Neuromuscular blockades	Suxamethonium	$N=5$ studies Desprez 2023,[6] Smith 1978,[37] Andersen 1962,[38] Roe 1962,[39] Spence 1967[40]	1	4	1 study: no change in oesogastric gradient pressure	3 studies: increase in intragastric pressure 1 study: administration associated with decreased pyloric distensibility	Not evaluated
	Others	$N=4$ studies Ahlstrand 2011,[41] Suganuma 2021,[42] Hunt 1984,[43] Pfeffekorn 2004[44]	3	6	3 studies: contradictory findings depending on the anesthetic agent used	Not evaluated	1 study: no effect on the detection of RAIR

Abbreviations: HV, healthy volunteers; LOS, lower esophageal sphincter; RAIR, rectoanal inhibitory reflex; RCT, randomized controlled trials.

min). A second study using high-resolution impedance esophageal manometry found similar results with relevant concentrations of remifentanil.[16] Regarding the use of impedance monitoring in this study, the authors also found that both the duration of bolus flow through (3.0 ± 0.3 vs. 5.0 ± 0.4 s; $p < 0.001$) and the presence of bolus flow at the OGJ (5.1 ± 0.5 vs. 7.1 ± 0.5 s; $p = 0.001$) decreased during remifentanil administration. Moreover, there was no evidence of increased bolus residue after remifentanil administration. Lastly, a study from 2021 using a cross-over design (remifentanil or placebo infusion) reported similar results.[18] Indeed, remifentanil induced more rapid bolus transit and peristaltic propagation (shorter contractile latency, increased distal bolus distension pressure) and a shorter emptying time of the bolus through the OGJ. In addition, in this last study, methylnaltrexone administration did not change the altered esophageal timing variable following remifentanil infusion (distal contractile velocity and distal latency), while distension pressures and bolus flow time returned to baseline. All these studies did not assess the potential impact of remifentanil on final diagnosis according to Chicago classification.

As well as esophageal motility, the influence of remifentanil infusion on gastric tone measured using gastric barostat was evaluated in nine HVs.[19] However, no clear conclusion can be drawn from this study due to high inter-individual variability observed during remifentanil infusion, although the mean gastric tone was significantly lower during the remifentanil wash-out period compared to baseline.

3.2 | Part. 2: Sedative agents

3.2.1 | Inhaled anesthetics

Halogens are a large family of inhaled gases, of which the main agent used today is sevoflurane. Their mechanisms of action are not fully understood, but they are known to act by agonizing GABA-A (gamma-aminobutyric acid) receptors and antagonizing NMDA (N-methyl-D-aspartate) receptors, and most often undergo hepatic metabolism.[59] They differ in their solubility coefficient in oil and blood, which determines their potency and uptake potential, respectively. Their action at the site of effect passes through three phases: pulmonary, circulatory, and then tissue. Their effect is more rapid if the tissue is vascularised and if the agent is not very soluble. Their cerebral concentration rapidly approaches the alveolar concentration as soon as the plateau phase is reached. Halogens are mainly used to maintain anesthesia after induction, achieving the target within a few minutes using targeted inhalational anesthesia.[59]

The influence of inhaled anesthetics on digestive motility has been poorly studied in literature, as only seven prospective studies are available to date on the subject. Five of these reports investigated the impact of these agents on esophageal motility.[20–24] A first rather old study investigated the effect of the administration of halothane and enflurane on the LOS resting pressure and found that the latter was significantly decreased after the administration

TABLE 4 Characteristics of the studies.

First author (year of publication)	Country	Study design	Motility testing	Anesthesia protocol	Sample size	Age (years)	Male, *n* (%)	Principal findings of each study
Ahlstrand (2011)[41]	Sweden	Prospective	High-resolution esophageal manometry	Iv. Bolus dose of rocuronium (0.6 mg/kg)	10 HV (minor surgery under general anesthesia)	25 ± 16	5 (50)	No change in oesogastric pressure gradient
Ahlstrand (2011)[13]	Sweden	Prospective	High-resolution esophageal manometry	A target-controlled infusion of remifentanil was started until a plasma target concentration of 2.5 ng/mL was reached. The infusion was then increased to a target concentration of 5.0 ng/mL	14 HV	23 (18–30)	7 (50)	Decrease in LOS pressure
Ahlstrand (2012)[8]	Sweden	Prospective study, randomization for anesthesia protocol, cross-over study	High-resolution esophageal manometry	Allocated randomly to receive Alfentanil (20 μg/kg) or placebo (isotonic saline solution) 1 min before administration of Propofol (2 mg/kg). Anesthetised on two occasions 1-week apart	17 HV	28 ± 6	11 (65)	No change in oesogastric pressure gradient
Ammoury (2022)[26]	USA	Prospective study, randomization for anesthesia protocol	Perfused colonic manometry (8 lumen)	Allocated randomly to receive inhaled 8% sevoflurane for induction and maintenance or combination of propofol (2 mg/kg) and ketamine (0.5 mg/kg)	20 constipated children	10 (6–17)	14 (70)	No difference in total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions
Ander (2017)[17]	Sweden	Prospective study, randomization for anesthesia protocol, cross-over study	High-resolution esophageal manometry	Allocated randomly to (a) esmolol administered as a bolus dose (1 mg/kg) over 1 min followed by an infusion (10 μg/kg/min) over 15 min and (b) remifentanil with a targeted effect site concentration of 4 ng/mL	14 HV	25 ± 3.6	8 (73)	Decrease in both the inspiratory and expiratory OGJ pressures.
Anderson (1962)[38]	Denmark	Prospective	Perfused intragastric manometry (1 lumen)	Iv. Suxamethonium (75 mg)	10 HV (minor surgery under general anesthesia)	ND	6 (60)	Rise in intragastric pressure
Arbizu (2021)[32]	USA	Prospective	High-resolution anorectal manometry	Iv. Propofol (no given dosage)	27 constipated children	9.2 (4–18)	17 (63)	Decrease in the anal sphincter resting pressure. The internal anal sphincter minimum pressure during RAIR was significantly lower.
Balko (2020)[10]	USA	Retrospective	High-resolution esophageal manometry	Iv. Fentanyl (no standardized protocol)	83 patients with acute opioid administration and 91 controls	54 ± 18	74 (43)	Higher distal contractile integral, but no difference in Chicago classification v3.0

TABLE 4 (Continued)

First author (year of publication)	Country	Study design	Motility testing	Anesthesia protocol	Sample size	Age (years)	Male, *n* (%)	Principal findings of each study
Cajander (2021)[18]	Sweden	Prospective study, randomization for anesthesia protocol, cross-over study	High-resolution esophageal impedance manometry	Allocated randomly to receive either an iv remifentanil (3 ng/mL) and methylnaltrexone (0.3 mg/kg), or a placebo infusion (physiological saline solution) and methylnaltrexone 0.3 mg/kg, and vice versa at the second occasion 7 days apart.	19 HV	24.4 ± 4.1	10 (55)	Shorter contractile latency, increased distal bolus distension pressure
Cock (2017)[16]	Australia	Prospective	High-resolution esophageal manometry	Iv. Target-controlled infusion was used to administer remifen- tanil with an effect-site concentration of 3 ng/mL	11 HV	23 ± 3	7 (64)	Decrease of the duration of the bolus flow through and the presence of bolus flow at the OGJ
Derrington (1987)[45]	England	Prospective	Perfused esophageal manometry (3 lumen)	Iv. thiopentone 4 mg/kg and pancuronium 0.1 mg/kg. Anesthesia was maintained with 70% nitrous oxide and 0%–1% enflurane in oxygen with morphine sulphate for analgesia. After the administration of neostigmine 2.5 mg and glycopyrrolate 0.5 mg, measurements were taken every 1 min for 20 min	12 HV (minor surgery under general anesthesia)	ND	ND	No conclusion can be drawn
Desprez (2023)[6]	France	Retrospective	EndoFLIP system	No standardized protocol	125 gastroparetic patients	55 (43–66)	46 (37)	Suxamethonium administration associated with decreased pyloric distensibility
Frenckner (1979)[33]	Sweden	Prospective	Perfused anorectal manometry	Iv. Penthotal (5 mg/kg)	15 healthy children	6 (5–7)	ND	Decrease in the anal pressure at rest, relaxation of the internal anal sphincter during RAIR less pronounced but still visualized
Hammas (2001)[29]	Sweden	Prospective study, randomization for anesthesia protocol	Gastric barostat	Allocated randomly to receive Iv. propofol (1 mg/kg) before Iv. morphine (0.1 mg/kg) or Iv. morphine solely (0.1 mg/kg)	20 HV	68 (43–79)	11 (53)	No effect on gastric tone
Heijke (1991)[46]	England	Prospective study, randomization for anesthesia protocol	Perfused esophageal manometry (3 lumen)	Iv. thiopentone 4 mg/kg, atracurium 0.4 mg/kg, ventilation with N_2O 70% and isoflurane 0.5%–1% in O2.N_2O. Allocated randomly to receive a combination of atropine 1.2 mg and neostigmine 2.5 mg or atropine 0.6 mg and edrophonium 1 mg/kg	22 HV (minor surgery under general anesthesia)	31 (24–36)	0 (0)	No conclusion can be drawn

(Continues)

TABLE 4 (Continued)

First author (year of publication)	Country	Study design	Motility testing	Anesthesia protocol	Sample size	Age (years)	Male, *n* (%)	Principal findings of each study
Hunt (1984)[43]	England	Prospective study, randomization for anesthesia protocol	Perfused esophageal manometry (3 lumen)	Allocated randomly to receive either Iv. pancuronium 0.1 mg/kg or vecuronium 0.1 mg/kg	24 HV (minor surgery under general anesthesia)	ND	0 (0)	Vecuronium administration did not change the oesogastric pressure gradient, but pancuronium infusion elicited an increase in oesogastric pressure gradient resulting from an increase of the LOS pressure
Keshtgar (2016)[35]	England	Prospective	Perfused anorectal manometry	$N=27$ Iv. Ketamine and $N=31$ without sedation	58 constipated children	10 (6–15)	37 (63)	No difference in anal resting pressure. Less pronounced relaxation of the IAS during RAIR
Kohjitani (1999)[22]	Japan	Prospective study, randomization for anesthesia protocol	Perfused esophageal manometry (3 lumen)	Sevoflurane and 66% nitrous oxide in oxygen or enflurane and 66% nitrous oxide in oxygen	14 HV (minor surgery under general anesthesia)	10 ± 4	4 (29)	Decrease in LOS resting pressure
Kohjitani (2002)[23]	Japan	Prospective	Perfused esophageal manometry (3 lumen)	Inhalation of sevoflurane and 66% nitrous oxide in oxygen and iv. vecuronium (0.2 mg/kg), and maintained with sevoflurane and 66% nitrous oxide in oxygen	10 HV children	4.2 (2–8)	5 (50)	No difference in LOS resting pressure
de Leon (2010)[47]	Sweden	Prospective	High-resolution esophageal manometry	Iv. Propofol (2–2.5 mg/kg), rocuronium (0.7 mg/kg). After intubation, remifentanil (4 ng/mL) and ventilated with 50% oxygen in sevoflurane and air.	17 obese patients undergoing laparoscopic gastric by-pass	42 (28–68)	5 (30)	No conclusion can be drawn
de Leon (2010)[48]	Sweden	Prospective	High-resolution esophageal manometry	Iv. Propofol (2–2.5 mg/kg), rocuronium (0.7 mg/kg). After intubation, remifentanil 4 ng/mL and ventilated with 50% oxygen in sevoflurane and air.	17 obese patients undergoing laparoscopic gastric by-pass	43 (27–63)	2 (12)	No conclusion can be drawn
de Leon (2011)[28]	Sweden	Prospective	High-resolution esophageal manometry	Iv. Bolus dose of propofol (0.3, 0.6, and 0.9 mg/kg)	10 young HV and 10 elderly HV	25 (18–30) and 71 (60–87)	ND	Dose-effect of propofol administration on LOS resting pressure, but no difference in oesogastric pressure gradient
Liu (2009)[30]	Taiwan	Prospective	High-resolution anorectal manometry	Iv. Propofol (1.0–1.2 mg/kg)	18 HV	22 (19–28)	9 (50)	Decrease in lower anal sphincter resting pressure, no difference regarding the detection of RAIR

TABLE 4 (Continued)

First author (year of publication)	Country	Study design	Motility testing	Anesthesia protocol	Sample size	Age (years)	Male, *n* (%)	Principal findings of each study
Mather (1992)[21]	England	Prospective study, randomization for anesthesia protocol	Perfused esophageal manometry	Allocated randomly to one of seven groups, each to receive differing end-tidal concentrations of isoflurane (0.6% to 1.8%, 0.2%-step). suxamethonium 1 mg kg^{-1} (dosage for crush induction) was given to facilitate tracheal intubation	72 HV (minor surgery under general anesthesia)	55 (42–65)	23 (32)	No conclusion can be drawn
Paskins (1984)[36]	England	Retrospective	Perfused anorectal manometry	*N* = 255 without sedation, *N* = 142 Iv. Ketamine	397 constipated children	ND	ND	No difference in the detection of RAIR
Pfeffekorn (2004)[44]	USA	Retrospective	Perfused anorectal manometry	No standardized protocol	77 constipated children	ND	45 (56)	No difference in the detection of RAIR
Roe (1962)[39]	Ireland	Prospective	Perfused intragastric manometry (1 lumen)	Iv. Suxamethonium (75 mg)	25 HV (minor surgery under general anesthesia)	ND	ND	Increase in intragastric pressure
Savilampi (2013)[14]	Sweden	Prospective study, randomization for anesthesia protocol, cross-over study	High-resolution esophageal manometry	Allocated randomly to either methylnaltrexone (0.15 mg/kg) or saline subcutaneously 30 min before the target-controlled infusion of remifentanil (3 ng/mL)	10 HV	25 (21–31)	7 (70)	Decrease in both the inspiratory and expiratory OGJ pressures. Administration of methylnaltrexone abolished the effect
Savilampi (2015)[15]	Sweden	Prospective study, randomization for anesthesia protocol, cross-over study	High-resolution esophageal manometry	Allocated randomly to receive a naloxone bolus injection of 6 μg/kg and a naloxone infusion of 0.1 μg/kg/min iv or an equal amount of saline, 5 min after administration of iv remifentanil with 3 increasing effect-site concentrations (T1 = 1, T2 = 2, and T3 = 3 ng/mL)	14 HV	27 (18–38)	7 (50)	Increase in the integrated relaxation pressure and decrease in the distal latency, dose–response
Sehhati (1980)[20]	Germany	Prospective	Perfused esophageal manometry (3 lumen)	2:1 N_2O:O_2 alone during 15 min then addition of 2% halothane or 2% enflurane	10 HV	ND	ND	Decrease in the LOS resting pressure
Shurizek (1989)[11]	Denmark	Prospective study, randomization for anesthesia protocol	Perfused antro-duodenal manometry (4 lumen)	Allocated randomly to receive Iv. Pethidine (20–60 mg) or Fentanyl (50–100 μg)	22 HV	39 (18–71)	7 (32)	Reduction in the duration of the interdigestive motility complex

(Continues)

TABLE 4 (Continued)

First author (year of publication)	Country	Study design	Motility testing	Anesthesia protocol	Sample size	Age (years)	Male, *n* (%)	Principal findings of each study
Shurizek (1989)[25]	Denmark	Prospective	Perfused antro-duodenal manometry (6 lumen)	Induction with Iv. thiopentone, pethidine (30–50 mg), pancuronium (0.75–1 mg), suxamethonium (75–100 mg). Maintained with halothane and 67% NO in O_2	11 patients undergoing orthopedic surgery	[22–46,49–56]	5 (46)	No conclusion can be drawn
Smith (1978)[37]	Scotland	Prospective	Perfused esophageal manometry (3 lumen)	Iv. suxamethonium (100 mg)	15 patients undergoing pyloroplasty and vagotomy for duodenal ulcer and 14 HV	ND	ND	No change in oesogastric pressure gradient
Spence (1967)[40]	Scotland	Prospective	Perfused intragastric manometry (1 lumen)	Iv. suxamethonium (100 mg)	20 HV (minor surgery under general anesthesia)	ND	ND	Increase in intragastric pressure
Su (2020)[9]	USA	Prospective for HV and retrospective for patients	High-resolution esophageal manometry	Conscious sedation with 5–10 mg midazolam and 100–200 μg fentanyl	12 HV (prospective) and 7 patients (retrospective)	31 (23–44)	3 (25)	Both the supine and upright integrated relaxation pressure and the supine distal contractile integral were increased. No difference in Chicago classification v3.0
Suganuma (2021)[42]	Japan	Prospective study, randomization for anesthesia protocol, cross-over study	High-resolution esophageal manometry	Iv. fentanyl 2 mg/kg, remifentanil 0.05–0.10 mg/kg/min, propofol target controlled infusion 3–5 mg/mL and rocuronium 0.8–1.0 mg/kg. Allocated randomly to receive randomly either neostigmine 2 mg with 1 mg of atropine, or 2 mg/kg sugammadex	19 HV (minor surgery under general anesthesia)	59 ± 10	0 (0)	No change in oesogastric pressure gradient
Thorn (2005)[12]	Sweden	Prospective	Dent-sleeve device (5 cm long)	Iv. infusion of remifentanil (0.2 μg/kg/min) during 20 min and followed by bolus dose of propofol (1 mg/kg)	10 HV	23 (21–25)	5 (50)	No effect on the LOS resting pressure nor on the oesogastric pressure gradient
Thorn (2006)[24]	Sweden	Prospective	Dent-sleeve device (5 cm long)	Propofol 0.5 mg/kg iv to facilitate placement of the catheter. After 10 min induction with 8% sevoflurane in combination with oxygen. After muscle relaxation by means of rocuronium (0.6 mg/kg iv.) they were intubated.	9 HV (minor surgery under general anesthesia)	44 (29–51)	3 (33)	Decrease in LOS resting pressure
Tran (2014)[31]	USA	Prospective	Perfused anorectal manometry	Iv. Propofol (1 mg/kg)	20 constipated children	4.2 (2–6)	14 (70)	Decrease in the anal sphincter resting pressure

TABLE 4 (Continued)

First author (year of publication)	Country	Study design	Motility testing	Anesthesia protocol	Sample size	Age (years)	Male, *n* (%)	Principal findings of each study
Turan (2010)[27]	USA	Prospective study, randomization for anesthesia protocol, cross-over study	Perfused esophageal manometry (4 lumen)	Randomly assigned to receive propofol or dexmedetomidine, target-controlled infusion. Propofol (aivoc): 1, 2, and 4 μg/mL; dexmedetomidine 0.6, 1.2, and 2.4 ng/mL ("low," "medium," and "high"). Anesthetised on 2 occasions 1-week apart.	11 HV	24 ± 4	8 (73)	Dose-dependent decrease in LOS resting pressure but the oesogastric pressure gradient was still preserved at high-dose sedation
Varandajulu (2017)[34]	USA	Prospective	Perfused sphincter of Oddi manometry (3 lumen)	Iv. Ketamine, no standardized protocol	30 patients with recurrent pancreatitis	48 (42–61)	20 (67)	No effect on sphincter of Oddi resting pressure nor on the results of sphincter of Oddi dysfunction classification
Wallden (2008)[19]	Sweden	Prospective	Gastric barostat	Iv. Remifentanil. The initial dose was 0.1 μg/kg/min, after 15 min the dose was increased to 0.2 μg/kg/ min and after a further 15 min the dose was increased to 0.3 μg/kg/min	9 HV	24 (19–31)	9 (100)	No conclusion can be drawn

Abbreviations: FLIP, functional lumen impedance planimetry; HV, healthy volunteers; iv: intravenous; LOS, lower esophageal sphincter; ND, not detailed; OGJ, oesogastric junction; RAIR, recto-anal inhibitory reflex.

of these drugs.[20] A second study using different alveolar concentrations of isoflurane showed that the median effective concentration to suppress spontaneous lower esophageal contractions was 1.27 (1.12–1.43)% and 1.31 (0.93–3.49)% to suppress provoked lower esophageal contractions.[21] These results were confirmed by two other studies in HVs children and adults[22,24] but not in another study in children.[23] These two studies also exhibited a concentration-dependent decrease in LOS resting pressure and consequently a decrease in oesogastric pressure gradient after the administration of both sevoflurane and enflurane.[22,24] However, it is of importance to underline that this effect was rather small in these studies: a positive oesogastric pressure gradient was preserved.[22,24] In addition, even if the dosage used those for daily practice, most of the inhalation anesthetics evaluated in these studies are no longer used in most countries, such as halothane and enflurane. All these studies did not assess the potential impact of inhaled anesthetics on final diagnosis according to Chicago classification.

One report evaluated the effect of halothane on antroduodenal motility, but as other anesthetics were used during a non-standardized protocol, no conclusion can be clearly drawn from this solely study.[25] Lastly, one prospective study investigated the effect of inhaled sevoflurane used to induce and maintain sedation on colonic motility ($N = 10$ patients).[26] No difference was reported in colonic manometry results (total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions) between recordings starting 4 h after anesthesia or after 24 h in most patients.

3.2.2 | Propofol

Propofol is an intravenous hypnotic drug used for the induction or maintenance of sedation and general anesthesia.[49] It acts by agonizing GABA-A receptors and has a hepatic metabolism. It has an onset of action of less than 1 min and an elimination half-life of around 3 h, with a volume of distribution between 0.20 and 0.79 L/kg. Its main undesirable effects are the induction of hypotension and a respiratory depressant effect.[49]

The effect of propofol on digestive motility was evaluated in the literature in nine studies to date. Although propofol was part of the anesthesia protocol in seven reports,[8,12,24,27,28,47,48] only four of these studies[8,12,27,28] were specifically designed to prospectively study its influence on esophageal motility. A report on 10 HVs found no difference in either the esophagogastric pressure gradient or LOS resting pressure before and after administration of propofol.[12] Even if low doses of propofol were used in this first study (light sedation, bolus dose of propofol of 1 mg/kg), these results were confirmed in a more recent study with a cross-over design with usual dose used in clinical practice (2 mg/kg).[8] A third study evaluated several ranges of dosing of propofol using a cross-over design in 11 HVs.[27] A significant dose-dependent decrease in LOS resting pressure was found (−7.4 [−1.6 to −13.2] mmHg lower with high-dose than low-dose sedation [$p < 0.01$]). However, the esophagogastric pressure gradient

was still preserved at high-dose sedation (propofol aivoc from 1 to 4 μg/mL). In this report, the administration of dexmedetomidine, an α-2 receptor agonist, elicited similar dose-dependent decrease in LOS resting pressure.[27] Lastly, another report found similar results with a low dose of propofol (0.3 mg/kg).[28] On the contrary, higher doses (0.9 mg/kg) were associated with an increase in LOS resting pressure in young HVs, but the esophagogastric pressure gradient remained unchanged.[28] All these studies did not assess the potential impact of propofol on final diagnosis according to Chicago classification. In addition, the effect of propofol on gastric tone measured using a barostat was assessed in 20 HVs in one study before the administration of morphine.[29] No effect of low dose of propofol on gastric tone was found in this study.

Propofol administration was also assessed in colonic and anorectal motility in four studies.[26,30–32] One prospective study investigated the effect of anesthesia protocols on colonic motility ($N = 10$ patients).[26] No difference was observed on colonic manometry results (total motility index, gastro-colonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions) between recordings starting 4 h after anesthesia or after 24 h in most patients. However, propofol administration was associated with ketamine use to induce and maintain sedation and so it was not the sole agent in this study. The impact of administration of propofol at conscious sedation level on anal canal measurements using anorectal manometry was evaluated in three prospective studies.[30–32] A group of 18 HVs adults (age range 19–28 years) exhibited lower anal sphincter resting pressure compared to baseline after the induction of conscious sedation (15 ± 2 vs. 44 ± 4 mmHg, $p < 0.001$), but no difference was found regarding the detection of the recto-anal inhibitory reflex (RAIR, the difference between the lowest anal pressure during balloon inflation and anal pressure at rest) nor the volume required to elicit it.[30] Similar results were found in two studies performed in 20 and 27 constipated children (excluding those with Hirschsprung's disease), with a significant reduction observed in the anal sphincter resting pressure after propofol administration ($p < 0.001$ in both studies).[31,32] The volume required to induce RAIR were also comparable before and after propofol sedation in both studies.[31,32] However, the internal anal sphincter minimum pressure during RAIR was significantly lower after propofol administration in the most recent study.[32]

3.2.3 | Thiomebuthal sodium

Thiopental is an intravenous hypnotic drug of the barbiturate family which is used to induce general anesthesia.[50,51] It acts by agonism of GABA-A receptors and undergoes hepatic metabolism. It has an onset of action of less than 1 min and an elimination half-life of around 11 h, with a volume of distribution of around 2 L/kg. Its main undesirable effects are the induction of hypotension and a respiratory depressant effect.[50,51]

Two studies used thiopental in literature,[25,33] but only one of these studies used a standardized anesthesia protocol. This latter study[33] prospectively investigated the effect of thiomebuthal sodium administration (general anesthesia dosage) on the results of anorectal manometry in 15 children without any gastrointestinal disease. Anal pressure at rest decreased significantly after thiomebuthal sodium administration in comparison to baseline ($p < 0.05$). The relaxation of the internal anal sphincter during RAIR was less pronounced under anesthesia with thiomebuthal sodium ($p < 0.05$) but could still be visualized. To our knowledge, no other study has investigated the effect of thiomebuthal on digestive motility.

3.2.4 | Ketamine

Ketamine is an intravenous drug that acts by antagonizing NMDA receptors and which plays a role in sedation and analgesia.[52,53] It can be used for induction of anesthesia as a hypnotic agent, with the advantage of having no hypotensive effects; and for maintenance, due to its analgesic properties and its effects in antagonizing the hyperanalgesia induced by opioids. It is metabolized in the liver, with an onset of action of around 3 min and an elimination half-life of 3 h.[52,53] Its main side-effects are possible agitation with a feeling of derealisation and hypersalivation.

The literature on the effects of ketamine on digestive motility remains scarce, with only four studies published to date. One study prospectively assessed the impact of ketamine administration as adjunctive sedation (20 mg dosage) on sphincter of Oddi motility during sphincter of Oddi manometry ($N = 30$ patients without prior intervention on the sphincter of Oddi).[34] No effect of ketamine administration on the sphincter of Oddi was found in this study, as well as no impact on the results of sphincter of Oddi dysfunction classification if evidenced. A second prospective study investigated the effect of anesthesia protocols on colonic motility ($N = 10$ patients).[26] No difference was observed in colonic manometry results (total motility index, gastrocolonic reflex, and spontaneous or bisacodyl-induced high amplitude propagating contractions) between recordings starting 4 h after anesthesia or after 24 h in most patients. However, ketamine was used to maintain sedation in association with propofol, with subsequent interpretation bias. Two other studies[35,36] investigated the effect of ketamine administration on the anal sphincter resting pressure and RAIR in children with constipation. The first[35] compared the results of anorectal manometry between two groups of constipated children ($N = 27$ who underwent intravenous ketamine administration at moderate dosage [1–2 mg/kg] and $N = 31$ age-matched). Symptomatic scores were more severe in the ketamine administration group. No difference was seen in anal resting pressure, but children from the ketamine administration group exhibited less pronounced relaxation of the IAS during RAIR ($p < 0.006$). However, this difference in RAIR was not confirmed by a second study[36] with a retrospective design ($N = 142$ intravenous or intramuscular ketamine administration at moderate dosage and $N = 255$ awaken).

3.3 | Part. 3: Neuromuscular-blocking agents

Neuromuscular blocking agents (NMBAs) paralyze skeletal muscles at the myoneural junction by blocking the binding of acetylcholine to the post-synaptic receptor. Several neuromuscular blockades are available, differing in their mechanism of action and their onset and duration of action. Suxamethonium belongs to the family of depolarising NMBAs that act by activating the actin–myosin complex and muscle contraction by opening the Na/Ca/K channel.[54] The onset of action is less than 1 min, with a duration of action of around 10 min. It is metabolized by plasma pseudocholinesterases. Because of its rapid onset of action, it is indicated when there is a risk of inhalation requiring a quick tracheal intubation. Other NMBAs belong to the family of non-depolarising NMBAs, which act by competitively antagonizing the Na/Ca/K channel. Non-depolarising NMBAs are classified into two groups:

- Isoquinoline derivatives: atracurium, cisatracurium, and mivacurium; plasma metabolism through Hofmann elimination (atracurium, cisatracurium) or plasmatic pseudocholinesterase (mivacurium).
- Steroid derivatives: rocuronium, vecuronium, and pancuronium; hepatic and renal metabolism.

Rocuronium can be used in different doses, altering its onset of action.[55] At higher doses, its onset of action is less than 1 min, making it the second molecule of choice for inhalation risks. The other molecules have an onset of action of around 3 min and a variable duration of action, generally ranging from 15 min (mivacurium) to 2 h (pancuronium).[56]

The effect of NMBAs on digestive motility has been poorly studied in literature, as only 11 studies are available to date. These agents were part of the anesthesia protocol in 10 reports,[22,24,25,37,41–43,46–48] but only four of these studies[37,41–43] were specifically designed to study their effects on esophageal motility, and different drugs were used in each study. A first report found that vecuronium administration did not change the oesogastric pressure gradient, but pancuronium infusion elicited an increase in oesogastric pressure gradient resulting from an increase of the LOS pressure rather than a decrease in intra-gastric pressure.[43] A second study did not report any change in oesogastric pressure gradient following the administration of suxamethonium,[37] with similar results in two other studies after the administration of rocuronium.[41,42] Moreover, the administration of atropine (muscarinic antagonist) and neostigmine (parasympathomimetic) or sugammadex (reversal of rocuronium NMBAs) following rocuronium infusion did not change the LOS resting pressure in one of these reports.[42] These studies did not assess the potential impact of NMBAs on final diagnosis according to Chicago classification.

The effect of suxamethonium administration on intragastric pressure was prospectively evaluated in three studies.[38–40] A rise in intragastric pressure following the administration of suxamethonium was exhibited in three out of 10 patients in one study, which was attributed to fasciculations of the abdominal muscles.[38] These results were confirmed in a larger sample of 25 HVs, which showed in most cases a minor effect of suxamethonium injection on intragastric pressure.[39] Moreover, another study including 20 HVs demonstrated similar results, with a decrease in intragastric pressure observed after the ending of fasciculations.[40] Lastly, a more recent study using the EndoFLIP® system to assess pyloric distensibility in gastroparetic patients found that suxamethonium administration was associated with decreased pyloric distensibility (OR: 3.9; 95% CI: 1.3–11.4; $p = 0.013$), but its retrospective design and the absence of a standardized anesthesia protocol brought limitations to the interpretation of its results.[6]

Lastly, only one study[44] assessed the effect of the administration of NMBAs on the detection of RAIR using anorectal manometry in 77 children with constipation (excluding those with Hirschsprung's disease). However, although the intravenous administration of neuromuscular-blocking agents (succinylcholine, mivacuronium, or rapacuronium) had no effect on the detection of RAIR, the design of the study did not allow a conclusion to be reached. This was a retrospective study, without standardization of the anesthesia protocol, and most patients received a combination of several anesthetic agents.

4 | CONCLUSION

The literature remains scarce regarding the impact of anesthetics on digestive motility. Most published studies have been of patients undergoing esophageal manometry. We found heterogeneity in both the dose and timing of administration of anesthetics among studies, which limited the interpretation of their results. Remifentanil analgesia was the most studied anesthetic drug in literature, showing a decrease in both distal latency and lower esophageal sphincter pressure after its administration but the impact on Chicago classification was not studied. Inhaled anesthetics administration elicited a decrease in lower esophageal sphincter pressure, but contradictory findings were shown on esophageal motility following propofol or NMBAs' administration. There is a need for further prospective studies performed with usual doses of anesthetics for daily practice to study the impact of anesthetics in non-esophageal motility studies.

AUTHOR CONTRIBUTIONS

Study conception and design: DR, TC, GG, CD. *Articles selection*: DR, CD. *Analysis of articles*: DR, CD. *Paper writing*: DR, TC, GG, CD.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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