Endoscopy International Open

Impact of Virtual Reality Distraction During Colonoscopy Compared to Intravenous Deep Sedation: Results of a Monocentric Randomized Controlled Trial

Anastasia Pavlidi, Lotfi Triki, Julien Mortier, Jacques Deviere, Arnaud Lemmers, Vincent Huberty, Patrice Forget, Mark Hannen, Caroline Quolin, Turgay Tuna, Daniel Blero, Marianna Arvanitakis.

Affiliations below.

Abstract:

Abstract

Background and aims: Colonoscopy is associated with discomfort that requires intravenous sedation (IVS). The aim of this randomized controlled trial (RCT) was to explore the feasibility of virtual reality distraction (VRD) for colonoscopy using two primary endpoints: cecal intubation rate and the rate of rescue with IVS.

Methods: Patients scheduled for elective colonoscopy with IVS were randomized in a 2:1 ratio in favor of VRD, with rescue IVS by propofol if needed. VRD involved the use of a device providing a visual and auditive experience similar to clinical hypnosis.

Results: Ninety patients were included (VRD:60, IVS: 30). Caecal intubation rate was similar in both groups (92.8% for VRD vs 100% for IVS, p=0.3). The rescue IVS in the VRD group was 63.6%. There was a decrease in median total dose of propofol per patient in the VRD group (1.15 mg/kg for VRD and 4.41 mg/kg for IVS, p<0.001) and in the subgroup of VRD patients who received IVS rescue (3.17 mg/kg for VRD and 4.41 mg/kg for IVS, p =0.003). The median level of pain was higher, and the median level of comfort was lower in the VRD group (respectively 3 vs 0, p <0.001 and 7 vs 10, p <0.001).

Conclusions: The RCT provides preliminary data to better understand the feasibility of VRD for colonoscopy . We have not identified differences in procedural outcomes compared to conventional IVS, nevertheless higher pain and lower comfort scores were reported.

Corresponding Author:
Prof. Marianna Arvanitakis, Université Libre de Bruxelles - Campus Erasme, Gastroenterology, Route de Lennik 808, 1070 Bruxelles, Belgium, marianna.arvanitaki@erasme.ulb.ac.be

Affiliations:
Anastasia Pavlidi, Université Libre de Bruxelles - Campus Erasme, Gastroenterology, Bruxelles, Belgium
Lotfi Triki, Université Libre de Bruxelles - Campus Erasme, Gastroenterology, Bruxelles, Belgium

Thieme

Julien Mortier, Université Libre de Bruxelles - Campus Erasme, Anesthesiology, Bruxelles, Belgium
[...]
Marianna Arvanitakis, Université Libre de Bruxelles - Campus Erasme, Gastroenterology, Bruxelles, Belgium

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Thieme

Impact of Virtual Reality Distraction During Colonoscopy Compared to Intravenous Deep Sedation: Results of a Monocentric Randomized Controlled Trial

Anastasia Pavlidi[1],* (MD), Lotfi Triki[1],*(MD), Julien Mortier[2](MD), Jacques Deviere[1](MD,PhD), Arnaud Lemmers[1](MD,PhD), Vincent Huberty[1](MD,PhD), Patrice Forget[3] (MD,PhD), Mark Hannen[4] (MD), Caroline Quoilin[5] (PhD), Turgay Tuna[2] (MD,PhD), Daniel Blero[6]**(MD,PhD), Marianna Arvanitakis[1]** (MD,PhD)

[1] *Department of Gastroenterology, Digestive Oncology and Hepatopancreatology, HUB Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium*

[2] *Department of Anesthesiology, HUB Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium*

[3] *Institute of Applied Health Sciences, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen; Department of Anaesthesia, NHS Grampian, Aberdeen, United Kingdom. Pain AND Opioids after Surgery (PANDOS) European Society of Anaesthesiology and Intensive Care (ESAIC) Research Group, Brussels, Belgium. IMAGINE UR UM 103, Montpellier University, Anesthesia Critical Care, Emergency and Pain Medicine Division, Nîmes University Hospital, 30900 Nîmes, France.*

[4]*Department of Anesthesiology, University of Aberdeen, United Kingdom*

[5] *European Organisation for Research and Treatment in Cancer (EORTC), Brussels, Belgium*

[6] *Department of Gastroenterology, CHR Namur, Namur, Belgium*

*Shared first authorship

**Shared last authorship

Corresponding author:
Marianna Arvanitakis
Marianna.arvanitaki@hubruxelles.be

Keywords: Virtual reality, sedation, colonoscopy

Manuscript Word count: 3514

Introduction

Colonoscopy plays a crucial role in colorectal cancer (CRC) screening due to its high diagnostic sensitivity and therapeutic potential for treating premalignant colorectal lesions [1, 2]. Guidelines from the American College of Gastroenterology recommend screening in average-risk individuals between the ages of 50 and 75 years and suggest screening in average-risk individuals between ages 45 and 49 years to reduce the incidence of advanced adenoma, CRC, and CRC-related mortality [3]. Nevertheless, according to the U.S. Preventive Services Task Force (UPSTF), in 2016, 26% of eligible adults in the United States had never been screened for CRC and, in 2018, 31% were not up to date with screening [4].

Colonoscopy is perceived as a painful and anxiety-generating experience associated with emotional discomfort and embarrassment, leading patients to be reluctant to undergo the procedure [5]. Reflex spasms caused by colonic stimulation and acute distention secondary to inflation are the main causes of pain during colonoscopy that require intravenous sedation (IVS) with propofol, either alone or in combination with benzodiazepines and narcotics [6].

Although propofol sedation is largely used for endoscopic procedures, there is considerable variation in IVS practice between different centers and countries [7, 8]. The main reason for this is the differing sociocultural backgrounds that influence the choices and attitudes of patients and endoscopists [9].

Furthermore, the use of sedation can be associated with adverse events (AE), particularly in older patients [8, 10, 11]. Also, in some countries, propofol may only be administered by an anesthesiologist, resulting in potentially higher costs for the patient and the community [7]. Finally, IVS during colonoscopy can prolong recovery-room stay, delay discharge, and increase total medical costs [12].

Therefore, it is imperative to find safe, easy-to-use, and cost-effective ways to relieve pain and anxiety for patients undergoing colonoscopy. Clinical hypnosis and virtual reality (VR) have demonstrated effects on pain and anxiety reduction when delivered during medical procedures [13, 14, 15, 16, 17]. Immersive VR technology can guide the patient through the same steps as those used when clinical hypnosis is induced through an interpersonal process [18, 19]. However, the efficacy of the clinical use of VR distraction (VRD) during endoscopic procedures is still not well documented.

A VRD module, the Aqua module of the Oncomfort device (Oncomfort SA, Wavre, Belgium) was designed for management of pain and anxiety related to medical and surgical procedures. The purpose of this pilot study was to explore efficacy, safety, and pharmacoeconomic outcomes in patients undergoing colonoscopy with either VRD using the Aqua module or standard-of-care IVS with propofol.

Methods

Study center

This randomized controlled trial (RCT) was conducted at Erasme University Hospital in Brussels, Belgium, a teaching hospital associated with Université Libre de Brussels, between the 25th of June, 2020 and the 21st of December, 2021. The protocol was approved by the Ethics Committee of the study center (P2020/250) on the 27/05/2020 and was registered at ClinicalTrials.gov (NCT04465383). Written, informed consent was obtained from all subjects before their inclusion in the study and the trial has been performed in accordance with the principles of the Helsinki Declaration. This report is written in accordance with the CONSORT recommendations.

Study population

The study population included male and female adult patients (≥ 18 years old) with an indication for screening or diagnostic colonoscopy under conventional IVS (propofol), scheduled in the outpatient setting in the Day Clinic. Exclusion criteria can be found in Supplementary Table 1.

Randomization

A prospective, randomized, controlled design was used. Participants were proposed for inclusion during the pre-procedural consultation with the anesthesiologist and, if they were willing to participate in the study, they were randomly assigned to one of two arms via computer-generated randomization concealed using opaque envelopes:

1. Group A- Experimental arm: VRD. Administration of rescue IVS (propofol) if needed upon patient's request (VRD+IVS group).

2. Group B - Control arm: conventional IVS (propofol).

Random assignment to the study arms was done on a 2:1 basis (2:1 in favor of the experimental arm). This was decided upon to provide calibration of the results observed in the control arm as well as to allow an increased sample size in the experimental arm, providing more information about VRD. Participants were informed of their group allocation directly before the initiation of the colonoscopy procedure.

DS protocol

The VRD session consisted of VR software (Aqua module Version 3.0 or subsequent version, Oncomfort SA, Wavre, Belgium) including a clinical hypnosis script. Patients in the intervention group underwent a 30-minute VRD program through the device. The duration of the session could be adapted according to the duration of the procedure through the device controller.

For the VR protocol, the patient was asked to lay on their left side and the medical device was installed as a mask, projecting an underwater experience while playing a hypnotic script designed to induce a change in state of consciousness, increasing parasympathetic system tone and relaxation response, and reducing the perception of painful stimuli (Figure 1).

In case of patient complaint and at the discretion of the anesthesiologist, rescue propofol sedation could be administered to the patient at any time (VRD + IVS). Rescue propofol sedation was administered to the patient in case of discomfort and/or patient complaint according to the score on the Behavioral Pain Scale (BPS). Patients with a BPS score more than 3 were eligible for rescue propofol sedation. Propofol was administered with a target-controlled infusion, at a starting effect dose concentration (Ce) of 1 μg/mL to 6 μg/mL, adapted to weight (Marsh model) and incrementally increased by 0.5 μg/mL if needed, depending on the patient's reaction. Practically, this corresponds to a starting dose of 20-30 mg at the beginning of procedure with additional doses of 10 to 20 mg administered during the procedure. Doses were adapted according to the level of comfort and needs of the patient. Recorded parameters throughout the procedure included: peripheral oxygen saturation, mean arterial pressure (MAP), and continuous electrocardiogram.

Conventional IVS protocol

The procedure was performed under propofol sedation, with a target-controlled infusion at a starting effect-site concentration (Ce) of 1 μg/mL to 6 μg/mL depending on the patient's reaction and incrementally increased (by 0.5 μg/ml). Doses were adapted according to the level of comfort and patient needs. This sedation corresponds to ASA level of sedation and analgesia of 3-4 (moderate/conscious- to deep sedation/analgesia). The use of other drugs, such as midazolam, ketamine, or fentanyl, was not prohibited but was avoided as much as possible. Recorded parameters throughout the procedure were not different to the VRD

4

group. Patients discharge from the recovery room was based on the Aldrete Score System (≥9/10) [20].

Study endpoints

In the first stage, the primary objective of this study was to evaluate the feasibility of using VRD in colonoscopy. To facilitate this evaluation focusing on two primary endpoints, cecal intubation rate and the rate of rescue sedation requirement in the VRD group, were used. Secondary endpoints are listed in Table 1.

Sample size

The sample size of the study was computed based on expectations for the experimental arm at final analysis. Randomization (2:1 in favor of the experimental arm) was aimed mostly at providing calibration of the results observed in the control arm. However, hypothesis testing was planned for selected secondary efficacy endpoints, even though no power calculations had been done for these tests. In order to demonstrate that the caecal intubation rate in the experimental arm was ≥90%, 107 evaluable patients would be needed in the experimental arm, in order for the one-sided 95% exact confidence interval for the observed caecal intubation rate to be entirely above 90% (considering an expected observed rate of 95%, or 102/107 patients with cecal intubation). Assuming the loss of data or follow-up in the experimental arm of 10%, a total of 118 patients needed to be randomized to the experimental arm. Given the 2:1 randomization, the initial calculated total number of patients needed for the study was 177. Both co-primary endpoints were considered to assess study positivity; for this reason, no multiple-testing corrections were needed for calculation of the confidence intervals and sample sizes.

Interim analysis

An interim analysis was planned when 25% of the evaluable patients had been recruited to the experimental arm (27 evaluable patients). If 21 or fewer of the 27 patients had successfully undergone cecal intubation (i.e., a cecal intubation rate of 78%), the probability that the true rate would have been at least 90% was below 5%, and, therefore, continuation of the trial would be deemed futile. Likewise, if 19 or more of the 27 evaluable patients had received rescue sedation (a rate of 70%), the probability that the true rate would have been at most 50% was below 5%, and futility could be declared. Both futility boundaries were non-binding, which meant that definitive decisions about stopping the trial were left to the investigator's discretion and had no formal regulatory implications.

Analysis sequence

The interim analysis and the final analysis of the co-primary endpoints was conducted in the per-protocol population, defined as patients who did not request rescue IVS before introduction of the colonoscopy (in the experimental arm) and did not withdraw their consent (in both arms).

Thereafter, the study was initially divided into three stages, with randomization (2:1) maintained throughout. In the first stage, accrual was halted when about 45 patients had been randomized, at least 27 of whom being evaluable patients randomized to the experimental arm. A non-binding futility analysis was planned for the primary outcome. In the second stage, accrual was halted when about 90 patients had been randomized. A non-binding futility analysis was planned for the primary outcome. At the end of the recruitment of Stage 1 and 2, an analysis of the secondary outcomes would also be made. The data obtained until that stage was consistent with statistical power. Adding to this, the study took place during the pandemic which complicated recruitment and organization of the study. Thereafter, the study did not

6

continue to the planned final accrual of 177 patients (118 to experimental and 59 to control arm, respectively) and recruitment was completed at phase 2.

Statistical Analysis

The analysis was applied using R-studio software. This consisted of a per-protocol analysis with no replacement of missing data. Qualitative data are described by frequencies and percentages. Normally distributed quantitative data are described by means and standard deviations. We estimated the probability density of the data using violin plots to see if our data were normally distributed. Non-normally distributed data are described by the median, first and third quartile values. Chi-squared tests were used to compare frequencies and rates between groups. In cases where the assumptions of the chi-squared test were violated, particularly when the expected values were lower than 5, Fisher's exact test was used as an alternative.. A Student's t-test was used to determine whether there were any significant differences between the means of normally distributed data between the two groups. Alternatively, the Mann-Whitney-Wilcoxon test was used to compare asymmetrical distributions. The level of significance was taken at 5% throughout all analysis.

Results

A total of 109 patients were initially screened and were consented for the study, of whom 19 were excluded (withdrawal because of stress, claustrophobia, and preference for IVS). Consequently, a total of 90 patients entered the study and were randomized between the two colonoscopy arms on a 2:1 basis: 60 in the VRD group, 30 in the IVS propofol group (Figure 2). Five patients did not undergo colonoscopy and were excluded. Thus, a total of 85 patients underwent colonoscopy (28 IVS, 57 VRD) and data for these procedures were entered into the final statistical analyses. No significant differences were observed between the groups

7

regarding demographic factors. Demographic details of the two groups are presented in table 2.

Primary and secondary endpoints

Results for primary and secondary endpoints are shown in Table 3. Cecal intubation rate were 92.8% in the VRD group vs 100% in the IVS group (p= 0.365). The rescue sedation rate was 63.6% in the VRD group (38/60 patients). There was a reduction in the median total dose of propofol (mg/kg) per patient: 73.9% reduction in the VRD group as compared to the IVS group (1.15 vs 4.41 mg/kg, p<0.001) and in the subgroup of VRD patients who received IVS rescue (3.17 mg/kg for DS and 4.41 mg/kg for IVS, P =0.003), as well as a shorter median duration of sedation in the VRD group (6 vs 20.5 [min], p <0.001).

There was no difference between the groups regarding other colonoscopy parameters such as adenoma detection rate, biopsies performed, the need to change position, and procedure duration. A higher rate of patients required abdominal compressions during colonoscopy in the VRD group compared to the IVS group (75% vs 53%, p = 0.367). Concerning the impact on hospital flow, patients in the VRD arm stayed longer in the procedure room compared to IVS arm (median time 46.5 vs 41.5 [min], p = 0.031) but stayed for a shorter time in the recovery room (median time 39.5 vs 54 [min], p = 0.020) with no difference in the total duration of stay in the hospital.

The reported median level of pain during colonoscopy was higher in the VRD group as compared to the IVS group (3 vs 0, p <0.001) and the median level of comfort during colonoscopy was lower in the VRDVRD group (7 vs 10, p <0.001) (Table 3).

Regarding the healthcare professionals' (HCPs) experience, there was an overall lower satisfaction level for both anaesthesiologists and endoscopists in the VRD group, as well as a higher level of stress. The anesthesiologists' evaluation was correlated with patient pain (r = -

8

0.44, p=0.017) and the gastroenterologists' evaluation was correlated with the number of manipulations (r = -0.35, p=0.04).

Regarding physiological measures, there was no difference between the groups regarding oxygen saturation. There was a higher MAP in the VRD group compared to the IVS group. Four AEs occurred in four different patients, two in the IVS group (bradycardia, hypotension) and two in the VRD group (tiredness, hand tremors).

Discussion

This RCT is the first, to our knowledge, to investigate feasibility of colonoscopy with VRD without showing differences in terms of rate of cecal intubation compared to standard IVS with propofol. Even though more than half of the patients in VRD arm needed propofol rescue IVS, we found that the total dose of propofol was lower compared to the IVS arm, suggesting that pharmacological sedation can be minimized or even eliminated for some patients. Nevertheless, it must be noted that reported pain levels were higher in the VDR group, thus suggesting that the best alternative method to sedation is still to be determined, especially regarding the diversity of patient experience.

One of the advantages of VRD is the reduction in hemodynamic AEs such as arterial hypotension, which requires increased hemodynamic monitoring and a longer stay in the recovery room. In a retrospective study, it was reported that sedation with propofol could lead to up to 30% rates of arterial hypotension [21]. Compared to this study, there was no occurrence of arterial hypotension in the VRD group, even with rescue IVS, whereas there was one patient in the IVS group who presented with hypotension.

Visual distraction during colonoscopy is an effective way for improving patient pain, with higher rates of willingness to repeat the procedure, suggesting that audiovisual diversion techniques, such as VR, can improve patient acceptance and satisfaction of colonoscopy [6, 12,

22, 23, 24]. Table 4 summarizes the results of all studies that have been conducted using VR during gastrointestinal endoscopic procedures in adult populations. Three previous RCTs comparing colonoscopy without sedation and colonoscopy with some type of VRD, observed lower pain and anxiety scores in the intervention groups [25, 26, 27]. A small RCT compared colonoscopy under conscious sedation (midazolam) to colonoscopy with VRD, showing comparable performance measures (duration and completion of colonoscopy) [23]. Finally, a recent cohort study assessing the use of VR in patients undergoing colonoscopy without sedation, showed that 96.3% completed their colonoscopy without requesting or receiving any sedative medication [24].

In contrast to these other studies, this study showed that the level of pain during colonoscopy was significantly higher in the VRD group compared to the IVS group but the level of pain after the procedure was similar between the two groups. There could be several explanations for why VRD did not significantly reduce the level of pain. First, this could be correlated with patient anxiety due to their concern about the VRD procedure which is a first-time experience and probably perceived as having a limited antalgic effect due to of lack of public awareness on this type of alternative modality [29]. Perin et al. demonstrated that an immersive 3D-supported informed consent improved patient comprehension of their condition without increasing anxiety [29]. Therefore, such standard pre-procedural three-dimensional reconstructions could be applied in our protocol, offering an immersive informed consent procedure prior to undergoing colonoscopy and thus acting as a psychological form of reassurance regarding the procedure [30]. Another hypothesis that could explain the higher levels of pain observed in this study is the increased number of abdominal compressions needed during colonoscopy in the VRD group. This could provoke a more painful and less comfortable experience for the patient, as well as distracting them from the VR experience

and decreasing its effect. In addition, this could be correlated to the higher level of stress of the HCPs, both gastroenterologists and anesthesiologists, since the patient is conscious during the procedure and can still interact with the HCP team. The current study could not identify any predictive actors of response to VRD due to the small sample size. Finally, there may be discrepancies between reported level of pain (depending on consciousness level), and patient experience.

Compared with sedation modalities, VRD has potential advantages. First, VRD is standardized and does not depend on the skill or availability of the clinician compared to IVS which needs a trained HCP who is responsible for maintenance of sedation and patient monitoring while using IVS. This could eliminate the need for a clinician's physical presence and increase the capacity for reaching a greater number of patients who could benefit from VRD. Also, this could be useful for patients in rural areas and underserved regions [24]. In addition, without IVS, patients can return to work and drive almost immediately post-procedure, improving patient satisfaction levels. VRD during colonoscopy could also reduce health care costs compared the use of IVS, especially when an anesthesiologist is required. Comparatively, VRD equipment is a one-time buy and dedicated software subscriptions are becoming more affordable with increasing use of the technology [28]. Another potential benefit of VRD is its lower environmental impact as it consists of a reusable machine with which a significant reduction of the total dose of propofol was needed compared to IVS. Interestingly, it has been shown that propofol represents 45% of all drug-related waste in hospitals since the remaining propofol after each use cannot be stored [31]. Finally, the deployment of non-anesthesia sedation is crucial after consideration of the risks of over-sedation and related AEs. Consequently, VRD could be more appropriately used in patients who are at increased risk for AEs during IVS. High risk factors for AEs during endoscopy procedures such as male sex, ASA

11

class of 3 or higher, and increased body mass index[10] could be used for early identification of these complex cases for whom DS could be proposed.

Limitations

This study has several weaknesses which should be taken into consideration when interpreting the results. First, the small sample size, as well as the fact that it is a monocentric study, means that there is a possibility that our results may not be reproducible, and the study power may be overestimated, especially regarding ceacal intubation rate. Additionally, other quantitative parameters such as time to cecal intubation were not reported. Second, this study had some real-life issues because of the pandemic with difficulties in recruitment and organization. Third, all gastroenterologists involved in the study were trained to perform their examinations with IVS, which could lead to involuntary painful scope handling. Moreover, the study took place in an academic hospital with a high total number of HCPs participating in the study, each one with a different background. A fourth limitation is the selection process of the rescue sedation group. Indeed, the BPS score was not strictly respected and applied, therefore, the selection process was not solely based on objective criteria, but mostly on the anesthesiologist's professional experience and confidence. Moreover, the use of additional drugs during the anesthesia were not reported. A fifth limitation is that the anesthesiologists were not blinded to patient assignment and could potentially introduce bias to outcomes.

Conclusions

In conclusion, this is the first RCT to explore VRD, with optional IVS when needed, for colonoscopy. Despite similar procedure outcomes compared to conventional IVS, VRD has a less favourable pain and comfort profile. Furthermore, the group of patients who could benefit the most from non-sedative alternative modalities is still to be defined. Further developments for alternative non-sedative modalities providing satisfactory management of

12

colonoscopy-related pain and discomfort while assuring high quality procedures could help in

increasing screening rates for CRC.

Tables:

TABLE 1. Secondary endpoints

1	To compare the use of sedation medication in both arms: Average (per patient) total doses of sedation medication per arm
2	To compare the performance of colonoscopy in both arms: Adenoma detection rates, total duration of colonoscopy, total duration of sedation, total length of stay in the procedure room, total length of stay in the recovery room, total length of stay in the hospital
3	To assess the difficulty or ease of the procedure in both arms: Number of abdominal compressions and the need for patient position changes
4	To compare the patient's experience in both arms: Pain by Visual Analogue Scale (VAS 0 to 10), anxiety by Visual Analogue Scale (VAS 0 to 10), comfort by Visual Analogue Scale (VAS 0 to 10), preferred type of sedation, recall of the procedure , willingness to repeat the same procedure, AE rates
5	To assess gastroenterologists' and anesthesiologists' satisfaction in both arms: Measure of satisfaction of perceived facilitation or impediment of the procedure by digital sedation as measured by Likert scale (0 to 5)
6	To assess gastroenterologists' and anesthesiologists' stress in both arms: Measure of stress by Visual Analogue Scale (VAS 0 to 10)
7	To compare physiologic measures in both arms: Oxygen saturation (minimal observed during procedure) and MBP (minimal/maximal values)

VAS: Visual Analogue Scale, MBP: mean blood pressure, AE: adverse events

TABLE 2. Demographic characteristics of the study population

Variable	VRD Group (n=57)	IVS Group (n=28)	Total (n=85)
Age, yr, mean (SD)	55.4 (13.5)	55.7 (16.3)	55.5 (14.4)
Male Sex, no. (%)	23 (40.4)	17 (60.7)	40 (47.1)
Height, cm, mean (SD)	168.2 (8.7)	172.8 (9.3)	169.8 (9.1)
Weight, kg, mean (SD)	75.3 (13.7)	74.4 (14.1)	75.0 (13.8)
BMI, mean (SD)	26.6 (4.9)	24.8 (4.0)	26.1 (4.7)
Presence of significant medical comorbidities, no. (%)	40 (70.1)	16 (57.1)	56 (65.9)
History of sleep apnea, no. (%)	8 (14.0)	2 (7.1)	10 (11.8)
Previous colonoscopy, no. (%)	39 (68.4)	20 (71.4)	59 (69.4)

VRD : Virtual reality distraction IVS: Intravenous sedation, yr: year, SD: Standard deviation, cm: centimeter, kg: kilogram

TABLE 3. Results of primary and secondary endpoints

Variable	VRD Group	IVS Group	P value
Primary endpoints			
Caecal intubation rate, no./total no. (%)	53/57 (92.8)	28/28 (100)	0.365
Rate of rescue sedation, no./total no. (%)	38/60 (63.6)	-	-
Secondary endpoint: Amount of sedation			
Total dose of sedation (mg/kg) per patient, median (IQR)	1.15 (0 – 4.01)	4.41 (3.58 – 6.83)	<0.001
Total duration of sedation in min, median (IQR)	6 (0 – 19.5)	20.5 (15.25 – 29.75)	<0.001
Secondary endpoint: Colonoscopy performance measures			
Adenoma detection rate, %	44.6	46.4	1
Biopsies taken, %	60.0	60.7	1
Need to change position rate, %	19.6	10.7	0.367
Need for abdominal compressions, %	75	53	0.367
Total procedure duration in min, median (IQR)	22 (16.7 – 34)	20.5 (15 – 28.7)	0.599
Secondary endpoint: Hospital flow			
Total length of stay in procedure room in min, median (IQR)	46.5 (40.7 – 58.5)	41.5 (35 – 50.5)	0.031
Total length of stay in recovery room in min, median (SD)	39.5 (21.4)	54 (20.2)	0.020
Total length of hospital stay in min, median (IQR)	200 (139 – 259)	184 (150 – 216)	0.500

Secondary endpoint: Patient experience during the procedure			
Anxiety, VAS scale Median (IQR) **(0= not at all anxious, 10=extremely anxious)**	3 (1-5)	2 (1-3.25)	0.115
Comfort, VAS scale, Median (IQR) **(0= not at all comfortable, 10=extremely comfortable)**	7 (5-8)	10 (9-10)	<0.001
Pain, VAS scale, Median (IQR) **(0=not at all painful, 10=extremely painful)**	3 (2-5)	0 (0-0)	<0.0001
Capacity of recalling the procedure, Likert scale, Median (IQR) **(0 = negative memory of the experience, 5 = positive memory)**	4 (3-5)	5 (4.7-5)	<0.0001
AEs (number)	2:weakness,hands tremor	2: bradycardia, hypotension	
Secondary endpoint: HCP Experience			
Evaluation of anesthesiologist, Likert Scale, Median (IQR) **(0 = not at all satisfied, 5 = totally satisfied)**	3 (2-5)	5 (5-5)	<0.001
Evaluation of gastroenterologist, Likert Scale, Median (IQR) **(0 = not at all satisfied, 5 = totally**	4 (3.7-5)	5 (5-5)	0.010

satisfied)			
Level of stress of anesthesiologist, VAS scale, Median (IQR) **(0= not at all stressed, 10= totally stressed)**	3 (1-5)	0 (0-1)	<0.001
Level of stress of gastroenterologist, VAS scale, Median (IQR) **(0= not at all stressed, 10= totally stressed)**	2 (0-3)	0.5 (0-1)	<0.001
Secondary endpoint: physiologic measures			
Oxygen saturation, % (median minimal value observed during procedure, IQR)	97 (95-99)	97 (96-99)	0.736
MAP, mmHg **(median minimal and maximal value observed during procedure, IQR)**	Minimal value= 87 (75-103) Maximal value= 111 (96-123)	Minimal value= 75 (68-82) Maximal value= 97 (83-113)	<0.001 0.003
Heart rate, beats per minute **(mean minimal and maximal value observed during procedure, SD)**	Minimal value= 66.7 (12.2) Maximal value = 86 (14.2)	Minimal value= 61.7 (10.3) Maximal value = 77 (13.1)	0.079 0.010

AE: Adverse event, VRD: Virtual Reality Distraction, HCP: Healthcare professional, IVS: Intravenous sedation, MAP: Mean arterial pressure, VAS: Visual analogue scale, mg: milligram, kg: kilogram, IQR: Interquartile range, Q1-Q3 values, SD: Standard Deviation

TABLE 4. Results of studies using VR during gastrointestinal endoscopic procedures in adult populations

Author (year)	Country	No of patients (Intervention group/ control group if applicable) Study type	Procedure type	Device used	Primary outcomes
Lee (2004) (31)	China	52/53 RCT	Colonoscopy under propofol	Eyetrek system with earphones (Olympus,Japan)	Significantly lower dose of propofol in intervention group (0.81 mg/kg +/ 0.49 vs 1.18 mg/kg +/- 0.60) (p <0.01).
Umezawa (2015) (26)	Japan	28/29 RCT	Colonoscopy without sedation	Head-mounted display (MOVERIO EPSON® ; SEIKO EPSON CORPORATION , Japan)	No significant difference in anxiety score between groups (median scores, 20 vs 24). Lower pain score in intervention group but not significantly different (median scores, 24.5 vs 42). Significantly higher median post-procedural satisfaction levels (median scores, 89 vs 72, p= 0.04).
Veldhuijzen (2020) (23)	Netherlands	10/9 RCT	Colonoscopy under conscious sedation with midazolam and/or alfentanyl	Samsung Gear VR (Consumer Edition– SM-R322, combined with Galaxy S7, Korea)	Comparable values concerning: time to reach the cecum (median 10.48 minutes in the control group, versus 6.83 minutes in the intervention group) time to complete procedure (median 21.20 minutes vs 22.60 minutes) completed colonoscopies (100 % versus 90%)

					initial intravenous bolus of sedatives and analgesics, i.e., dose of midazolam (median, 2.5mg in both groups), dose of alfentanyl (median, 0.25mg in both groups).
Karaveli Çakır (2021) (27)	Turkey	30/30 RCT	Colonoscopy without sedation	Cardboard Super Flex Goggles	No significant difference between pre- and post-operative state anxiety score between both groups but significant difference found between anxiety scores (p <.000) and pain scores (p<.03) during the procedure in favor of the intervention group.
Friedman (2021) (24)	USA	27 Cohort prospective study	Colonoscopy with pharmacological rescue if needed	Samsung (Ridgefield Park, New Jersey, United States) Gear VR Oculus headset	96.3% (26/27) completed their colonoscopy without requesting or receiving any sedative medication.
Liu (2022) (25)	China	58/59 RCT	Colonoscopy without sedation	Head-mounted VR display (Nibiru 3.50.005, Nanjing, China) and wristband (Empatica, Milan, Italy)	The median (IQR) pain scores were 7 (6–8) and 5 (4–6) in the control and intervention groups, respectively (p<0.001).
Boonreunya (2022) (33)	Thailand	32/32 RCT	Upper GI endoscopy with topical anesthesia	Oculus GO (Standalone VR headset)	No statistical difference in pain during esophageal intubation between the groups (2.7 ± 2.4 in the intervention group vs 2.3 ± 2.3, p=0.751).

RCT: Randomized controlled trial, mg: milligram, kg: kilogram, VR: virtual reality, IQR: interquartile range, GI: gastro-intestinal

Figure legends

Figure 1. The Oncomfort device for virtual reality distraction.

Figure 2. Study Flowchart. VRD: Virtual Reality Distraction, IVS: Intravenous sedation.

References

1.   Dekker E, Rex DK. Advances in CRC Prevention: Screening and Surveillance. Gastroenterology 2018;154:1970-84. DOI: https://doi.org/10.1053/j.gastro.2018.01.069.

2.   Chan MTV, Wu WKK, Tang RSY. Optimizing depth of sedation for colonoscopy. Can J Anesth 2015;62:1143-8. DOI: https://doi.org/10.1007/s12630-015-0462-4.

3.   Shaukat A, Kahi CJ, Burke CA, et al. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol 2021;116:458-79. DOI: https://doi.org/10.14309/ajg.0000000000001122.

4.   U.S. Preventive Services Task Force. Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 2008;149:627-37. DOI: https://doi.org/10.7326/0003-4819-149-9-200811040-00243.

5.   Lauriola M, Tomai M, Palma R, et al. Intolerance of Uncertainty and Anxiety-Related Dispositions Predict Pain During Upper Endoscopy. Front Psychol 2019;10:1112. DOI: https://doi.org/10.3389/fpsyg.2019.01112.

6.   Zhang YY, Vimala R, Chui PL, et al. Effect of visual distraction on pain in adults undergoing colonoscopy: a meta-analysis. Surg Endosc 2023;37:2633-43. DOI: https://doi.org/10.1007/s00464-022-09724-7.

7.   Wernli KJ, Brenner AT, Rutter CM, et al. Risks Associated With Anesthesia Services During Colonoscopy. Gastroenterology 2016;150:888-94. DOI: https://doi.org/10.1053/j.gastro.2015.12.018.

8.   Macken E, Dongen SV, Francque S, et al. Parameters influencing the quality of colonoscopy in Belgium: a critical evaluation. Acta Gastroenterol Belg 2018; 81:29-38. No DOI.

9.   Shamseddine A, Chehade L, Al Mahmasani L, et al. Colorectal Cancer Screening in the

Middle East: What, Why, Who, When, and How? Am Soc Clin Oncol Educ Book 2023;43:e390520. DOI: https://doi.org/10.1200/edbk_390520.

10.   Coté GA, Hovis RM, Ansstas MA, et al. Incidence of Sedation-Related Complications With Propofol Use During Advanced Endoscopic Procedures. Clin Gastroenterol Hepatol 2010;8:137-42. DOI: https://doi.org/10.1016/j.cgh.2009.07.008.

11.   Kollmann CM, Schmiegel W, Brechmann T. Gastrointestinal endoscopy under sedation is associated with pneumonia in older inpatients—results of a retrospective case-control study. United European Gastroenterol J 2018;6:382-90. DOI: https://doi.org/10.1177/2050640617735059.

12.   Elkins G, White J, Patel P, et al. Hypnosis to Manage Anxiety and Pain Associated with Colonoscopy for Colorectal Cancer Screening: Case Studies and Possible Benefits. Int J Clin Exp Hypn 2006;54:416-31. DOI: https://doi.org/10.1080/00207140600856780.

13.   Rousseaux F, Dardenne N, Massion PB, et al. Virtual reality and hypnosis for anxiety and pain management in intensive care units: A prospective randomised trial among cardiac surgery patients. Eur J Anaesthesiol 2022;39:58-66. DOI: https://doi.org/10.1097/eja.0000000000001633.

14.   Faruki AA, Nguyen TB, Gasangwa DV, et al. Virtual reality immersion compared to monitored anesthesia care for hand surgery: A randomized controlled trial. PLOS ONE 2022;17:e0272030. DOI: https://doi.org/10.1371/journal.pone.0272030.

15.   Moon J, Shin J, Chung J, et al. Virtual Reality Distraction during Endoscopic Urologic Surgery under Spinal Anesthesia: A Randomized Controlled Trial. J Clin Med 2018;8:2. DOI: https://doi.org/10.3390/jcm8010002.

16.   Tefikow S, Barth J, Maichrowitz S, et al. Efficacy of hypnosis in adults undergoing surgery or medical procedures: A meta-analysis of randomized controlled trials. Clin Psychol

Rev 2013;33:623-36. DOI: https://doi.org/10.1016/j.cpr.2013.03.005.

17.   Cornelis FH, Monard E, Moulin MA, et al. Sedation and analgesia in interventional

radiology: Where do we stand, where are we heading and why does it matter? Diagn Interv

Imaging 2019;100:753-62. DOI: https://doi.org/10.1016/j.diii.2019.10.002.

18.   Askay SW, Patterson DR, Sharar SR. Virtual reality hypnosis. Contemp Hypn

2009;26:40-7. DOI: https://doi.org/10.1002/ch.371.

19.   Rousseaux F, Bicego A, Ledoux D, et al. Hypnosis Associated with 3D Immersive

Virtual Reality Technology in the Management of Pain: A Review of the Literature. J Pain Res

2020;13:1129-38. DOI: https://doi.org/10.2147/jpr.s231737.

20. Fang L, Wang Q, Xu Y. Postoperative Discharge Scoring Criteria After Outpatient

Anesthesia: A Review of the Literature. erianesth Nurse 2023; 38(4):642-649.e1.

 doi: 10.1016/j.jopan.2022.11.008

21.   Sneyd JR, Absalom AR, Barends CRM, et al. Hypotension during propofol sedation for

colonoscopy: a retrospective exploratory analysis and meta-analysis. Br J Anaesth

2022;128:610-22. DOI: https://doi.org/10.1016/j.bja.2021.10.044.

22.   Xiaolian J, Xiaolin L, Lan ZH. Effects of Visual and Audiovisual Distraction on Pain and

Anxiety Among Patients Undergoing Colonoscopy. Gastroenterol Nurs 2015;38:55-61. DOI:

https://doi.org/10.1097/sga.0000000000000089.

23.   Veldhuijzen G, Klaassen NJM, Van Wezel RJA, et al. Virtual reality distraction for

patients to relieve pain and discomfort during colonoscopy. Endosc Int Open 2020;08:E959–

66. DOI: https://doi.org/10.1055/a-1178-9289.

24.   Friedman M, Rand K, Patel T, et al. A pilot study of virtual reality as an alternative to

pharmacological sedation during colonoscopy. Endosc Int Open 2021;09:E343-7. DOI:

https://doi.org/10.1055/a-1339-0724.

24

25.   Liu Q, Zang Y, Zang W, et al. Implementation of virtual reality technology to decrease patients' pain and nervousness during colonoscopies: a prospective randomised controlled single-blinded trial. Clin Med 2022;22:237-40. DOI: https://doi.org/10.7861/clinmed.2022-0001.

26.   Umezawa S, Higurashi T, Uchiyama S, et al. Visual distraction alone for the improvement of colonoscopy-related pain and satisfaction. World J Gastroenterol 2015;21:4707-14. DOI: https://doi.org/10.3748/wjg.v21.i15.4707.

27.   Karaveli Cakir S, Evirgen S. The Effect of Virtual Reality on Pain and Anxiety During Colonoscopy: A Randomized Controlled Trial. Turk J Gastroenterol 2021;32:451-7. DOI: https://doi.org/10.5152/tjg.2021.191081.

28.   Găină MA, Szalontay AS, Ștefănescu G, et al. State-of-the-Art Review on Immersive Virtual Reality Interventions for Colonoscopy-Induced Anxiety and Pain. J Clin Med 2022;11:1670. DOI: https://doi.org/10.3390/jcm11061670.

29.   Perin A, Galbiati TF, Ayadi R, et al. Informed consent through 3D virtual reality: a randomized clinical trial. Acta Neurochir 2021;163:301-8. DOI: https://doi.org/10.1007/s00701-020-04303-y.

30.   Hoffman HG, Richards T, Coda B, et al. The Illusion of Presence in Immersive Virtual Reality during an fMRI Brain Scan. Cyberpsychol Behav 2003;6:127-31. DOI: https://doi.org/10.1089/109493103321640310.

31.   Rajaratnam V, Abdelwahab M, Jeffries S, et al. A novel app to calculate the environmental impact of general anesthesia using propofol or volatile anesthetics. J Clin Anesth 2022;82:110942. DOI: https://doi.org/10.1016/j.jclinane.2022.110942.

32.   Lee D, Chan A, Wong S, et al. Can Visual Distraction Decrease the Dose of Patient-Controlled Sedation Required During Colonoscopy? A Prospective Randomized Controlled

Trial. Endoscopy 2004;36:197-201. DOI: https://doi.org/10.1055/s-2004-814247.

33.   Boonreunya N, Nopawong E, Yongsiriwit K, et al. Virtual reality distraction during

upper gastrointestinal endoscopy: a randomized controlled trial. J Gastroenterol Hepatol

2022;37:855-60. DOI: https://doi.org/10.1111/jgh.1578

Supplementary Table 1. Exclusion criteria.

	1. Scheduled therapeutic procedure (resection, dilation) 2. Active Crohn's disease 3. Low auditory acuity that precludes use of the device 4. Low visual acuity that precludes use of the device 5. Head or face wounds precluding use of the device 6. Schizophrenia 7. Dizziness 8. Water/sea phobia 9. Non-proficiency in French or Dutch (research language) 10. Factors precluding examination taking place in the Day clinic setting (important co-morbidity factors etc)