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Letter to Editor

Virtual Reality as Auxiliary Technology in the Operating Room

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Patients experience anxiety before the operating room for many reasons. These include fear of complications and pain, nausea or vomiting after surgery. There is also sometimes a fear of complete recovery after surgery. Unfortunately, the impact of such stresses on patients is manifested by increased blood pressure and heart rate and so on. Researchers found that patients who experience less postoperative pain experience faster recovery and longer hospital stay when using methods to reduce anxiety before surgery. Such anxieties can be resolved with the short acting benzodiazepine midazolam before surgery, but can also cause various side effects. Benzodiazepines have adverse effects, such as hemodynamic perturbations; respiratory depression; and paradoxical effects, such as hostility, aggression, and psychomotor agitation. It should be kept in mind that the patient's acceptance and willingness to use them should be assessed before providing the patient with complementary or alternative options to relieve anxiety. A number of cases that have been shown to be effective in reducing anxiety in these conditions include acupuncture, aromatherapy, music, dog therapy, visiting (OR team members), training and virtual reality [1].

Virtual reality (VR) has already been shown to be one of the most effective clinical cases. VR technology, which can alleviate acute pain through distraction in burn care and other settings, is becoming more available with recent advances in technology [2-3]. This technology can be used not only during the burn treatment process, but in most age groups before surgery and sometimes even during local anesthesia and any type of medical intervention [2-3].

The first use of the term "virtual reality" is attributed to Jaron Lanier, the founder of VPL Research, a pioneer in virtual reality development [4].

The first "virtual reality mirror box" was introduced by Ramachandran and Rogers-Ramachandran to investigate the effect of sight on false emotions. Huffman and his colleagues also examined the effect of VR distraction on pain-related human brain activity. Despite various limitations, VR researchers have achieved success in feasibility, satisfaction, and innovation to reduce pain associated with medical interventions. VR technology has also been shown to be effective in minimizing drug therapy, thereby reducing the risks associated with sedation. VR significantly reduced mental pain scores in addition to decreasing pain-related brain activity in all five areas of interest including the anterior cingulate cortex, primary and secondary somatosensory cortex, insula, and thalamus. Pain studies in children age groups have focused mainly on interventions such as coping strategies proposed by the US Department of Health and Human Services, such as imagery, breathing, relaxation, positive thinking, and social support [5].

In addition to the advertising applications seen in the entertainment industry of this technology, virtual reality techniques are now used in the industry as well. Power plant workers in Japan experience the next opportunity from computer-made virtual control rooms before taking on real-life situations [4].

Reports of mental pain and functional magnetic resonance imaging results indicate that there is evidence of convergence on the analgesic effect of opioid use alone or the use of VR technology alone. In addition, pain-related brain activity patterns provide evidence that demonstrates the significant analgesic effects created by

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VR distraction when used as an adjunct to opioid analgesia. These results provide data supporting the clinical use of multimodal analgesic techniques (e.g., combination pharmacologic and no pharmacologic) [6].

Obstetricians often report anxiety during epidural delivery. Anxiety medications are rarely prescribed because of concerns about fetal exposure, and nonpharmacological methods such as music therapy and hypnosis are used with little efficacy; And increased satisfaction with using this method without side effects has been reported. Limitations of VR include side effects such as nausea, motor disease and dizziness and cost-effectiveness. These findings also suggest that VR can be a low-cost, low-risk complement to the distraction tools offered to patients undergoing epidural placement [7].

Subjective and objective evidence about the effectiveness of VR provides the pain relief experienced at TUMT. In addition, a statistically significant decrease in prostate blood flow index during VR use indicates that physiological changes occur as a result of VR distraction rather than its analgesic specificity. The hardware costs VR $ 25100 ($ 22,050 cap, $ 3000 hardware, trackball $ 50). The VR system is also easily portable into a small cart [3].

Finally, it can be noted that this technique leads to a pleasant feeling in the actual treatment of the patient and consequently reduces anxiety. The training of anesthesiologists is evolving, and compliance with the highest standards in the field should make people more secure. The importance of the role of training and evaluation of programs is important. With the increasing application of simulator technology, there is a need for further validation studies and efforts to investigate the results of knowledge translation in surgeries when using these devices. Demand for non-technical skills is evident despite demand.

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Virtual Reality Distraction during Endoscopic Urologic Surgery under Spinal Anesthesia: A Randomized Controlled Trial

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Abstract: Sedation protocols during spinal anesthesia often involve sedative drugs associated with complications. We investigated whether virtual reality (VR) distraction could be applied during endoscopic urologic surgery under spinal anesthesia and yield better satisfaction than pharmacologic sedation. VR distraction without sedative was compared with pharmacologic sedation using repeat doses of midazolam 1–2 mg every 30 min during urologic surgery under spinal anesthesia. We compared the satisfaction of patients, surgeons, and anesthesiologists, as rated on a 5-point prespecified verbal rating scale. Two surgeons and two anesthesiologists rated the scale and an overall score was reported after discussion. Thirty-seven patients were randomized to a VR group (n = 18) or a sedation group (n = 19). The anesthesiologist's satisfaction score was significantly higher in the VR group than in the sedation group (median (interquartile range) 5 (5–5) vs. 4 (4–5), p = 0.005). The likelihood of both patients and anesthesiologists being extremely satisfied was significantly higher in the VR group than in the sedation group. Agreement between the scores for surgeons and those for anesthesiologists was very good (kappa = 0.874 and 0.944, respectively). The incidence of apnea was significantly lower in the VR group than in the sedation group (n = 1, 5.6% vs. n = 7, 36.8%, p = 0.042). The present findings suggest that VR distraction is better than drug sedation with midazolam in terms of patient's and anesthesiologist's satisfaction and avoiding the respiratory side effects of midazolam during endoscopic urologic surgery under spinal anesthesia.

Keywords: virtual reality; sedation; spinal anesthesia; endoscopic urologic surgery

1. Introduction

Virtual reality (VR) technology has been investigated for its clinical applications [1,2]. Studies have investigated the educational use of VR for simulation-based training [3–7]. VR has also been evaluated as a non-pharmacological means of mitigating acute procedural pain and has also been demonstrated to be effective for the attenuation of pain perception, anxiety, and general discomfort in both adults and children [1,8–11].

VR may distract patients from noisy, scary, and uncomfortable environments during surgery under spinal or regional anesthesia. A recent pilot study investigated whether immersive VR therapy can be used as an adjunctive nonpharmacolgic sedating strategy in patients who receive drug sedation with propofol [12] and found no significant difference in the propofol requirement between the groups,

although there was less propofol consumption in the VR group [12]. However, the effect of VR distraction alone under spinal anesthesia has not been evaluated. It is still unknown whether VR can provide safe and effective distraction and replace pharmacologic sedation.

During endoscopic urologic surgery under spinal anesthesia, the patient may receive pharmacologic sedation to lessen the effect of noise in the operation room, the unpleasantness of the procedure, and the fear of surgery. However, sedative drugs may cause complications, such as respiratory depression or hemodynamic instability [13,14]. Distraction by a VR program that includes visual and audio suggestions for relaxation may achieve the intended goals of pharmacologic sedation without drug-related side effects.

Therefore, we hypothesized that VR distraction might achieve greater patient satisfaction without the side effects of drug sedation during urologic surgery under spinal anesthesia. To this end, we conducted a randomized controlled trial comparing patient satisfaction between VR distraction and midazolam-based sedation in patients undergoing endoscopic urologic surgery under spinal anesthesia.

2. Methods

2.1. Study Design

The protocol of this prospective, parallel, non-crossover, single-blind, randomized controlled clinical trial was approved by the Institutional Review Board of Seoul National University Hospital (No. 1611-069-808) and was registered prior to patient enrollment at http://www.clinicaltrials.gov (NCT03055663, Principal investigator: Won Ho Kim, data of registration: 14 February 2017). All patients provided written informed consent. This study was conducted at the Seoul National University Hospital, Seoul, Republic of Korea between March and November of 2017.

2.2. Patients

The eligibility criteria were scheduled endoscopic urologic surgery, including holmium laser enucleation of the prostate (HOLLEP) or transurethral resection of bladder tumor), and an American Society of Anesthesiologists (ASA) physical status classification of I–III. The exclusion criteria were as follows: history of chronic use of sedatives or narcotics (>6 months), alcohol or drug abuse, baseline pulse oximetry saturation of less than 90%, and baseline hemodynamic or respiratory instability (initial systolic arterial pressure <80 mmHg, respiratory rate >25 or <10 breaths/min). Medication history was screened in all patients and chronic user of the listed drugs was excluded because the response to the midazolam in these patients may differ. Patients were randomly assigned to a VR group or a sedation group. Randomization was conducted by a number table generated from an internet-based computer program (www.randomization.com). A staff anesthesiologist who is independent of our study made a random allocation sequence, enrolled participants and assigned participants to interventions. The study participants were allocated using sequentially numbered, opaque, sealed envelopes containing random allocation numbers. The sealed envelope was opened after induction of anesthesia by the attending anesthesiologist, who was not one of the trial investigators. Surgeons who reported their satisfaction score and the outcome assessor who measured the satisfaction score of the patients in the recovery room were blinded to group assignment. The patients and attending anesthesiologists could not be blinded to group assignment.

2.3. Anesthesia Protocol

All patients underwent routine monitoring, including electrocardiography, non-invasive arterial pressure monitoring, pulse oximetry, and capnography. Mean arterial pressure, respiratory rate, and heart rate were measured every 3 min and oxygen saturation (SpO_2) and end-tidal CO_2 concentration (ET_{CO2}) were monitored continuously. No premedication was administered. Spinal anesthesia was induced by intrathecal injection of hyperbaric bupivacaine 12–14 mg with fentanyl 20 μg at the L4–L5 or L5–S1 spinal level to achieve a spinal sensory block level of at least T10.

After induction of spinal anesthesia, all patients received their allocated study intervention. All patients were observed postoperatively in the recovery room for at least 30 min.

2.4. VR Group

The patients assigned to the VR group were subjected to a 30-min VR program (Aqua 30 Korean Version 4.0, Oncomfort SA, Wavre, Belgium) via a head-mounted display and earphone connected to an android cell phone (Galaxy 7.0, Samsung, Seoul, Korea) (Supplemental Figure S1). This program was designed for relaxation and distraction from anxiety or pain of patients (www.oncomfort.com/en). The patients watched a VR underwater view of the ocean while listening to narrations designed to induce relaxation and meditation. If the surgery was not completed within 30 min, the patient watched the VR program again. Details of the narration are provided in Supplemental Text S1 and screenshots are shown in Supplemental Figures S2–S4. The sedation group underwent pharmacological sedation with midazolam using an initial bolus dose of 1–2 mg and a maintenance dose of 1–2 mg every 10–30 min. Oxygen was supplied at 5 L/min via a facemask in the sedation group but not in the VR group. However, to blind the surgeon to group assignment, the VR headset and earphone were also used in the sedation group and a facemask was also used but without an oxygen supply in the VR group. If a patient assigned to the VR group wanted to stop watching the VR program, propofol could be administered as rescue medication and the incidence of rescue medication was recorded.

2.5. Study Outcomes

Baseline demographic data, including age, sex, and body mass index, were recorded preoperatively. The type of surgery and the total operating time were also recorded. The primary outcome variable was the patient-reported satisfaction score measured by a 5-point Likert-like verbal rating scale according to a prespecified score-defining table (1, extremely dissatisfied; 2, dissatisfied; 3, undecided; 4, satisfied; 5, extremely satisfied; Table 1). Patient's satisfaction score was measured at the recovery room when the patient became alert. The surgeon's and anesthesiologist's satisfaction scores were also measured at the end of surgery according to the same prespecified score table (Table 1) as secondary outcomes. The criteria for reporting the satisfaction score were explained to the patients, surgeons, and anesthesiologists before induction of anesthesia. To minimize reporting bias, two surgeons and two anesthesiologists were involved in reporting the satisfaction score. These two surgeons and two anesthesiologists discussed and reported a single satisfaction score. The two anesthesiolgists included the attending anesthesiologist and a supervising staff anesthesiologist, who were not otherwise involved in the study. Any discrepancy in the satisfaction score was resolved by discussion and a single overall satisfaction score was reported for each patient. The assigned surgeons and anesthesiologists did not change throughout the study period.

The incidence of patient discomfort intraoperatively for any reason, requests by patients to stop watching the VR program, and unnecessary patient movements were recorded. Episodes of SpO_2 desaturation (<90% for more than 5 s), apnea (undetectable ET_{CO2} for more than 5 s), and administration of rescue sedation with propofol (if an optimal level of sedation was not achieved, as judged by agitation or intolerance) were also recorded. Hypotension was defined as a decrease in mean arterial pressure to <55 mmHg or up to a 20% reduction from baseline and bradycardia was defined as a heart rate <50 beats/min or a 20% reduction from baseline. Hypotension was treated by ephedrine 5 mg and bradycardia by atropine 0.5 mg intravenously. Desaturation or apnea was treated with supplemental oxygen (10 L/min) via a face mask and respiratory assistance was provided by a chin lift or jaw thrust maneuver or assisted mask ventilation. Laryngeal mask airway insertion or tracheal intubation was allowed in the event of persistent apnea according to the decision of the attending anesthesiologists.

The Ramsay Sedation Scale (RSS) could not be used because the patients in the VR group were watching the VR program [15]. The incidence of nausea ($\geq$3 on an 11-point numeric rating scale reported by the patient where 0 is no nausea and 10 is the worst nausea imaginable) and vomiting

during surgery and in the recovery room was documented. During their stay in the recovery room, the patients were presented with score table again and asked to rate their satisfaction when they became completely alert. If the patient was confused by the residual effect of midazolam, the scoring of satisfaction was performed after transfer to the general ward. The patients were also asked about their memory of the surgical procedure or procedural pain they experienced during surgery (measured a 0–10 numeric rating scale where 0 is no pain and 10 is the worst pain imaginable). Length of stay in the recovery room was recorded. The criteria for discharge to the recovery room in our hospital is a modified Aldrete score ≥9 (Supplemental Table S1) [16].

Table 1. Satisfaction score.

Rater	Score	Description
Surgeon	1 (extremely dissatisfied)	Any of the following: 1. Patients involuntarily moved or repeatedly spoke, which made the surgical procedure stop more than twice. 2. Persistent penile erection (3 or more episode lasting >10 s) that significantly interfered with the surgical procedure and required phenylephrine injection.
	2 (dissatisfied)	Any of the following: 1. Patients involuntarily moved or repeatedly spoke, which made the surgical procedure stop once. 2. Persistent penile erection (2 or more episodes >10 s) that interfered with the surgical procedure, but not used phenylephrine.
	3 (undecided)	Any of the following: 1. Patients involuntarily moved or spoke a little, but no interference with the surgical procedure. 2. Transient penile erection (<10 s) that did not interfere with surgical procedure significantly.
	4 (satisfied)	All of the following: 1. No patient's voluntary movement or speaking. No interference with the surgical procedure. 2. Transient penile erection (<10 s) which did not interfere with the surgical procedure at all.
	5 (extremely satisfied)	All of the following: 1. No patient's voluntary movement or speaking. No interference with the surgical procedure. 2. No penile erection at all.
Patient	1 (extremely dissatisfied)	Any of the following: 1. Patients recalled all steps of the surgical procedure. 2. Patients felt severe pain during surgery (NRS ≥ 7). 3. Patients repeatedly moved due to discomfort.
	2 (dissatisfied)	Any of the following: 1. Patients recalled about two-thirds of the surgical procedure time (including recall of inserting and withdrawing the fiberoptic scope into the urethra). 2. Patients felt moderate pain (NRS of 4 to 6). 3. Patients moved several times due to discomfort.
	3 (undecided)	Any of the following: 1. Patients recalled less than one-third of the surgical procedure time. 2. Patients felt mild pain (NRS of 2 to 3).
	4 (satisfied)	All of the following: 1. No patient's recall of surgery. 2. No pain at all. 3. Patients felt comfortable during surgery.
	5 (extremely satisfied)	All of the following: 1. No patient's recall of surgery. 2. No pain at all. 3. Patients felt extreme comfort and were not concerned about the lithotomy position and surgery at all.
Anesthesiologist	1 (extremely dissatisfied)	Any of the following: 1. Patients involuntarily moved 3 or more times and repeatedly spoke which interfered the surgical procedure. 2. More than three events of apnea. 3. Desaturation (SpO_2 < 90% more than 5 s) more than twice. 4. Assisted ventilation required due to desaturation and apnea.
	2 (dissatisfied)	Any of the following: 1. Patients involuntarily moved or spoke 1 to 2 times, which interfered the surgical procedure. 2. Apnea developed twice. 3. Desaturation (SpO_2 < 90% more than 5 s) once. 4. Oral or nasal airway insertion due to desaturation or apnea.
	3 (undecided)	All of the following: 1. Patients involuntarily moved or spoke 1 to 2 times, but did not interfere with the surgery. 2. Apnea developed once but did not require oral or nasal airway insertion or assisted ventilation.
	4 (satisfied)	All of the following: 1. No patient's voluntary movement or speaking. 2. Apnea developed once but did not require oral or nasal airway insertion or assisted ventilation.
	5 (extremely satisfied)	All of the following: 1. No patient's voluntary movement or speaking. 2. No Apnea.

NRS = Numerical Rating Scale.

Finally, considering all the variables mentioned above, the incidence of a composite of optimal patient, anesthesia and surgical conditions was determined for each study participant when all the following five criteria were satisfied: (1) the patient did not complain of discomfort, did not move unnecessarily, did not try to detach the monitoring devices, and remained lying still; (2) desaturation or

apnea did not occur; (3) the patient did not need assisted ventilation, laryngeal mask airway insertion, or tracheal intubation; (4) there was no need for rescue medication; and (5) hypotension or bradycardia did not occur or occurred only once.

2.6. Statistical Analysis

No previous study has compared satisfaction scores between VR and drug sedation groups. We calculated that a sample size of 17 subjects would be needed in each group based on a power analysis assuming a mean difference in the satisfaction score of 1.0 and a standard deviation of 1.0. Allowing for a dropout rate of 10%, 37 patients were required.

The final results were evaluated by intention-to-treat analysis. Categorical variables were analyzed by the chi-squared or Fisher's exact test. Continuous variables were compared using the unpaired *t* test or Mann-Whitney *U* test according to the normality of the variables, and mean differences were calculated with the confidence intervals (CIs). The Shapiro-Wilk test and Q-Q plots were used to test the normality of the data distribution. The Cohen's kappa statistic was used to determine the agreement beyond chance between the two surgeon's and two anesthesiologist's satisfaction scores. The agreement was interpreted according to the following scale: 0.80 to 1.00, very good; 0.60 to 0.80, good; 0.40 to 0.60, moderate; 0.20 to 0.40, fair; less than 0.20, poor agreement. $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS Version 22.0 (IBM Corp., Armonk, NY, USA).

3. Results

Of the 40 patients assessed for eligibility to be included in this study (Figure 1), three patients refused to participate. The remaining 37 patients were enrolled and randomized to the VR group ($n = 18$) or to the sedation group ($n = 19$). All 37 patients finished the study protocol and were included in the analysis. No patient in the VR group asked to stop watching the VR program and no rescue medication was administered in either study group. All patients were able to report their satisfaction score in the recovery room. There were no missing data for any of our study variables. The patient characteristics at baseline are shown in Table 2. The patient demographics and comorbidity were comparable. The duration of surgery and weight of the prostate were not different between the groups.

The satisfaction scores failed the normality test. The distribution of the satisfaction scores of the patients and anesthesiologists were significantly different between the groups ($p = 0.025$ and $p = 0.001$, respectively), while the score of the surgeons was not significantly different (Figure 2). The incidence of extreme satisfaction (satisfaction score 5) for patients and anesthesiologists was significantly higher in the VR group than in the sedation group (patients, $n = 17$, 94.4% in the VR group vs. $n = 12$, 63.2% in the sedation group, $p = 0.042$). Two independent assessors of the satisfaction score showed very good agreement beyond that expected by chance (surgeons, kappa = 0.874, 95% CI = 0.730–1.000, $p < 0.001$; anesthesiologists, kappa = 0.944, 95% CI = 0.739–1.000, $p < 0.001$). There were two cases of discrepancy in reporting the satisfaction score of the surgeons and one case of discrepancy for the score of the anesthesiologists. The difference was one-point and a higher score was selected for all cases.

Table 3 shows the comparison of outcome variables between the groups. Most patients did not move inadvertently during surgery in the VR group. There were significantly more patients who developed apnea in the sedation group than in the VR group ($n = 1$, 5.6% in group VR vs. $n = 7$, 36.8% in the sedation group, $p = 0.042$, risk difference (95% CI) −0.34, (−0.09 to −0.58)). One patient in the sedation group received assisted mask ventilation. Two patients in the VR group fell asleep while watching the VR program. They did not receive propofol and their group assignment was not changed. The hemodynamic variables during surgery, including the incidence of hypotension and bradycardia, were not different between the groups. The duration of stay in the recovery room was not different between the groups.

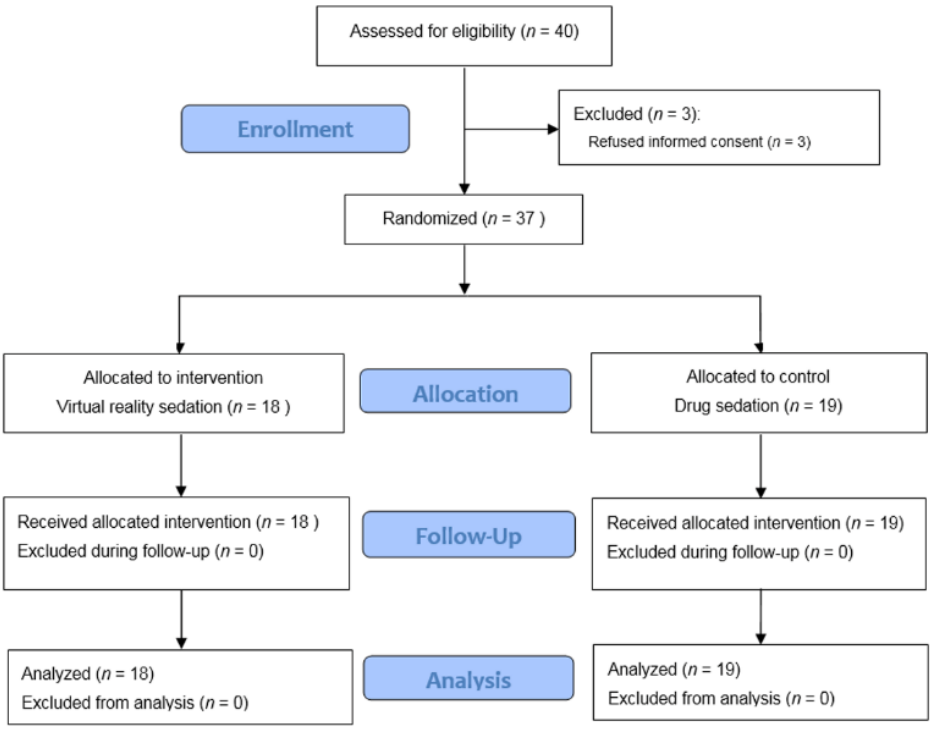

Figure 1. Flow diagram of the study according to CONSORT 2010.

Table 2. Baseline characteristics of patients and surgical characteristics.

Variables	VR Group	Sedation Group
Case number, *n*	18	19
Age, years	69 (65–70)	69 (63–72)
Weight, kg	69 (64–73)	64 (62–69)
Height, cm	167 (163–170)	167 (162–170)
Body-mass index, kg m^{-2}	24.8 (23.3–26.9)	23.9 (21.3–25.1)
ASA PS, 1/2/3	7/7/4	9/7/3
Underlying disease (*n*)		
Hypertension	8 (44.4)	8 (42.1)
Diabetes Mellitus	3 (16.7)	3 (15.8)
Angina pectoris	3 (15.8)	3 (16.7)
Stroke	2 (11.1)	-
Chronic obstructive pulmonary disease	-	1 (5.3)
Chronic kidney disease	2 (11.1)	-
Prostate weight (g)	65 (38–98)	75 (39–110)
Duration of anesthesia (min)	65 (55–100)	65 (60–85)
Duration of surgery (min)	40 (35–75)	45 (30–60)
Fluid administration (mL)	200 (60–200)	100 (70–150)
Colloid administration (mL)	-	-

The values are expressed as the median (interquartile range) or number (%). VR Group = virtual reality group; ASA PS = American society of anesthesiologist physical status classification. *p*-values are the results of Mann-Whitney U test for continuous variables and Fisher exact test for categorized variables.

The incidence of optimal patient, anesthesia and surgical conditions was significantly higher in the VR group than in the sedation group (n = 17, 94.4% in VR group vs. n = 13, 68.4% in the sedation group, p = 0.043, risk difference (95% CI) 0.17 (−0.08 to 0.42)). There was no harmful or unintended effect of the study interventions other than the reported outcomes.

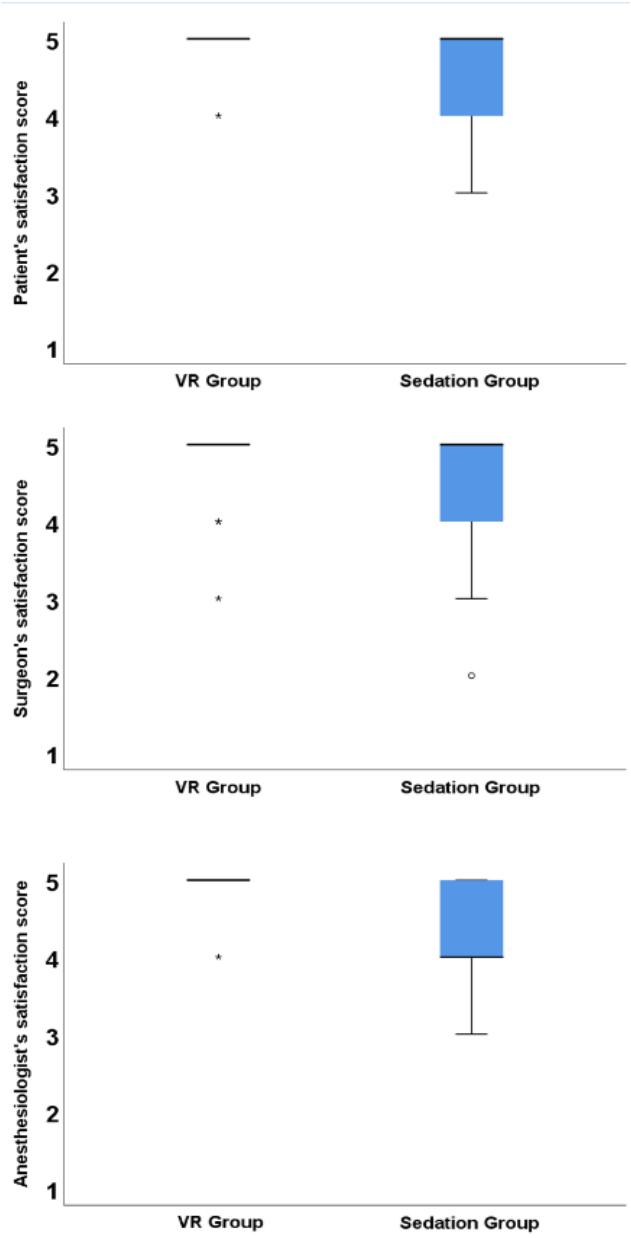

Figure 2. Box-and-whisker plots of the satisfaction scores of patients, surgeons, and anesthesiologists. Thick horizontal bars, boxes, and error bars represent the median, 25th, 75th, 10th and 90th percentile. VR group = Virtual Reality group, 1 = extremely dissatisfied, 2 = dissatisfied, 3 = undecided, 4 = satisfied, 5 = extremely satisfied, ○ means outlier and * means extreme outlier. Extreme outlier is determined when outliers is located distal to 1.5× interquartile range from 25 or 75 percentile.

Table 3. Sedation-related characteristics.

Variables	VR Group	Sedation Group	*p*-Value
Case number, *n*	18	19	
Intraoperative variables			
Patients who do not move involuntarily during surgery, *n*	16 (88.9)	13 (68.4)	0.001
Patients who requested to stop watching VR, *n*	0	-	
Midazolam administration, mg	4 (4–6)	-	
Administration of rescue sedative, *n*	0	0	
Desaturation (SpO_2 < 90%, more than 5 s), *n*	0	1 (5.3)	0.999
Apnea (flat $ETco_2$, more than 5 s)			
Develop, *n*	1 (5.6)	7 (36.8)	0.042

Table 3. *Cont.*

Variables	VR Group	Sedation Group	*p*-Value
Frequency in the patients with apnea, range	1–2	1–5	
Assisted mask ventilation, *n*	0	1	0.999
Conversion to general anesthesia, *n*	0	0	
Ephedrine administration			
Incidence, *n*	2 (11.1)	6 (31.6)	0.232
Dose, median (IQR) (range), mg	0 [0,0] (5–10)	0 (0–5) (5–10)	0.313
Atropine administration			
Incidence, *n*	1 (5.6)	4 (21.1)	0.340
Dose, median (IQR) (range), mg	0 [0,0] (0–0.5)	0 (0–0) (0–0.5)	0.425
Nausea (≥3 of numerical rating scale), *n*	0	2	0.486
Vomiting. *n*	0	0	
Satisfaction score as a continuous variable			
Patient	5 (5–5)	5 (4–5)	0.105
Surgeon	5 (5–5)	5 (4–5)	0.558
Anesthesiologist	5 (5–5)	4 (4–5)	0.005
Incidence of extreme satisfaction			
Patient	17 (94.4)	12 (63.2)	0.042
Surgeon	14 (77.8)	13 (68.4)	0.714
Anesthesiologist	17 (94.4)	8 (42.1)	0.001
Recovery room parameters			
Remember the operative procedure, *n*	0	3 (15.8)	0.230
Felt procedural pain during surgery, *n*	0	0	
Duration of recovery room stay, min	27 (21–44)	29 (22–53)	0.620
Nausea (≥3 of numerical rating scale), *n*	1	2	0.999
Vomiting, *n*	0	0	
Optimal patient, anesthesia, and surgical condition, *n*	17 (94.4)	12 (63.2)	0.042

The values are expressed as the median (interquartile range) or number (%). VR Group = Virtual reality group; ASA PS = American society of anesthesiologist physical status classification, $ETco_2$ = end-tidal carbon dioxide. *P*-values are the results of Mann-Whitney U test for continuous variables and Fisher exact test for categorized variables. Hypotension was determined when heart rate <50/min or 30% or more decrease from baseline. Bradycardia was determined when heart rate <50/min or 30% or more decrease from baseline.

4. Discussion

We conducted a randomized controlled trial comparing VR distraction and drug sedation in patients undergoing endoscopic prostatectomy under spinal anesthesia. The satisfaction score of the anesthesiologists was significantly higher in the VR group than that in the sedation group. The incidences of extreme satisfaction reported by the patients and anesthesiologists were significantly higher in the VR group than those in the sedation group. Our study results suggest that VR distraction may be preferable for both patients and anesthesiologists during endoscopic urologic surgery under spinal anesthesia.

VR has been studied for its potential use in simulated medical training [17,18], pain control for medical procedures and physical trauma [19–21], and rehabilitation of patients with stroke or Parkinson's disease [22,23]. Recently, VR distraction has been studied in regional anesthesia to assess its sedation and analgesic-sparing effects [12,24]. However, the studies included only a small number of patients as a pilot and feasibility study or were retrospective in nature. Furthermore, the commercial VR programs used did not aim to improve patient relaxation and included no verbal narration inducing relaxation. In this prospective randomized controlled trial, we used a commercially available VR sedation program specifically designed for perioperative settings to evaluate participants' satisfaction. The supplemental text and figures present a glimpse of the program, including the narration and a silent scene of the three-dimensional undersea environment inducing relaxation and sedation. Our study may have value as the first trial to investigate the effect of a specific VR program as a single modality to replace drug sedation during spinal anesthesia.

The incidence of extreme satisfaction reported by both patients and anesthesiologists was higher in the VR group than in the sedation group and the anesthesiologist's satisfaction scores were significantly higher in the VR group. However, there was no difference in the surgeon's satisfaction scores between

the groups. From a surgeon's perspective, the respiratory depression caused by midazolam may not influence the surgical conditions, although the patient may move purposelessly during respiratory depression or snoring. The incidence of apnea caused by respiratory depression also influenced the rate of adequate sedation in our study.

The persistent penile erection that occurs during HOLLEP may interfere with the surgical procedure because any movement of the cystoscope could be interrupted. Drug sedation with midazolam may cause sleep-related penile erection [25], whereas VR distraction may avoid this sleep-related problem and contribute to better surgical conditions. A previous study that monitored penile tumescence reported that sleep-related erectile episodes occurred in nearly all patients who received midazolam. Therefore, we included penile erection in our criteria for the surgeon's satisfaction score (Supplemental Table S1). However, there was no difference in this regard between the groups, suggesting that our study was not adequately powered to detect the small difference in the incidence of penile erection during midazolam sedation under spinal anesthesia.

We compared VR distraction with drug sedation with midazolam. However, this benzodiazepine has a relatively long duration of action and is not a preferred sedative nowadays compared with propofol or dexmedetomidine. Our study results indeed showed a high incidence of apnea during sedation with midazolam. Propofol or dexmedetomidine are also used frequently for procedural sedation [26–29]. Propofol is associated with rapid recovery, although arterial hypotension may develop in response to suppression of reflex tachycardia. Sedation with dexmedetomidine provides improved analgesia and causes less respiratory depression than other sedatives, including benzodiazepines and propofol [30,31]. Further studies are required to compare VR sedation with drug sedation using propofol or dexmedetomidine.

Our study has several limitations. First, the primary outcome variable was the patient-reported satisfaction score. Our sample size was calculated based on the difference in this score. Other secondary variables were not considered when calculating the sample size; therefore, our study may have lacked statistical power for the secondary outcomes. Furthermore, the satisfaction score of the patient was reported by different patients who were not blind to the group assignment. To decrease the patient-dependent reporting bias, our patients determined their satisfaction score according to a prespecified scoring scale (Table 1). However, our score was not validated in any previous study. Although the satisfaction scores of the surgeons and anesthesiologists were reported by two personnel after discussion and their kappa statistics were analyzed, the patient scores could not be analyzed in that manner. Second, our study was a small single-center trial, so its external validity may be limited. The effect of VR distraction may be different in different surgical settings and age groups. Third, the attending anesthesiologists and patients could not be blinded to group assignment, which could have confounded the satisfaction scores of anesthesiologists and patients.

5. Conclusions

Our study results suggest that VR distraction is preferable to pharmacologic sedation with midazolam in terms of patient's and anesthesiologist's satisfaction and avoiding the respiratory side effects of midazolam during endoscopic urologic surgery under spinal anesthesia in patients with ASA physical status classification of I–III. Further studies are required to detect a true clinical advantage of VR distraction over drug sedation.

Supplementary Materials: The following are available online at http://www.mdpi.com/2077-0383/8/1/2/s1, Supplemental Table S1: Modified Aldrete Score, Supplemental Figure S1: Patient during Holmium laser enucleation of the prostate under spinal anesthesia with virtual reality distraction, Supplemental Figure S2: A Screenshot of 'Aqua 30', Supplemental Figure S3: A Screenshot of 'Aqua 30', Supplemental Figure S4: A Screenshot of 'Aqua 30', Supplemental Text S1: Script of 'Aqua 30' (Introduction part only).

Author Contributions: Conceptualization, J.Y.M. and W.H.K.; Data curation, J.C. and W.H.K.; Formal analysis, J.C. and W.H.K.; Investigation, J.C. and W.H.K.; Methodology, J.Y.M. and W.H.K.; Visualization, W.H.K.; Writing—Original draft, W.H.K.; Writing—Review and editing, J.Y.M., J.S., J.C., S.-H.J. and S.R.

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Original research

Perioperative Outcomes of Immersive Virtual Reality as Adjunct Anesthesia in Primary Total Hip and Knee Arthroplasty

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ABSTRACT

Background: Immersive virtual reality (IVR) is utilized as an adjunct to anesthesia to distract patients from their intraoperative environment, thereby potentially reducing sedative and narcotic medication usage. This study evaluated intraoperative and acute postoperative results of patients undergoing primary total hip (THA) and total knee arthroplasty (TKA) with and without IVR.

Methods: Utilizing IVR as an adjunct to spinal anesthesia, 18 primary THAs (n = 8) and TKAs (n = 10) were performed. These cases were 1:2 matched based on procedure type, age, sex, and body mass index to those performed without IVR. Intraoperative and postanesthesia care unit sedative/narcotic usage, vital signs, and pain scores were compared. Acute perioperative outcomes, including 24-hour oral morphine equivalent (OME), first ambulation distance, length of stay, and 30-day complications, were also analyzed. Pearson Chi-square and Wilcoxon-Mann-Whitney tests evaluated categorical and continuous variables, respectively.

Results: When compared to non-IVR primary THAs and TKAs, those performed with IVR utilized significantly less intraoperative sedation (48 mg vs 708 mg of propofol; $P < .001$) and trended toward less narcotic usage (13 mcg vs 39 mcg of fentanyl; $P = .07$). In the postanesthesia care unit, IVR and non-IVR patients showed no significant differences ($P > .3$) in vital signs, pain scores, or OME received. Additionally, similar ($P > .3$) postoperative outcomes were noted in both cohorts' 24-hour OME use, distance at first ambulation, length of stay, and 30-day complications.

Conclusions: The use of spinal anesthesia with the IVR adjunct to perform primary THAs and TKAs appears to be well-tolerated and associated with less intraoperative sedative medication usage than spinal anesthesia alone.

Introduction

Immersive virtual reality (IVR) is the creation of an artificial environment with a 3-dimension-enabled head-mounted device and noise-canceling headphones [1]. Most IVR devices aim to provide soothing experiences by using natural environments such as forests, beaches, snowy canyons, space, or botanical gardens to replicate calming surroundings [2–4]. Recently, IVR has been applied as a form of distraction in medical patient care to attenuate anxiety and general discomfort during interventions such as wound care, physical therapy, dental procedures, and perioperative processes of peripheral nerve blocks and anesthesia induction [1,5–10]. IVR utilization has further expanded intraoperatively as an adjunct to surgeries performed under regional or neuraxial anesthesia [11–14].

For orthopedic surgeries, early studies have provided favorable results on IVR's application, safety, and efficacy in reducing patients' anxiety and sedation requirements although utilization has been primarily for outpatient procedures [11,12]. This success has led to growing interest in IVR usage as an adjunct to spinal anesthesia during total hip arthroplasty (THA) and total knee arthroplasty (TKA) [13,14]. Despite the known advantages and pain-

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reduction seen with spinal anesthesia compared to general anesthesia, sedative and narcotic medications are often still required to attenuate noxious stimuli associated with these procedures [15]. The addition of IVR as an adjunct would appear to be complementary to spinal anesthesia and perhaps decrease the need for these medications during THA and TKA.

The goal of this study was to compare the intraoperative, immediate postoperative, and 30-day acute postoperative results of patients undergoing primary THA or TKA with IVR as an adjunct to spinal anesthesia to those of procedures performed with spinal anesthesia alone. We hypothesized that IVR patients would require less intraoperative sedation and narcotics, maintain similar perioperative pain scores, and utilize fewer postoperative narcotics.

Material and methods

After the institutional review board approval was obtained, a single institutional retrospective review identified 18 patients from January 1, 2021 to July 1, 2021 who underwent primary THA (n = 8) or TKA (n = 10) with spinal anesthesia and IVR as an adjunct. Patients were excluded if aged ≤18 years, they had indications other than osteoarthritis, or were unable to tolerate the IVR experience fully during the surgery. IVR patients were matched 1:2 to controls that did not use IVR based on procedure type (THA or TKA), age (±3 years), sex (exact), and body mass index (±5 kg/m^2).

During the routine preoperative evaluation, elective total joint arthroplasty patients met with both surgeon and anesthesia providers to review the risks and benefits of the procedure and the choice of anesthetic options. Patients were provided information related to anesthesia options of general, spinal, or spinal with IVR and eventually self-selected into a surgery performed with or without IVR. Spinal anesthesia remains our current institutional recommendation and preference for THA and TKA and was solely utilized in both cohorts. For those patients interested in the adjunct, the IVR hardware (PICO G2 4K Enterprise [PICO, San Francisco, CA] goggles and Bose Quiet Comfort QC 35 noise-canceling headsets [Bose, Framingham, MA]), choice of the 4 different visual content environments created by HypnoVR (Strasbourg, France; https://hypnovr.io/en/solutions/softwares/), and voice-guided relaxation techniques/sounds were demonstrated (Fig. 1). On the day of surgery, both the anesthesiologist and surgeons confirmed the informed consent, including the patient's anesthetic plan and preference. If patients elected to receive an ultrasound-guided, single-shot nerve block, fascia iliaca for THA or saphenous (adductor canal) for TKA was performed. In the operating room, patients received a 10- to 30-mg dose of propofol prior to spinal anesthesia with 1.5% mepivacaine. Further sedation or narcotic dosing was titrated based on a subjective evaluation of patients' requirement as indicated by comfort level, pulse oximetry, and noninvasive arterial pressure monitoring. Specifically, both IVR and non-IVR patients initially received no sedation unless they felt uncomfortable or anxious about being fully awake per their request or abnormal vital signs/monitoring. In this case, propofol infusion was given to a level of minimal to moderate sedation as assessed by purposeful response to verbal or tactile stimuli, airway protection, and hemodynamic stability. Those patients selecting IVR were fitted for the IVR headset and headphones and informed of expected sounds, vibrations, or smells associated with the surgery. High-volume arthroplasty surgeons performed the THAs and TKAs at a single institution via the same approach (direct anterior for THA and medial parapatellar for TKA), contemporary techniques/implants, and standardized acute postoperative recovery protocols.

Perioperative results were separated and compared according to preoperative, intraoperative, immediate postoperative, and acute postoperative outcomes. Patient demographics, American Society of Anesthesiologists score, Charlson Comorbidity Index, anesthesia type (ie, spinal alone vs spinal and peripheral nerve block), and quantity of sedation (both preoperative and intraoperative) were recorded. There were no patients in either the IVR or non-IVR matched cohort that required intraoperative conversion to general anesthesia. Intraoperative outcomes included maximum heart rate, maximum systolic blood pressure, anesthesia time, intraoperative oral morphine equivalents (OMEs), and complications. Immediate postoperative outcomes included postanesthesia care unit (PACU) sedative/narcotic usage, vital signs, pain scores (Numerical Pain Rating Scale from 0 to 10), and recovery duration. Acute outcomes analyzed 24-hour OMEs, first ambulation distance with physical therapy, length of stay, and 30-day complications (readmissions or reoperations).

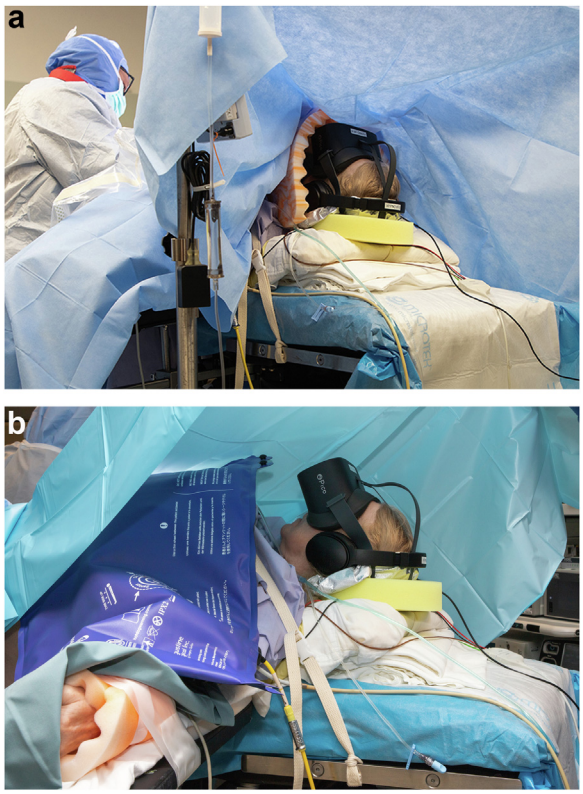

Figure 1. A patient undergoing primary total hip arthroplasty under spinal anesthesia with immersive virtual reality goggles and noise-canceling headphones including a view from anesthesia (a) and side profile (b).

For patients undergoing THA and TKA with IVR-adjunct anesthesia, the mean age was 74 years (range, 54-93 years), 67% were female, and the mean body mass index was 28 kg/m^2 (range, 20.0-34.5 kg/m^2). No significant difference existed between cohorts except for the IVR patient cohort having significantly ($P = .007$) more patients who were American Society of Anesthesiologists score 3 (Table 1). Additionally, there were no significant differences in preoperative hemoglobin levels, heart rate, systolic blood pressure, or OMEs provided before the surgery.

Statistical analysis

Matched cohorts were evaluated on differences in preoperative, intraoperative, immediate postoperative, and acute postoperative outcomes. Study demographics and outcomes were described as frequency and percentages or means and standard deviations. Pearson Chi-square tests were used for categorical variables while Wilcoxon-Mann-Whitney tests were used for continuous variables.

Table 1
A comparison of baseline characteristics between patients undergoing total joint arthroplasty with and without IVR-adjunct anesthesia.

Characteristics	IVR	No IVR	*P* value
Age (mean, range)	74 (57-93) y	73 (54-89) y	.601
Sex			
Female	12	24	.999
Male	6	12	
Body mass index (mean, range)	28 (20-35) kg/m^2	28 (22-34) kg/m^2	.659
ASA score			
2	8	29	.007
3	10	7	
Anesthesia type			
Spinal	5	6	.203
Spinal with block	13	30	
Procedure			
Total hip arthroplasty	8	16	.999
Total knee arthroplasty	7	14	
Robotic-assisted total knee arthroplasty	3	6	
Preoperative heart rate (mean, SD)	81 (±14) beats/min	84 (±15) beats/min	.588
Preoperative systolic blood pressure (mean, SD)	125 (±24) mm/Hg	114 (±20) mm/Hg	.106
Preoperative hemoglobin (mean, SD)	13.8 (±1.4) g/dL	13.5 (±1.2) g/dL	.653
Preoperative OME given (mean, range)	24 (0-55) OMEs	28 (1-58) OMEs	.178

ASA, American Society of Anesthesiology score; SD, standard deviation.

Stata/MP 17.0 (StataCorp, College Station, TX) was used to conduct the analysis, and *P* values of less than 0.05 were considered statistically significant.

Results

Intraoperative outcomes

Primary THA and TKA performed with IVR utilized significantly less intraoperative sedation (48 mg vs 708 mg of propofol; $P < .001$) than those without IVR. Although not significant with the numbers available, there was a trend toward less narcotic usage (13 mcg vs 39 mcg of fentanyl; $P = .07$) for the IVR patients. The operating room time was not different between cohorts ($P = .4$), and no IVR cases were intraoperatively abandoned. No significant differences were noted in maximum heart rate ($P = .1$) or systolic blood pressure ($P = .3$), and there were no intraoperative complications in either cohort (Table 2).

Immediate postoperative outcomes

The overall recovery duration in the PACU was 1.7 hours for IVR patients and 2.3 hours for controls ($P = .4$) (Table 3). There remained no significant difference between cohorts' maximum heart rate ($P = .4$), systolic blood pressure ($P = .4$), utilization of OMEs ($P = .7$), or antiemetics ($P = .7$). Additionally, pain scores upon patient arrival to the PACU and final pain scores were not significantly different ($P \geq .2$).

Acute postoperative outcomes

During the first 24 hours of acute hospital stay, no significant difference in OME ($P = .3$) or antiemetic utilization ($P = .9$) was seen between IVR and non-IVR patients (Table 4). Similarly, ambulation distance with physical therapy during the first attempt ($P = .5$), hospital length of stay ($P = .9$), and discharge home ($P = .2$) were not significantly different. Two complications (1 patient with postoperative anemia requiring a gluteal artery embolization and 1 patient with a postoperative hematoma requiring aspiration at 6 weeks) and 1 readmission/reoperation for a periprosthetic hip fracture at 2.5 weeks after the surgery occurred in the non-IVR cohort; none occurred in the IVR patients.

Discussion

The use of IVR-adjunct anesthesia represents a novel technology with the potential to reduce the use of sedative and narcotic medication during a major elective lower-extremity joint replacement. Less is known about the possible subsequent physiologic, psychologic, and pain-reduction benefits of a distraction therapy in this setting. According to our results, patients undergoing THA and TKA with IVR adjunct to spinal anesthesia required significantly less sedation and showed a trend toward less narcotics during the procedure compared to non-IVR controls. Otherwise, postoperative pharmacologic requirements, pain scores, and 30-day outcomes were similar between the groups.

The application of the IVR adjunct appeared to be well-tolerated by THA and TKA patients with intraoperative outcomes such as operative time, vital signs, and anesthetic complications that were not different from those of matched non-IVR surgeries. Perhaps the most encouraging finding was that IVR patients' maximum heart rate and systolic blood pressure remained well-controlled throughout the surgeries, which we believe confirms a calming, anxiolytic effect of the IVR experience despite significantly less sedation being utilized. Chan and Scharf found similar decreased sedation requirements in their pilot study of patients undergoing

Table 2
Intraoperative outcomes of patients undergoing total joint arthroplasty with and without IVR-adjunct anesthesia.

Intraoperative outcomes	IVR	No IVR	*P* value
Intraoperative maximum HR (mean, SD)	80 (±13) beats/min	86 (±12) beats/min	.079
Intraoperative maximum SBP (mean, SD)	134 (±12) mm/Hg	134 (±22) mm/Hg	.315
Operating room time (mean, SD)	128 (±22) min	131 (±17) min	.373
Intraoperative OME (mean, SD)	1.7 (±3.8) OMEs	2.1 (±5.5) OMEs	.93
Intraoperative propofol sedation (mean, SD)	48 (±27) mg	708 (±293) mg	<.001

HR, heart rate; SBP, systolic blood pressure.

Table 3
Immediate postoperative outcomes in the PACU of patients undergoing total joint arthroplasty with and without IVR-adjunct anesthesia.

Immediate postoperative outcomes	IVR	No IVR	*P* value
PACU duration (mean, SD)	1.8 (±1.3) h	2.3 (±1.8) h	.404
Initial pain score (mean, SD)	0.6 (±1.7)	1.2 (±2.4)	.329
Final pain score (mean, SD)	1.2 (±1.5)	2.1 (±2.1)	.159
Maximum heart rate (mean, SD)	81 (±14) beats/min	85 (±15) beats/min	.368
Maximum systolic blood pressure (mean, SD)	150 (±17) mm/Hg	145 (±23) mm/Hg	.378
Antiemetics (mean, SD)	6.1 (±2.5) mg	5.5 (±3) mg	.738
OMEs (mean, SD)	61 (±44) OMEs	64 (±42) OMEs	.645

various hip, knee, and foot procedures [11]. However, the results were not significant, likely due to inadequate power [11]. In contrast, a randomized controlled trial by Huang et al. showed no significant decrease in sedation medication between IVR and non-IVR THA and TKA cohorts [13]. It is important to note that in this study, intraoperative sedation needs were self-administered by the patient, and the treating anesthesiologist provided adjunct analgesia. As seen in our results with IVR patients, the benefits of reducing sedation requirements may only be evident if the anesthesia provider solely controls sedation during the case.

Although it did not reach significance, there was also a trend toward less narcotic requirements during THA and TKA performed with an IVR adjunct. Similar pain-mitigating effects of IVR have been seen in burn victims undergoing physical therapy sessions, which are crucial for minimizing long-term disability and preventing contractures. Burn patients performing physical therapy with virtual reality for distraction reported significantly lower visual analog scores than those without virtual reality. The magnitude of pain reduction did not diminish with repeated use of IVR in subsequent therapy sessions [5]. A randomized controlled trial of patients with hand injuries undergoing dressing changes also demonstrated significantly lower visual analog scores with the use of virtual reality [16]. Preliminary pain and narcotic use reduction during surgeries performed with IVR is encouraging; however, such a difference appears to be limited intraoperatively as pain scores and OMEs in the PACU and during hospitalization were not different between groups. The study is likely underpowered to determine such difference; thus, further research will be required to fully realize if the utilization of IVR during any potential painful episodes (ie, physical therapy, dressing change, sleeping etc.) could impact postoperative pain and narcotic requirements.

The immediate postoperative PACU experience of the IVR patients, including factors like overall time, vital signs, pain medication/antiemetic usage, and serial pain scores, is noninferior to that of the non-IVR group indicating at least an equal experience. Despite less sedation being utilized in the IVR group, we believe the nondifferent immediate postoperative outcomes may be due to the relatively quick half-life of the propofol sedation itself (estimated to be 40 minutes) [17]. A similar amount of time often elapses as the surgery is completed, dressings are placed, patients are transferred from the OR bed to a stretcher and transported to the PACU, and PACU arrival intake is completed by nursing. Given this duration, the propofol sedation is likely to be worn off in both groups. Any potential differences in vital signs, pain scores, or medication usage between the IVR and non-IVR patients may have been less evident.

IVR may also have a role in enhanced recovery programs after THA and TKA which are known to provide cost-efficient and high-quality patient care. Patient expectations and motivation are key components to ensuring their success [18–20]. Additionally, the in-hospital and 30-day postoperative outcomes between the 2 groups were also equivocal, with no significant differences in discharge location or complications, readmissions, or reoperations. Given our findings of decreased sedation and noninferior acute outcomes, IVR appears to be a safe, novel adjuvant for the rapid recovery protocol and/or same-day discharge for outpatient total joint replacements.

The major limitation of our study includes the relatively small sample size, which can result in inadequate power for insignificant findings. Patient selection bias is inherent as patients were offered and eventually self-selected the IVR experience for their surgery. Despite standardized care pathways, multiple anesthesia providers and surgeons were involved in the patients' surgical care episode, and subjective differences in anesthesia practice and procedural techniques exist. Furthermore, no blinding can be performed given the application of the IVR device, and such ongoing interactions may have also led to differences in the amount of sedation given by the treating anesthesia providers. It is important to note that no universally accepted or superior scale of assessing the depth of sedation and subsequent dosing currently exists [21]. Nevertheless, our anesthesia practitioners routinely perform anesthesia for a high volume of THAs and TKAs, and the practice standard is to minimize sedation based on the response to verbal and tactile stimulation similar to previously published sedation-assessment methods [22–24]. Baseline and postoperative mental status or health assessments were not obtained and could further elucidate the benefits of decreased pharmaceutical requirements between the groups. A well-powered randomized controlled trials will be needed to further delineate the potential benefits of IVR in total joint arthroplasty.

Conclusions

In summary, the use of spinal anesthesia with an IVR adjunct to perform primary THAs and TKAs appears to be well-tolerated and

Table 4
Postoperative outcomes of patients undergoing total joint arthroplasty with and without IVR-adjunct anesthesia.

Acute postoperative outcomes	IVR	No IVR	*P* value
Antiemetics (mean, SD)[a]	5.1 (±2.5) mg	5.9 (±5.4) mg	.871
Oral morphine equivalents (mean, SD)[a]	55 (±24) OMEs	64 (±30) OMEs	.306
Postoperative day 1 hemoglobin (mean, SD)	10.9 (±1.3) g/dL	10.7 (±1.6) g/dL	.427
Ambulation distance on first attempt (mean, SD)	84 (±67) feet	71 (±67) feet	.520
Length of stay (mean, SD)	30 (±9) h	35 (±27) h	.898
30-D complications	0	2	.547
30-D readmissions	0	1	.999
30-D reoperations	0	1	.999

[a] Antiemetic medication and OMEs administered during the first 24 h of hospital admission.

associated with less intraoperative sedative medication usage than spinal anesthesia alone. Additionally, with the numbers available, the surgical experience with IVR does not lead to worse immediate and acute postoperative outcomes for interested patients undergoing an elective arthroplasty. The utilization of the IVR adjunct may be considered a novel, safe anesthetic approach to total joint arthroplasty, and further investigation is warranted, particularly on the utility in outpatient total joint programs.

Conflicts of interest

Dr. C. K. Ledford is a committee member of American Academy of Orthopaedic Surgeons, American Association of Hip and Knee Surgeons, and American Board of Orthopaedic Surgery. All other authors declare no potential conflicts of interest.

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BMC Emergency Medicine

RESEARCH

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Virtual Reality for Pain Relief in the Emergency Room (VIPER) – a prospective, interventional feasibility study

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Abstract

Background: Pain is one of the most common, yet challenging problems leading to emergency department (ED) presentation, despite the availability of a wide range of pharmacological therapies. Virtual reality (VR) simulations are well studied in a wide variety of clinical settings, including acute and chronic pain management, as well as anxiety disorders. However, studies in the busy environment of an adult ED are scarce.

The aim of this study is to explore the feasibility and effectiveness of a VR simulation for pain and anxiety control in a convenience sample of adult ED patients presenting with traumatic and non-traumatic pain triaged 2–5 (i.e., urgent to non-urgent) with a pain rating of ≥ 3 on a numeric rating scale (NRS 0–10).

Methods: Prospective within-subject, repeated measures interventional feasibility pilot study at a Swiss University ED. The intervention consisted of a virtual reality simulation in addition to usual care. Pain and anxiety levels were measured using a verbally administered numeric rating scale (NRS) before and after the intervention. Information on patient experience was collected using established rating scales.

Results: Fifty-two patients were enrolled. The most common pain localisations were extremities ($n = 15$, 28.8%) and abdomen ($n = 12$, 23.1%). About one third of patients presented with trauma-associated pain ($n = 16$, 30.8%). Duration of pain was mainly acute (< 24 h) ($n = 16$, 30.8%) or subacute (> 24 h) ($n = 32$, 61.5%). The majority of patients were triage category 3, i.e. semi-urgent ($n = 48$, 92.3%). Significant reduction in pain (NRS median pre-VR simulation 4.5 (IQR 3–7) vs. median post-VR simulation 3 (IQR 2–5), $p < 0.001$), and anxiety levels (NRS median pre-VR simulation 4 (IQR 2–5) vs. median post-VR simulation 2 (IQR 0–3), $p < 0.001$) was achieved, yielding moderate to large effect sizes (Cohen's d estimate for pain reduction = 0.59 (95% CI 0.19—0.98), for anxiety level on NRS = 0.75 (95% CI 0.34—1.15). With medium immersion and good tolerability of the VR simulation, user satisfaction was high.

Conclusions: Virtual reality analgesia for pain and anxiety reduction in the busy setting of an ED is feasible, effective, with high user satisfaction. Further randomized controlled studies are needed to better characterize its impact on pain perception and resource utilization.

Keywords: Pain management, Anxiety, Virtual reality simulation, Emergency department, e-Health, Telemedicine, Telehealth

Background

Pain is one of the most common problems leading to emergency department (ED) presentation. However, pain management in the ED remains challenging [1–3]. Many barriers to effective pain management in the ED have

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been reported, and include the individual pain level of the patient (e.g., the highly subjective experience of pain) as an important influencing factor [1, 4]. A wide range of pharmacological therapies including both opioid and non-opioid medications exist and are broadly applied in the ED via different routes of application, yet there are specific side effects and contraindications to consider [3]. Furthermore, EDs are a major source of opioid prescription and thus, in some countries, contribute to the rising opioid dependency crisis [5, 6]. Non-pharmacological therapies (e.g. relaxation techniques, traditional distraction, and transcutaneous electrical nerve stimulation are recommended as well, but are oftentimes underused in the busy acute-care setting of an ED [3].

Virtual Reality (VR) affects the visual and the auditory senses allowing immersion in a virtual world thanks to a VR headset, giving participants the illusion of "being there" in the 3 dimensional computer generated world as if it is a place they are visiting. The mechanism of how VR works to alleviate pain is only partially known. The gate control theory postulates pain perception to be modulated by interaction among different neurons. VR or other stimuli might lead to a closure of the neural gateways, thus reducing pain perception [7]. In addition to distraction [8], there are novel mechanisms for VR treatment in pain, such as producing neurophysiologic changes related to conditioning and exposure therapies [9], or regulating autonomic, affective (mood, anxiety), and evaluative (subjective pain and enjoyment rating) responses associated with acute pain [10]. fMRI studies have demonstrated that VR can reduce pain comparable to a moderate dose of opioids [11, 12]. The effects of VR simulations are well studied in a wide variety of clinical settings, including acute and postoperative [13–21], as well as chronic pain management [13, 17, 22], neuropathic pain [23], in patients undergoing invasive procedures [22, 24, 25], and for treatment of burn patients [26, 27]. Furthermore, there is a growing body of evidence for the application of VR simulation especially in the pediatric population (burn pain, painful procedures, chemotherapy, anxiety, and palliative care [11, 21, 28–32]. Additionally, VR simulation can be used for the treatment of anxiety disorders [18, 20, 30, 33].

Studies in the busy environment of an adult ED are scarce [34], and mainly focus on procedural analgesia during painful medical interventions.

Thus, we conducted a within-subject, repeated measure interventional feasibility pilot study to investigate:

i) The feasibility of deployment of a VR simulation in the busy setting of the ED for an adult population presenting with traumatic or non-traumatic pain ≥ 3 on a numerical rating scale (NRS) (0–10).
ii) The effectiveness of the VR simulation in pain and anxiety control. Impact of gender and pain location on response.
iii) The acceptance of the VR simulation in the study population and patient experience (user satisfaction, simulator sickness, sense of presence and immersion).

Methods

Study design, setting, and ethical approval

This is a prospective self-controlled interventional feasibility pilot study at the ED of the University Hospital of Bern, Switzerland. Our ED is a tertiary care centre, caring for a patient population of around 2 million and treating over 45,000 adult patients each year with an interdisciplinary team [35, 36].

The study took place from March 22nd, 2021 until July 9th, 2021, during daytime hours depending on availability of the study investigator.

All patients admitted to the ED were triaged by registered nurses using the Swiss triage scale, a five-level triage scale with high inter-rater and intra-rater reliability [37]. Chief complaints, objective parameters (vital signs), and key questions are used to stratify the risk: 1—life-threatening emergencies requiring immediate care, 2—urgent conditions requiring medical evaluation within 20 min, 3 – semi-urgent conditions, requiring medical evaluation within 2 h, 4 – non-urgent conditions and 5—follow-ups.

This study was classified as a quality evaluation study by the local institutional review board (Kantonale Ethikkommission Bern (KEK), BASEC-Number Req-2020–01,266).

Inclusion/exclusion

We recruited a convenience sample ($n = 52$) of adult (≥ 18 years of age) ED patients triaged 2–5 on the Swiss triage scale, i.e. excluding critically ill/injured patients in shock, with a pain rating of NRS ≥ 3 on a numeric rating scale (0–10) who presented to the ED with the following complaints: traumatic and non-traumatic musculoskeletal pain (back, pelvis, neck, extremities), abdominal or chest pain, or headache.

Exclusion criteria were as follows:

- Hemodynamically unstable patient (e.g., planned for admission to the intensive care unit or deemed unstable by the physician in charge)
- Patients without decision-making capacity or with communication deficits (e.g., hearing loss, patient unable to communicate in German at a level suffi-

cient to give informed consent and answer questions about pain and anxiety)
- Altered mental status (e.g., intoxication, cognitive impairment, acute confusional state, acute psychosis, acute stroke, and developmentally delayed patients).
- History of drug abuse
- Patient unable to use VR due to vision problems (e.g., blindness or without his/her glasses).
- Patient suffering from epilepsy or other sensitivity to flashing light or motion
- Pregnancy or other medical condition prone to severe nausea and vomiting
- Patient suffering from claustrophobia
- Patients on non-invasive ventilation and patients requiring oxygen delivered by face mask
- Patients requiring droplet, aerosol and contact precautions
- Patient with injuries/skin affections (rashes, open wounds) to face/neck including traumatic brain injury that prevents the use of the VR headset
- Imprisoned patients
- Patient who participated in this study at a previous consultation
- Refusal to participate in the study

Baseline data

Sociodemographic data (gender, age, highest level of education, need to wear glasses, prior experience with VR), clinical data regarding pain presentation (localisation, association with trauma or tumor, presence of neuralgic pain, duration (acute < 24 h, subacute > 24 h, chronic > 3 months) and triage level according to the Swiss triage scale) [37] were collected in a survey.

Intervention

The study investigator (FB) informed the patient about the study aims, handed out the information form and ensured the absence of contraindications, responded to the patient's questions and collected the patient's free, informed and expressed consent.

The intervention consisted of the application of the Healthymind VR simulation (HEALTHY MIND, Paris, France), using a Pico G2 4 K VR headset (Pico Interactive Inc., San Francisco, California, USA) with resolution of 1920 × 2160 and a diagonal field of view of 101 degrees and Bose Quiet Comfort 35 II noise-cancelling headphones (Bose Corporation, Framingham, Massachusetts, USA) as an adjunct to usual care in the ED. Pain medication was administered throughout the patient's stay in the ED as it would be during a usual ED visit. In our ED, analgesia is administered according to a clearly defined standard and protocol, which was also adhered to unchanged during the study. If necessary the VR simulation was interrupted, so that medication (or other medical interventions) could be provided. The content of the simulation has been developed by a private company (HEALTHY MIND, Paris, France) and is a registered Class I medical device that is commercially available. The company was not involved in any aspects of the study. The immersive, but not interactive experience, consists of a contemplative relaxing landscape accompanied by a sound universe specifically composed to relax the patient. The patient could choose between either a forest or beach setting (Supplemental materials Figs. 1 and 2). The duration of the VR simulation was aimed at 20 min. If necessary, the simulation could be interrupted for important medical procedures or because of patient preference.

The application was controlled by the study investigator using an android tablet (Samsung Galaxy Tab A 2019, 4G; Samsung Electronics Co.,Ltd., Suwon, South Korea). The study investigator (FB) was always present during the simulation and worked with ED staff as necessary to ensure the patient was receiving appropriate clinical care throughout the duration of the intervention.

Primary and secondary outcomes

Primary outcome measures

Pain reduction Effectiveness of the VR simulation on the patients' self-assessment of their current pain intensity by a verbally administered numeric rating scale (NRS from 0 to 10 integers) immediately pre- and post-intervention. This scale has been demonstrated to be a valid and reliable tool for the assessment of acute pain in the ED [38].

Secondary outcome measures

Anxiety reduction Effectiveness of VR simulation on the patients' self-assessment of their current anxiety measured on a verbally administered numeric rating scale (NRS from 0 to 10 integers) immediately pre- and post-intervention. Furthermore, the validated Patient-Reported Outcomes Measurement Information System (PROMIS®) Anxiety short form 8a (8 Items) was filled out by the patient immediately before and after the intervention [39, 40].

To evaluate the raw score of the anxiety intensity on the PROMIS Anxiety short form 8a, the value of the response options ranging from one to five for each of the eight items is summarized (raw score ranges from 8 to 40, with higher scores indicating higher anxiety levels).

Vital signs Vital signs (blood pressure, heart rate, respiratory rate) were collected within a 10-min time-frame before and after the simulation.

Patient experience

Motion sickness Motion sickness was assessed on a verbally administered numeric rating scale (NRS 0 to 10), immediately before and after the procedure.

"Visually-induced motion sickness" was assessed with four-items (nausea, headache, blurred vision, dizziness) according to the Simulator Sickness Questionnaire (SSQ) adapted from Kennedy et al. (total score ranges from 1 = no simulator sickness to 5 = strong simulator sickness) [41].

Sense of presence and immersion Presence and immersion in the virtual world was determined according to the 6-item questionnaire developed by Slater-Usoh-Steed (total score ranges from 1 = no immersion to 7 = full immersion) [42].

User satisfaction User satisfaction was assessed using a 7-item questionnaire (1: I liked the experience with the simulation; 2: The headset and headphones were comfortable; 3: The audio quality was pleasant; 4: The image quality was pleasant; 5: The simulation improved my discomfort; 6: I would use this simulation again with these complaints; 7: I would recommend this simulation to others. Answers on a Likert Scale from 1 = totally disagree to 5 = totally agree) directly after the procedure.

Confounders

Information on the analgesic and anxiolytic medication administered in the ED was collected from the electronic patient healthcare dossier (e-care).

Statistical analysis

Data was analysed in Stata® 16.1 (StataCorp, The College Station, Texas, USA).

Baseline characteristics are presented as numbers and percentage or median and interquartile range (IQR) using descriptive statistics as appropriate. Comparisons between two independent groups (e.g. male vs. female) were carried out by Chi-square or Wilcoxon rank sum test depending on variable (categorial or continuous).

Pre- and post-simulation comparisons (e.g. pain) were performed with McNemars test or Wilcoxon signed rank test. Incomplete variables are indicated. No data were imputed. Only complete data pairs could be evaluated. A p-value < 0.05 was considered significant. There was no p-value adjustment in this exploratory data analysis. Effect sizes with 95% confidence intervals (CI) for pain and anxiety levels before and after the simulation were determined by Cohen's d. Effect size was determined as follows: Cohen's d < 0.5 small, 0.5 – 0.8 moderate, and > 0.8 large.

Results

Recruitment, missing data

A total of 310 ED patients were screened, with in 194 patients meeting eligibility criteria (Flowchart Fig. 1). After determining eligibility, 28 patients were missed by the study investigator due to patient undergoing a clinical evaluation, diagnostic study or procedure, 77 patients had already left the ED, and 37 patients refused to participate in the study. Finally, 52 patients were enrolled in this study, and all but 2 patients included completed at least 10 min of the VR simulation (two patients required urgent medical intervention leading to discontinuation of the simulation after one and two minutes, respectively).

Characteristics of patient population

Baseline characteristics of the patient population are detailed in Table 1. Overall, 52 patients were recruited, 32 females and 20 males. The most common pain localisations were extremities ($n = 15$, 28.8%), abdomen ($n = 12$, 23.1%), head ($n = 8$, 15.4%), back, and chest (each $n = 5$, 9.6%). About one third of patients presented with trauma-associated pain ($n = 16$, 30.8%). No patient presented with tumor-associated pain. Duration of pain was mainly acute (< 24 h) ($n = 16$, 30.8%) or subacute (> 24 h) ($n = 32$, 61.5%). Over ninety percent of patients were triaged level 3 ($n = 48$, 92.3%). Median pain level before VR on a NRS from 0 to 10 was 4.5 (IQR 3–7), median anxiety level was 4 (IQR 2–5). Median anxiety level on the 8-item PROMIS questionnaire was 14 out of a maximum of 40 points (IQR 11–21), with significant differences between females (median 18, IQR 12–26) and males (median 12.5, IQR 9.5–15), $p = 0.002$.

Simulation details

Technical details of the VR simulation are described in Supplement Table 1. 28.8% of simulations were interrupted at least once, mainly due to medical interventions. Mean simulation time was 20 min. No significant differences regarding gender were found.

Pain and anxiety reduction

Significant reduction in pain (NRS median pre-simulation 4.5 (IQR 3–7) vs. median post-simulation 3 (IQR 2–5), $p < 0.001$), and anxiety levels (NRS median pre-simulation 4 (IQR 2–5) vs. median post-simulation 2

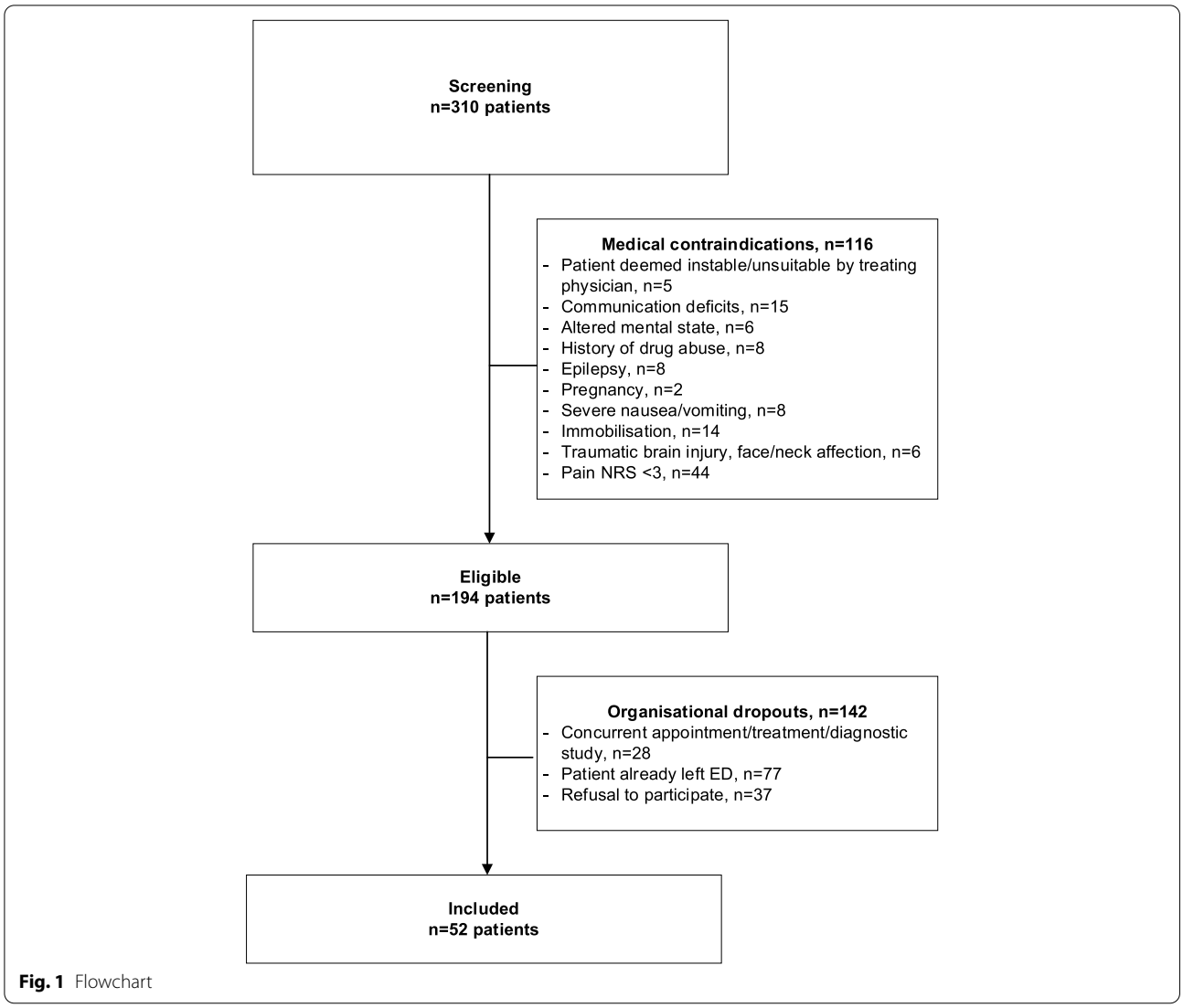

Fig. 1 Flowchart

(IQR 0–3), $p<0.001$; PROMIS median pre-simulation 14 (IQR 11–21) vs. median post-simulation 8 (IQR 8–11), $p<0.001$) was achieved (Table 2). Effect sizes were moderate to large (Cohen's d estimate for pain reduction = 0.59 (95% CI 0.19—0.98), Cohen's d estimate for anxiety level on NRS = 0.75 (95% CI 0.34—1.15), Cohen's d estimate for anxiety level on PROMIS = 1.15 (95% CI 0.72—1.57).

No significant differences in vital parameters were observed pre- and post-simulation (Supplement Table 2).

Pain and anxiety levels according to gender are detailed in Fig. 2.

Effects of the VR simulation on pain and anxiety levels (NRS 0–10) according to pain location are detailed in Fig. 3. No significant differences of the effectiveness of the VR simulation on pain and anxiety levels according to gender were found ($p=0.324$).

Forty-two percent of patients ($n=22$) received analgesics before the simulation, and only 11% ($n=6$) received opioids. Compared to males, the proportion of females receiving pain medications and opioids was significantly higher ($p=0.010$ and $p=0.040$, respectively) (Supplement Table 3). Only three patients received analgesics during the intervention.

A significant reduction of pain and anxiety levels was achieved using adjunctive VR (Fig. 4).

Patient experience

Presence and immersion in the virtual world according to the questionnaire of Slater, Usoh and Steed was "medium illusion of being there" (median 3.8 on a scale from 1 to 7, IQR (2.8–4.7). The 4-item Simulator Sickness Questionnaire in the intervention group revealed

Table 1 Baseline characteristics of the patient population as a whole and according to gender

	Total		Gender				
	Number	(*n* = 52)	Female	(*n* = 32)	Male	(*n* = 20)	*P*-value
Sociodemographic characteristics							
Age, med (IQR)	42	(35.5–55.5)	41.5	(36–56)	42.5	(34.5–56)	0.829
Gender, n (%)							
Male	20	(38.5)	0	(0.0)	20	(100.0)	
Female	32	(61.5)	32	(100.0)	0	(0.0)	
Highest education level, n (%)							
No formal education	1	(1.9)	1	(3.1)	0	(0.0)	
Obligatory	10	(19.2)	4	(12.5)	6	(30.0)	
Secondary	18	(34.6)	14	(43.8)	4	(20.0)	
Tertiary	23	(44.2)	13	(40.6)	10	(50.0)	0.184
Glasses, n (%)	22	(42.3)	15	(46.9)	7	(35.0)	0.399
Prior experience in VR, n (%)	22	(42.3)	13	(40.6)	9	(45.0)	0.756
Pain characteristics							
Pain localisation, n (%)							
Extremities	15	(28.8)	9	(28.1)	6	(30.0)	
Abdomen	12	(23.1)	5	(15.6)	7	(35.0)	
Head	8	(15.4)	7	(21.9)	1	(5.0)	
Back	5	(9.6)	3	(9.4)	2	(10.0)	
Chest	5	(9.6)	4	(12.5)	1	(5.0)	
Neck	2	(3.8)	2	(6.2)	0	(0.0)	
Pelvis	1	(1.9)	0	(0.0)	1	(5.0)	
Other	4	(7.7)	2	(6.2)	2	(10.0)	0.324
Trauma-associated pain, n (%)	16	(30.8)	11	(34.4)	5	(25.0)	0.476
Tumor-associated pain, n (%)	0	(0.0)	0	(0.0)	0	(0.0)	
Neuralgiform pain, n (%)	1	(1.9)	1	(3.1)	0	(0.0)	0.425
Duration of pain, n (%)							
Acute < 24 h	16	(30.8)	9	(28.1)	7	(35.0)	
Subacute > 24 h	32	(61.5)	21	(65.6)	11	(55.0)	
Chronic > 3 months	4	(7.7)	2	(6.2)	2	(10.0)	0.726
Triage level, n (%)							
2 (urgent)	2	(3.8)	2	(6.2)	0	(0.0)	
3 (semi-urgent)	48	(92.3)	29	(90.6)	19	(95.0)	
4 (non-urgent)	1	(1.9)	0	(0.0)	1	(5.0)	
5 (follow-up)	1	(1.9)	1	(3.1)	0	(0.0)	0.321
Pain level, pre [NRS 0–10], med (IQR)	4.5	(3–7)	5	(3–7.5)	4	(3–5.5)	0.255
Pain bearable, pre, n (%)	45	(86.5)	27	(84.4)	18	(90.0)	0.563
Anxiety level, pre [NRS 0–10], med (IQR)	4	(2–5)	5	(2–6)	3.5	(1–5)	0.205
PROMIS anxiety total, pre, med (IQR), [scores ranging from 8–40][a]	14	(11–21)	18	(12–26)	12.5	(9.5–14)	0.002
Pain level, pre [NRS 0–10], med (IQR)	4.5	(3–7)	5	(3–7.5)	4	(3–5.5)	0.255

[a] Number *n* = 51, due to incomplete questionnaire

Abbreviations: *IQR* Interquartile range, *med* Median, *PROMIS* Patient-Reported Outcomes Measurement Information System

a good tolerability of the VR simulation. Motion sickness measured on a NRS (0–10) was significantly lower after than before the simulation (median pre-simulation 0.5, IQR 0–3, median post-simulation 0, IQR 0–1, $p < 0.001$). The overall responses in the user satisfaction survey were positive. Over half of the patients agreed to the statement that the simulation helped with their pain ($n = 26$, 53.1%), and over 90% would recommend

Table 2 Pain and anxiety levels before and after the VR simulation. Median (IQR) if not mentioned otherwise

	Pre			Post			
	N	Result		N	Result		*P*-value
Pain level, [NRS 0–10]	52	4.5	(3–7)	50	3	(2–5)	< 0.001
Anxiety level, [NRS 0–10]	52	4	(2–5)	49	2	(0–3)	< 0.001
PROMIS anxiety total, scores ranging from 8–40	51	14	(11–21)	49	8	(8–11)	< 0.001
Pain bearable, n (%)	52	45	(86.5)	48	46	(95.8)	0.125

Abbreviations: *IQR* Interquartile range, *med* Median, *PROMIS* Patient-Reported Outcomes Measurement Information System

the simulation ($n = 46$, 93.9%) (Fig. 5). No significant differences in user satisfaction were found according to gender.

Discussion

Summary

In this prospective within-subject, repeated measure interventional pilot study, adjunctive virtual reality simulation proved to be feasible, effective and safe in a convenience sample of adult patients presenting with traumatic and non-traumatic pain, even in the busy setting of an adult ED, to reduce pain and anxiety.

Our patients mainly presented with acute and subacute musculosceletal, and abdominal pain, but also headache. We could demonstrate a significant pain and anxiety reduction after the 20 min VR distraction simulation, regardless of gender. Furthermore, the simulation proved effective regardless of the administration of analgesics before the intervention. We found good tolerability of the VR simulation with a high user satisfaction.

Recruitment

Mosadegi et al., studied feasibility of an immersive VR experience in hospitalized patients. Recruitment in their study proved crucial with only a small number of patients ultimately able and willing to participate. Consistent with the "digital divide" for emerging technologies, they found younger patients were more willing to participate, a finding we did not replicate [43, 44]. In the current study, patient recruitment was much less of an issue. The more advanced VR system used in the current study may contribute to the higher patient acceptance. The main reasons for exclusion were organizational (i.e. concurrent appointment, diagnostic study, medical treatment, or the fact that the patient had already left the ED after consultation). As we did not want to disturb normal patient diagnostic and treatment flow in our busy ED with the study intervention, this finding was not unexpected.

Effectiveness on pain and anxiety

The current study found a significant reduction in pain and anxiety levels through the VR simulation. Our results confirm the little existing evidence regarding effectiveness of VR on pain reduction in the ED. Sikka et al. were the first to study of the effect of VR in ED patients with acute pain [34]. In their convenience sample of 100 adult patients presenting to an urban academic ED with undifferentiated pain of at least 3 on a NRS (0–10), around 2/3 of the population were women and African American, presenting mainly with musculosceletal, abdominal and back pain. The mean VR application time in their study was shorter (6.9 ± 4.4 min). Both their reported pain and anxiety scores dropped significantly from pre- to post-intervention (pain 7.16 ± 2.5 to 6.49 ± 2.7, $p < 0.0001$; anxiety 2.06 ± 0.8 to 1.81 ± 0.8, $p < 0.0001$) with good tolerability. However, as a main limitation, they did not provide information regarding concurrent analgesic medication administered. In our study, we noticed a significant reduction of pain and anxiety levels, regardless of administration of analgesics before the simulation.

Spiegel et al. conducted a prospective randomized controlled study (VR on demand vs. specialized television program) in hospitalized patients with pain scores of at least 3 out of 10 on a NRS and achieved a similar level of pain reduction (mean within-subject difference in immediate pre- and post-intervention pain scores in the VR group (-1.72 points; SD 3.56), with a significantly greater pain reduction in the VR group than in the control group (-0.46 points; SD 3.01) [14]. Although the effect of VR on pre- and post-simulation pain scoring was statistically significant, the absolute reduction in pain scores in these and our patients was relatively small but clinically meaningful. The minimal clinical important difference (MCID) on the NRS usually lies between 1 and 2 points [45, 46]. A recent study demonstrated that patients perceived a change of 1.65 points on NRS in their pain severity as meaningful [47].

We did not find a significant change in physiological parameters, in line with the current lack of firm evidence that VR therapy can affect autonomic arousal or

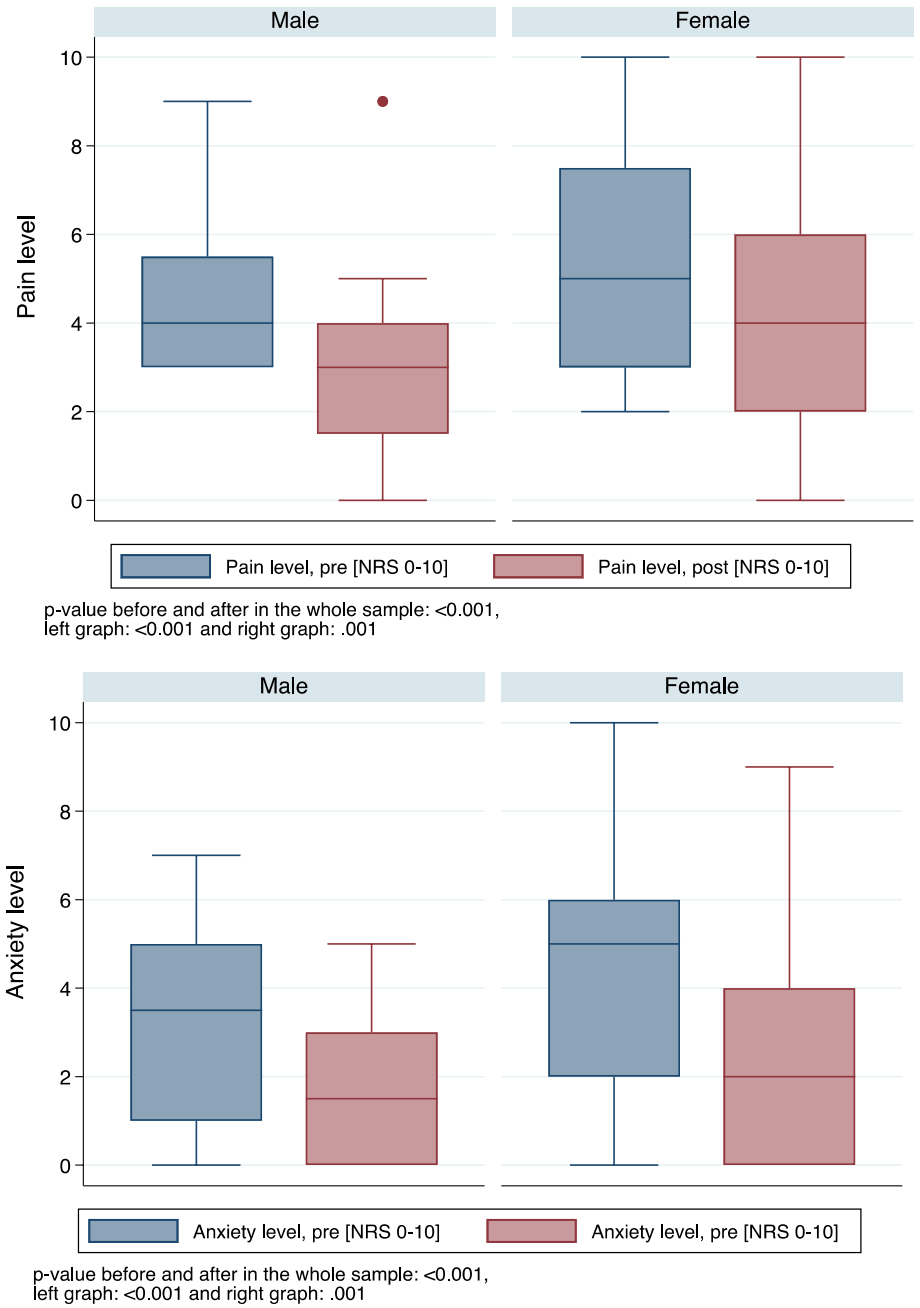

Fig. 2 Pain and anxiety levels (NRS 0–10) before and after the VR simulation according to gender

demonstrate its analgesic properties through modulation of these parameters [20].

Increased levels of anxiety can lead to worsening pain perception, decreased pain threshold and less cooperative patients [20, 48]. We found significantly higher levels of anxiety in women, and such gender differences have been reported elsewhere [49]. The ability of VR to remove patients from the anxiety-inducing clinical environment of a busy ED and immerse them in a relaxing virtual environment reduced both the associated pain and anxiety regardless of gender in our patients. One might also speculate, that VR pain and

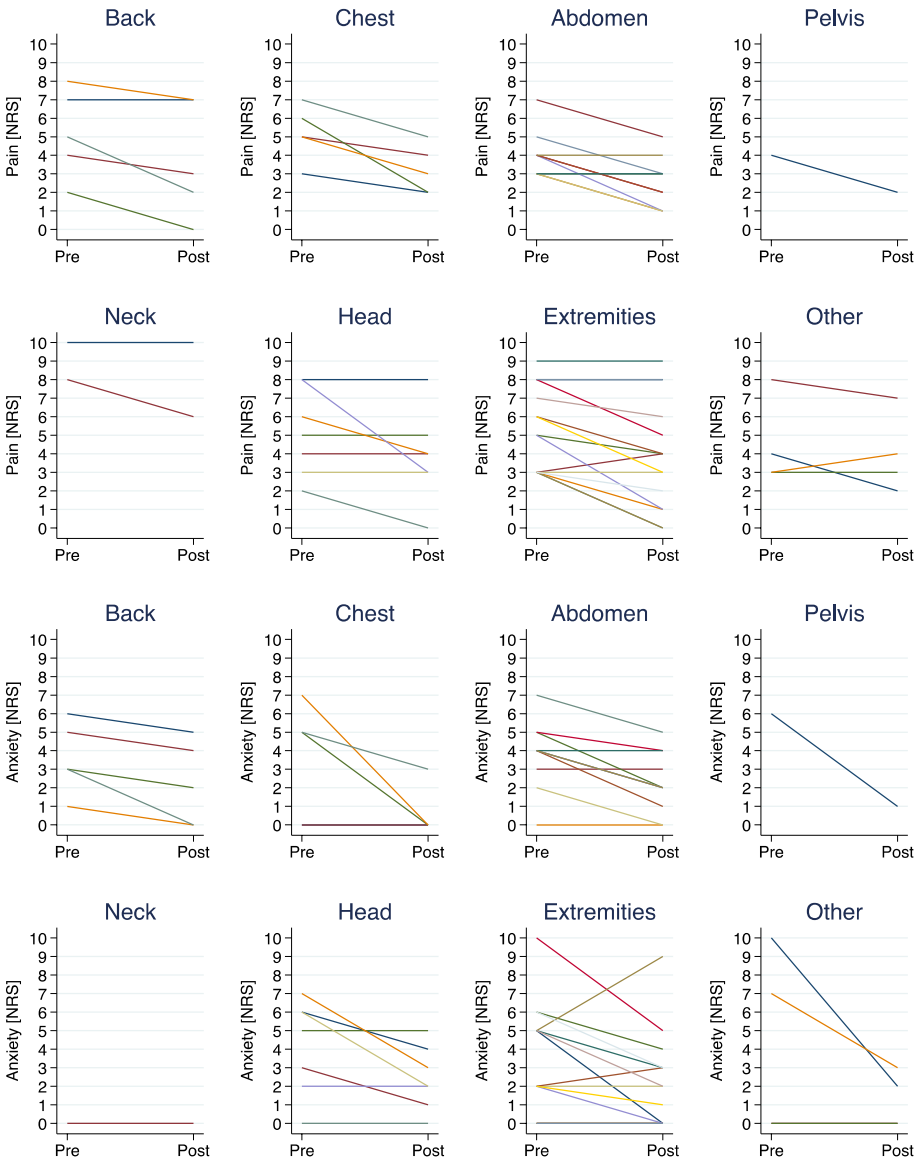

Fig. 3 Pain and anxiety levels (NRS 0–10) before and after the VR simulation according to pain location

anxiety control can potentially help reduce the patients risk of developing chronic pain or post-traumatic stress symptoms in the future.

Patient experience

Our simulation was well tolerated, with a low incidence of side effects such as nausea, headache, blurred vision or dizziness or motion sickness, in accordance with previous other reports [20, 21]. The use of calm VR worlds may have helped minimize simulator sickness in the current study.

Strong evidence has also shown that the quality of VR and the amount of immersion as well as interactivity delivered by the VR technology directly correlates with the measured quantity of analgesic effect [8, 9, 48]. Even though the sense of presence and immersion measured according to Slater in our patients was medium (probably due to interruptions, and the busy setting ED), our simulation still proved to be effective and safe with good subjective user satisfaction. In comparison to other VR systems, the interactivity of our simulation was deliberately low, in order not to overburden the VR inexperienced person. Further studies are needed to determine the optimal degree of presence and immersion as well as interactivity possible to achieve good results in the busy setting of an adult ED.

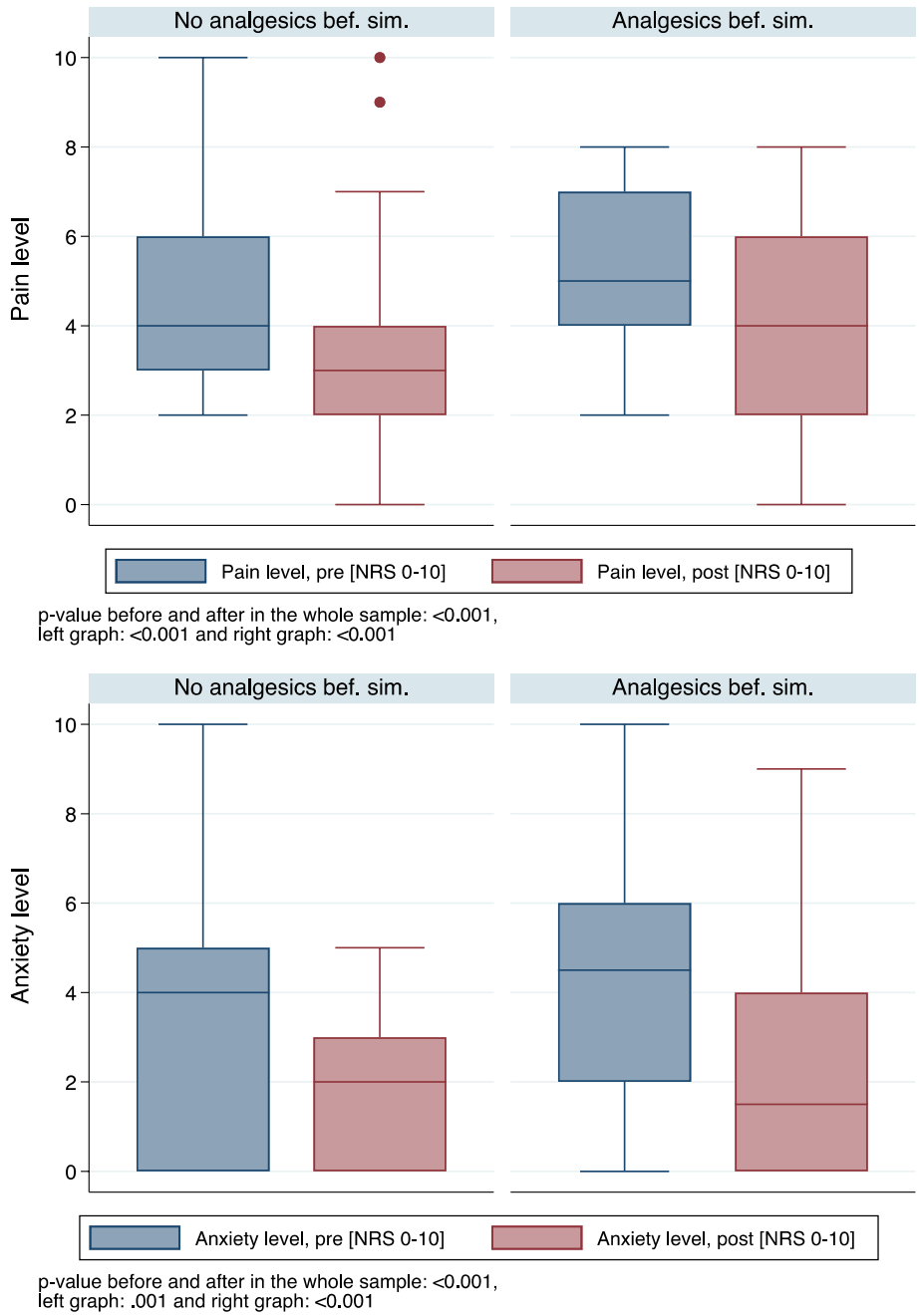

Fig. 4 Pain and anxiety levels (NRS 0–10) before and after the VR simulation according to administration of analgesics before the simulation

Limitations

These results need to be interpreted with some reservations. First, this was a single tertiary care academic center study with a limited number of participants, that may be affected by selection bias, and thus have impact on generalizability. Furthermore, as this was a feasibility study, we included an uncontrolled convenience sample (no randomization or blinding), and results may been influenced by performance bias. We cannot exclude the novelty effect of using a previously unknown technique [50], but other studies have shown VR continued to reduce pain with repeated use [32]. This research was limited to patients with a self-reported pain level of 3 or greater on a NRS but did not control for baseline medication, final diagnosis, or pharmacological interventions. But note that we report pre- and post-intervention measures for

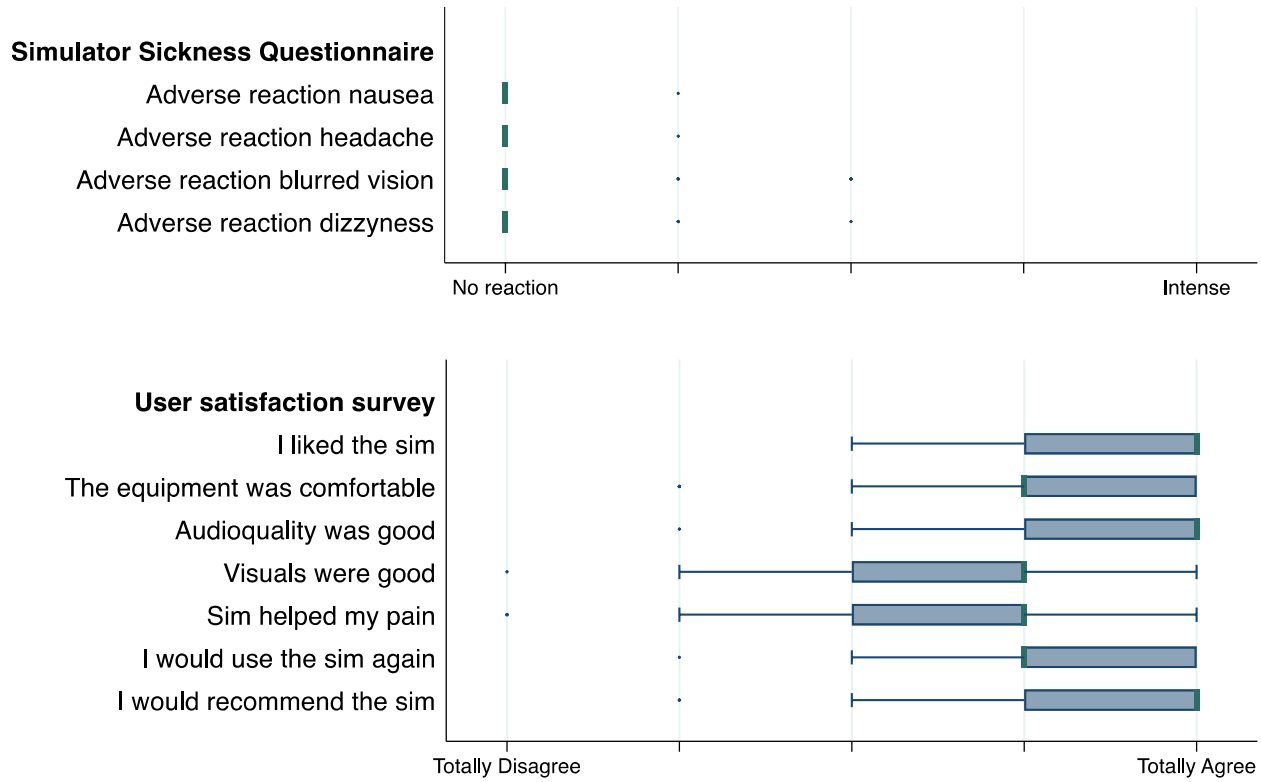

Fig. 5 Results of the Simulator Sickness Questionnaire and User Satisfaction Survey. The medians of the distribution are indicated by a bold line. Outliers, i.e., the last observed value ≤ 1.5 × interquartile range above the upper quartile/below the lower quartile, are indicated with a point marker

each individual patient, and only three patients received additional pain medications during the VR.

Although premature to recommend VR as standard of care in the ED, the current results warrant consideration of a multicenter study in a larger patient group. Further comprehensive and structured research is needed to measure additional confounders and outcomes to identify optimal use of the VR simulation application in the ED setting. In addition, studies on the exact mechanism of action of the VR simulation beyond simple distraction would be valuable.

Conclusion

VR simulation for pain and anxiety reduction in the busy setting of an ED is feasible, effective, and safe. Further and larger randomized controlled studies are needed to better characterize its impact on pain perception and resource utilization.

Abbreviations

CI: Confidence interval; ED: Emergency department; IQR: Interquartile range; MCID: Minimal clinical important difference; Med: Median; NRS: Numeric rating scale; PROMIS: Patient-Reported Outcomes Measurement Information System; SSQ: Simulator sickness questionnaire; VR: Virtual reality.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12873-022-00671-z.

Additional file 1: Supplement table 1. Technical details of the VR simulation. **Supplement table 2.** Vital parameters before and after the VR simulation. **Supplement table 3** Analgesics administered before, during or after the simulation, according to gender. **Supplement figure 1.** Beach simulation. **Supplement figure 2.** Forest simulation.

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Authors' contributions

TB: conception, design, acquisition, analysis, interpretation, drafting and revising. FB: conception, design, acquisition, drafting and revising. AKE: conception, design, drafting and revising. WEH: conception, design, interpretation, drafting and revising. MM: conception, design, analysis, interpretation, drafting and revising. TCS: conception, design, acquisition, interpretation, drafting and revising. All authors have approved the submitted version. All authors have agreed both to be personally accountable for their own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Availability of data and materials
Data contain potentially identifying or sensitive patient information. Data used in this study are available upon reasonable request from the corresponding author at the Emergency Department of the University Hospital Bern, Switzerland to researchers eligible under Swiss legislation to work with codified personal health care data. Eligibility will be determined by Cantonal ethics committee Bern.

Declarations

Ethics approval and consent to participate
This study was classified as a quality evaluation study by the local institutional review board (Kantonale Ethikkommission Bern (KEK), BASEC-Number Req-2020–01266). Informed consent for study participation was obtained from each patient. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication
Informed consent for publication of study results was obtained from each patient. No individual details are revealed in the publication.

Competing interests
WEH has received research funding from the European Union, the Swiss National Science foundation, Zoll foundation, Dräger Medical Germany, Mundipharma Research UK, MDI International Australia, Roche Diagnostics Germany, all outside the submitted work. WEH has provided paid consultancies to AO foundation Switzerland and MDI International Australia, all outside the submitted work.WEH has received financial support for a congress he chaired from EBSCO Germany, Isabel Healthcare UK, Mundipharma Medical Switzerland, VisualDx USA, all outside the submitted work.
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Publisher's Note

Critical Care

RESEARCH

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Discomfort improvement for critically ill patients using electronic relaxation devices: results of the cross-over randomized controlled trial E-CHOISIR (Electronic-CHOIce of a System for Intensive care Relaxation)

Lili Merliot-Gailhoustet[1], Chloé Raimbert[1], Océane Garnier[1], Julie Carr[1], Audrey De Jong[1], Nicolas Molinari[2], Samir Jaber[1] and Gerald Chanques[1*]

Abstract

Purpose: To assess the impact of different electronic relaxation devices on common stressful patient symptoms experienced in intensive care unit (ICU).

Methods: Sixty critically ill patients were enrolled in four relaxation sessions using a randomized cross-over design: standard relaxation (TV/radio), music therapy (MUSIC-CARE©), and two virtual reality systems using either real motion pictures (DEEPSEN©) or synthetic motion pictures (HEALTHY-MIND©). The goal was to determine which device was the best to reduce overall patient discomfort intensity (0–10 Numeric Rating Scale (NRS); primary endpoint). Secondary endpoints were specific stressful symptoms (pain, anxiety, dyspnea, thirst, and lack of rest feeling) and stress response measured by Analgesia/Nociception Index (ANI). Multivariate mixed-effect analysis was used, taking into account patient characteristics and multiple measurements.

Results: Fifty patients followed the full research protocol, and ten patients did at least one research planned session of relaxation. HEALTHY-MIND© was associated with a significant decrease in overall discomfort, the primary endpoint (median NRS = 4[2–6] vs. 2[0–5]; $p = 0.01$, mixed-effect model), accompanied by a significant decrease in stress response (increase in ANI, secondary endpoint; $p < 0.01$). Regarding other secondary endpoints, each of the two virtual reality systems was associated with a decrease in anxiety ($p < 0.01$), while HEALTHY-MIND© was associated also with a decrease in pain ($p = 0.001$) and DEEPSEN© with a decrease in lack of rest ($p = 0.01$). Three incidents (claustrophobia/dyspnea/agitation) were reported among 109 virtual reality sessions. Cybersickness was rare (NRS = 0[0–0]).

Conclusion: Electronic relaxation therapy is a promising, safe, and effective non-pharmacological solution that can be used to improve overall discomfort in alert and non-delirious ICU patients. Its effectiveness depends on technical characteristics (virtual reality using a synthetic imagined world versus a real world or music therapy alone without virtual reality), as well as the type of symptoms.

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Key messages

- Electronic relaxation therapies are effective supportive care tools for improving stressful symptoms in ICU patients.
- Effectiveness depends on the type of symptom and the characteristics of the devices.
- Overall discomfort and adrenergic stress response are more significantly improved by virtual reality using a synthetic imagined world than using a real world or music therapy alone.

Keywords: Virtual reality, Music therapy, Non-pharmacological therapies, Supportive care, Intensive care

Introduction

Admission in an intensive care unit (ICU) is associated with many causes of suffering, related to the illness or intensive therapies and environment [1, 2]. The consequences can be serious, from the development of an adrenergic stress response interfering with critical illness (tachycardia, polypnea, patient/ventilator asynchrony, agitation, immunosuppression, etc.) [3, 4] to the development of a post-intensive care syndrome (PICS), including neuro-psychological disorders (anxiety, depression, post-traumatic stress syndrome) and chronic pain that delay the return to a social and professional normal life [5, 6]. The link between suffering in ICU and the development of PICS has been highlighted for a long time [7], leading to conceptualize modern intensive care as the most humane possible [8, 9]. For all these reasons, supportive care has become part of intensive care, along with the treatment of organ dysfunctions. In order to prevent drug-related side effects that can be serious in critically ill patients [10], current guidelines for the management of pain, agitation, delirium, immobility, and sleep disruption (PADIS) suggest to develop non-pharmacological therapies [1, 11].

Electronic innovative technology has been developed in medical settings, such as music therapy using programmable shape and length of music score [12, 13], and immersive virtual reality (VR), to offer a non-pharmacological treatment of pain and anxiety [14]. The literature regarding the use of VR in medical care is beginning to be abundant, but its use to relieve overall discomfort and baseline stressful symptoms in ICU has never been the object of a randomized study.

In this context, we propose to assess the impact of different electronic relaxation devices to improve ICU patients' stressful symptoms, through a cross-over randomized study. The primary goal was to determine the best technique to improve overall patient discomfort (primary endpoint), among 3 different relaxation devices (VR system with real motion pictures, VR system with computer-generated pictures, music therapy provided through a computer and an headset), compared to a standard relaxation session (TV, radio available at bedside). Secondary goals were to measure the impact on 5 of the main stressful symptoms experienced by ICU patients (pain, anxiety, dyspnea, thirst, and lack of rest) and on electrophysiological measurement of stress response using the Analgesia/Nociception Index (ANI) and usual physiological variables (secondary endpoints).

Material and methods

Ethics approval

This randomized controlled trial (RCT) was approved by an ethics committee [*Comité de Protection des Personnes Sud-Méditerranée-1* (ID-RCB:2016-A00748-43)] according to French law [15] and registered on Clinical Trials NCT04017299, 12 July 2019. The research was funded by the French healthcare ministry (Direction Générale de l'Offre de Soins (DGOS)/General Healthcare Supply Direction).

Patient population

The trial took place in the medical-surgical ICU of the University Hospital of Saint Eloi, Montpellier, France, from July 2019 to December 2019.

All consecutive patients over 18 yo admitted to the ICU were eligible if they were alert and non-delirious, following the French validated versions of the Confusion Assessment Method for the ICU (CAM-ICU) [16, 17] and the Richmond Agitation Sedation Scale (RASS) that had to be ≥ 0 [18], and with current organ dysfunctions defined by a Sequential Organ Failure Assessment (SOFA) score ≥ 3 [19].

The exclusion criteria were: patient transferred from another ICU, dying patients, patients needing hygiene precautions limiting the access to the headsets, patients usually treated by antipsychotics or with previous known cognitive impairment, patients hospitalized for brain injury, and according to French law [15]: pregnant or breastfeeding women, patients under tutelage or curatorship, patients not registered with the national social security system, or who refused to participate.

Conduct of the study and description of the electronic relaxation tools

Patients were screened daily for eligibility by investigators and included in the study after written consent. Patients underwent four relaxation sessions consecutively, after randomization of the session order, using a cross-over design. The cross-over randomized design was chosen to take into account the possible impact of the session order on the outcomes, the subjective nature of the measurement, and the possible cumulative effect on memory for repeated sessions during a short time (intensive care). The randomization was made by the statistic department. The randomization table was generated by randomly drawing the permutations between the 4 interventions (relaxation sessions). The order of the 4 relaxation sessions was provided via sealed numbered envelopes available for the ICU investigators who opened the envelopes after enrolling the patient consecutively. At least one hour of washout was planned between two sessions. The four relaxation sessions are described as follows:

- *STANDARD SESSION*: a relaxation and distraction period of 15 min during which usual distraction was chosen by the patient (e.g., television, radio). The bedroom's door was kept closed, and any nursing or medical procedures of care were prevented during the session.
- *MUSIC-CARE*© (Paris, France)**:** a 15-min relaxation session of psycho-musical intervention (music therapy) using the MUSIC-CARE© device. As described previously [12], this device provides pieces of music played by musicians, with music score's components (tempo, intensity, number of instruments) decreasing slowly until a minimal stage, and re-increasing just before the end of the relaxation session (U-shaped score). The duration of the session is modifiable. Music therapy was provided through a high-quality audio headset, the style of music being chosen by the patient from the range offered by the software available at each bed-side computer, with the duration of the session set at 15 min.
- *HEALTHY-MIND*© *VR system* (Paris, France)**:** a 15-min relaxation session of VR immersing the patient into an artificial world created from computer-generated pictures using a software linked to the Occulus Rift© helmet and a headset. The patient is able to choose four kinds of environments (beach, mountain, snow and Japan) using synthetic motion pictures, breathing exercises and hypnotic speech, as proposed by the manufacturer.
- *DEEPSEN*© *VR system* (Saint-Didier-au-Mont-d'Or, France)**:** a 15-min relaxation session of VR, immersing the patient into a series of filmed sequences, using an "all-in-one" headset created by the company. The patient was able to choose the film among four kinds of videos (Norway, mountain countryside, India, and Camargue, a quiet seaside in South of France, near Montpellier) using real motion pictures, breathing exercises, and hypnotic speech, as proposed by the manufacturer.

Figure 1 shows an example of virtual reality's world and headsets. Headsets and headphones were cleaned

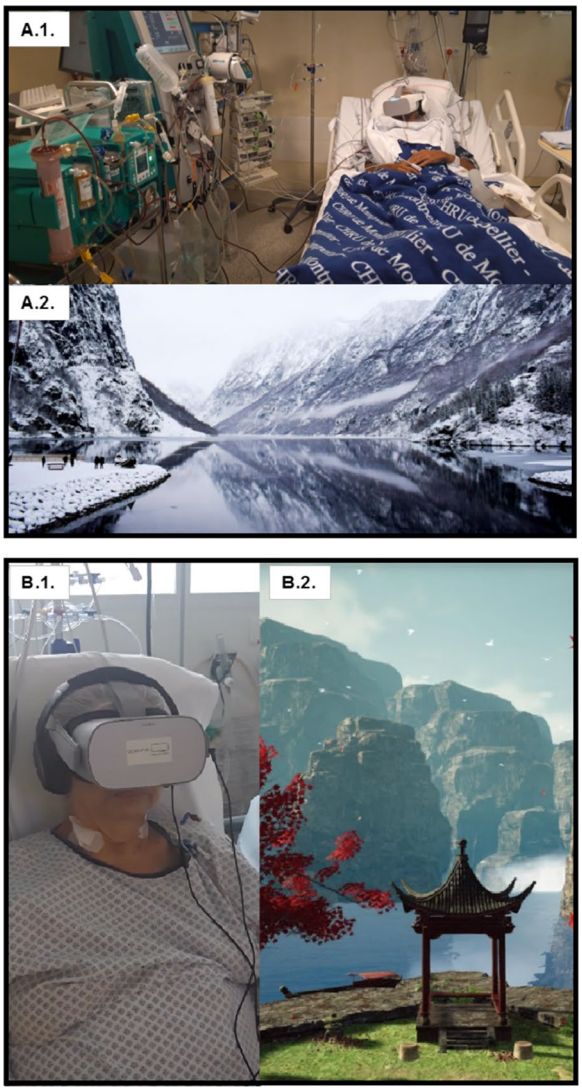

Fig. 1 Examples of virtual reality's worlds. A.1. ICU patient with DEEPSEN © Virtual Reality headset. A.2. DEEPSEN© provides motion pictures from real environment, here Norway. B.1. ICU patient with HEALTHY-MIND© Virtual Reality headset. B.2. HEALTHY-MIND© provides synthetic motion pictures from imagined environment, here Japan

before and after each session. Protections were placed between the device and the patient.

Data handling

After enrollment in the study, a relaxation technique was proposed to the patient at the time of the day she or he preferred, from morning to afternoon, in the order of randomization. At baseline, before starting the session, the following vital variables were recorded from the patient's bedside monitoring: heart rate, blood pressure, respiratory rate, and Analgesia/Nociception Index (ANI). ANI measures heart rate variability from the bed-side electrocardiographic monitoring of the patient, providing a number from 0 to 100 through spectral analysis. This number is an estimation of the balance between parasympathetic and sympathetic outflows: 100 means a high parasympathetic modulation (low stress level = low risk of suffering) and 0 means extremely low parasympathetic modulation (high stress level = high risk of suffering) [20]. Only instant-ANI (PhysioDoloris© monitor, MDoloris Medical Systems, Lille, France) was recorded because it provided an analysis of heart rate variability on 64 s compared to 4 min for mean-ANI. It had previously been reported that instant-ANI was more accurate than mean-ANI in ICU patients [20, 21]. Delirium was assessed before each session by the CAM-ICU. In the absence of delirium, the relaxation session was provided and the patient was asked to report her or his symptoms' intensity before and after the session using a large visual Numerical Rating Scale (NRS) ranging from 0 to 10 (0 = no symptom at all; 10 = the worst possible symptom). This scale is the most valid self-report pain scale in ICU patients [22] and is therefore the tool recommended to assess pain intensity in ICU patients who are able to communicate [1, 23]. Intensities of other stressful symptoms can also be measured using self-report pain scales such as the 0–10 NRS [2] and were currently used in studies investigating thirst [24], anxiety [25, 26], dyspnea [25], and sleep privation [1]. Overall discomfort (physical and psychological discomfort) and five current stressful symptoms were assessed: pain, anxiety, thirst, dyspnea, and lack of rest. All parameters were recorded again after the end of each relaxation session.

Statistical analysis

Primary endpoint

Variation in the intensity of overall patient discomfort before and after each relaxation session to determine which technique was the most effective to reduce discomfort.

Exploratory secondary endpoints

Secondary endpoint related to patient's suffering Variation in the intensity of five stressful symptoms: pain, anxiety, dyspnea, thirst, lack of rest [2]

Secondary endpoints: physiological stress response Variation in physiological variables (heart rate, arterial blood pressure, respiratory rate), and ANI, as an electrophysiological parameter related to the stress response.

Safety and feasibility

The intensity of cybersickness (defined as a visuospatial vertigo associated or not with nausea and vomiting) was self-reported by the patient after the relaxation session. The feasibility of the relaxation technique was assessed by the investigation team using the 0–10 NRS to report the ease of device installation/setting for the investigators (from 0 "not easy at all" to 10 "the easiest possible"). The investigation team collected also any incidents that occurred during the relaxation sessions.

Number of patients needed to be enrolled

Taking into account the exploratory nature of the study, the sample size was calculated based on the number of possible orders of relaxation sessions that was calculated as follows: 4 types of sessions $\times 3 \times 2 = 24$ possible orders of sessions. Two different patients were expected to be enrolled at least for each kind of sequence (i.e., 48 patients), to allow for a homogenous repartition of different possible relaxation orders among the studied population. To take into account lost to follow-up patients and missing data, 60 patients were expected to be enrolled in the study.

Presentation of data and analysis

Description of the data was made using usual descriptive statistics for quantitative variable (mean (standard deviation) or median [25th–75th percentiles] depending on the distribution of the data) and for qualitative data (n, number of data available (frequency in percentage)). All relaxation sessions were included in intent-to-treat analysis. Univariate analysis was carried out to compared data «before» versus «after» each relaxation sessions for NRS, ANI, and physiological variables, using the Student's t test or the Wilcoxon–Mann–Whitney's U test according to the distribution of data.

The comparison of electronic techniques between them and the standard relaxation session was carried out by a mixed-effect multivariate analysis, adjusted on session's order and significant patient's characteristics, to take into account potential biases (fixed factors) and repeated measurements (patient was considered as the

random factor). A backward selection was made manually by removing at each step the variable with the highest *p*-value to ultimately keep only the significant variables ($p < 0.05$) in the model. The type of relaxation technique and the session order were always maintained in the model during the selection.

For all statistical tests, a *p* value of 0.05 was considered statistically significant. Data were analyzed by an independent statistician using the SAS Enterprise Guide version 9.4 (SAS Institute, Cary, NC).

Results

Patient baseline characteristics

Among the 277 patients admitted to the ICU during the study period, 190 were eligible and 60 were enrolled. Figure 2 shows the study flow chart. Fifty patients (83%) achieved the full protocol (four relaxation sessions), and ten patients performed one to three sessions. Reasons to not perform all sessions were mainly sight problems, claustrophobia, patients who became too tired or delirious (CAM-ICU+), or who left the ICU before the end of the protocol. Patient demographic and medical characteristics are summarized in Table 1. Briefly, patients were admitted to the ICU for a surgical reason in 58% and for a medical reason in 42%. Multimodal analgesia was used preferentially with a minimal use of major opioids and a short duration of sedation in order to optimize the liberation from invasive mechanical ventilation. During the first session, 18 patients were assisted with high-flow oxygen therapy, two with non-invasive ventilation (facemask), and one was intubated; two patients were on continuous extra-renal replacement therapy; and seven required vasopressors.

Impact of relaxation sessions on overall discomfort (primary endpoint)

In univariate analysis, HEALTHY-MIND© VR system was associated with significant decrease in overall discomfort (median NRS = 4 [2–6]) before the session versus 2 [0–5] after the session, $p = 0.02$). The two other specific relaxation techniques and the standard relaxation were not associated with significant changes (Table 2). These results were confirmed by mixed-effect multivariate analysis, showing that HEALTHY MIND© VR system was the only relaxation technique associated with a significant decrease in overall discomfort (reduction by 0.8 point; $p = 0.01$, mixed-effect model) (Table 3).

Impact of relaxation sessions on five common ICU stressful symptoms (exploratory secondary endpoints related to patient's suffering)

Variation in symptoms' intensities is shown in Table 2 (univariate analysis) and Table 3 (multivariate analysis). HEALTHY-MIND© VR system was associated with a reduction in pain and anxiety intensities by 0.8 points compared to the standard relaxation ($p = 0.001$ and 0.004, respectively, mixed-effect model). DEEPSEN© VR system was associated with a reduction in anxiety by 0.9 point ($p = 0.004$) *and* a reduction in lack of rest by 1.6 points ($p = 0.01$).

Impact of relaxation sessions on analgesia/nociception index (ANI) and physiological variables (exploratory secondary endpoints)

ANI increased significantly after each relaxation session except for the standard relaxation (univariate analysis, Table 2). The multivariate analysis showed a significant change for HEALTHY-MIND© VR system only (estimate gain + 13, $p < 0.01$) (Table 3). Other physiological variables did not change significantly.

Safety

Incidents were reported in three patients during the 109 VR sessions: self-withdrawal related to claustrophobia ($n = 1$) or agitation ($n = 1$) and displacement of the headset to the nose and mouth associated with tachypnea and dyspnea ($n = 1$). In all, premature interruptions of relaxation sessions before the end of the 15-min planned session occurred in 12/218(6%) sessions (3/54(6%), 4/53(8%), 3/56(5%), 2/55(4%), for the standard relaxation, HEALTHY-MIND© and DEEPSEN© VR systems, and MUSIC-CARE©, respectively). Main reasons were eyesight problems, annoyance, interruptions related to visit of patient's relatives, or urgent care. Cyber-sickness was rarely observed after the use of music therapy or VR headsets, with a median NRS of dizziness of 0 [0–0]. Five on 56 patients (11%) reported a NRS ≥ 4 for dizziness after a session with DEEPSEN© VR system, 2/53 (4%) after a session with HEALTHY-MIND© VR system, 1/55 (2%) after standard session, and none after MUSIC-CARE© relaxation. No other serious side effects were observed. Ten patients (17%) did not complete the four sessions: three because of discharge from ICU, three because of fatigue or anxiety, two because of eyesight problems, one because of the appearance of delirium, and one who developed claustrophobia.

Feasibility

The placement and use of devices were easy according to the investigators (feasibility-NRS of 10 [10;10] for standard; 10 [9;10] for MUSIC-CARE©; 10 [8;10] for DEEPSEN©; 10 [8;10] for HEALTHY-MIND©). Investigators were present for the placement and configuration of headset. Some patients learned their use very quickly and used it with autonomy after the end of the research protocol.

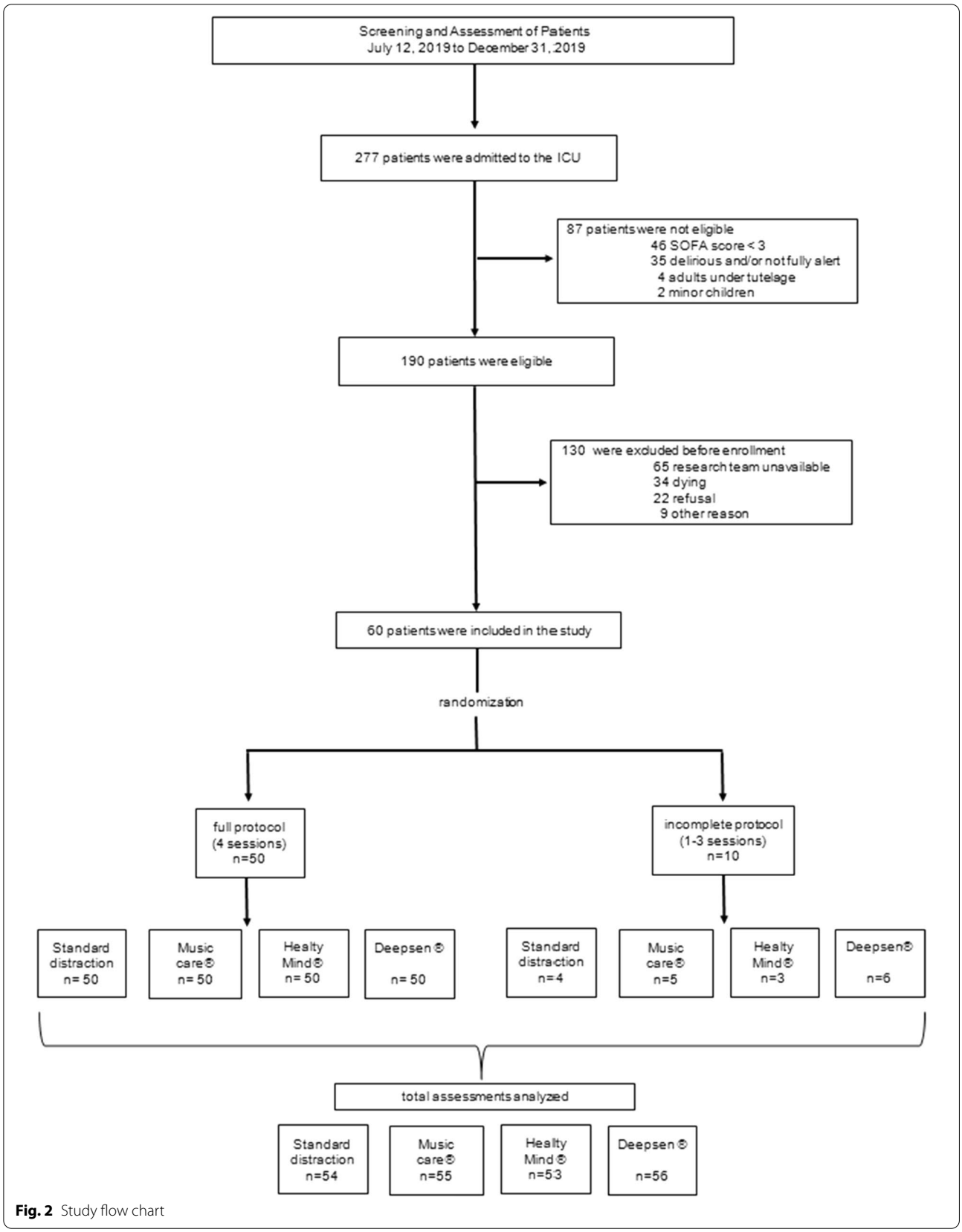

Fig. 2 Study flow chart

Table 1 Demographic and medical characteristics

Medical characteristics upon admission to ICU	
Age (yr)	62 [51–69]
Sex (F/M)	20/40
BMI (kg.m^{-2})	27 [22–30]
SAPS II score	36 [28–44]
SOFA score	6 [4–8]
Reason for admission to the ICU	
Liver transplant, *n* (%)	18 (30%)
Post-operative, *n* (%)	17 (28%)
ARDS, *n* (%)	6 (10%)
Hemorrhagic shock, *n* (%)	5 (8%)
Septic shock, *n* (%)	4 (7%)
Others, *n* (%)	10 (17%)
Characteristics upon enrolment into the study	
RASS level	0 [0–0]
CAM-ICU negative, *n* (%)	60 (100%)
Length of stay in ICU before enrollment (days)	2.7 [1.1–3.6]
Invasive mechanical ventilation before enrollment, n (%)	36 (60%)
Time between extubation and enrollment (hours)	25 [14–42]
Sedation before enrollment, *n* (%)	36 (60%)
Number of tubes or catheters at inclusion	4 [2–5]
Medical characteristics of patients on the first relaxation session	
Mechanical ventilation, *n* (%)	1 (2%)
Non-invasive ventilation, *n* (%)	2 (3%)
High flow nasal oxygen therapy, *n* (%)	18 (30%)
Dialysis, *n* (%)	2 (3%)
Vasopressors, *n* (%)	7 (12%)
Sedation at enrollment, *n* (%)	0 (0%)
Analgesic administration at enrollment, *n* (%)	45 (75%)
Acetaminophen, *n* (%)	19 (32%)
Nefopam, *n* (%)	38 (63%)
Tramadol, *n* (%)	32 (53%)
Major opioid, *n* (%)	2 (3%)
Epidural analgesia, *n* (%)	3 (5%)
Anxiolytic administration at enrollment, *n* (%)	16 (27%)
Patients' outcomes	
Length of stay in ICU (days)	8.0 [5.2–12.1]
Mortality in ICU, *n* (%)	3 (5%)
Total length of stay in hospital (days)	21.8 [12.6–39.3]
Total mortality in hospital, *n* (%)	7 (12%)

Continuous data are expressed in median [25th–75th percentiles].

BMI Body mass index; *SAPS II* Simplified acute physiology score II; *SOFA* Sequential organ failure assessment score; *RASS* Richmond agitation-sedation scale; *CAM-ICU* Confusion assessment method for the ICU; *ARDS* Acute respiratory distress syndrome

Discussion

The main findings of this cross-over randomized study are that using electronic relaxation devices is feasible, safe, and well tolerated in more than 90% of alert and non-delirious critically ill patients. Some devices are more effective than others to relieve ICU patients from stressful symptoms. VR with synthetic motion pictures (imagined world) is the most effective to decrease overall discomfort, compared to real world or music therapy only (primary endpoint). This result is reinforced by a significantly greater increase in ANI with this kind of VR compared to other devices. Exploratory secondary endpoints may explain this result because this relaxation device was also associated with a significant decrease in both pain and anxiety, while the other kind of VR (real world) was associated with a significant decrease in anxiety and lack of rest, but not pain (multivariate analysis). These findings should be discussed and nuanced by the fact that some symptoms (pain, anxiety, dyspnea) had a light intensity (< 4/10) in the included population. These devices could demonstrate different properties in other populations of ICU patients, and these results should not discourage further research in patients with moderate to severe pain, anxiety, or dyspnea. Such research is mandatory because similar relaxation devices may have different impacts depending on the type of symptoms, as reported by the present study.

The study highlights also that today pain is not always the most important stressful symptom in ICU patients, contrary to other symptoms like thirst. Pain management has been improved in ICU for many years [27], including the elaboration of new pain scales [22, 28], the measurement and recognition of pain and related outcomes [29, 30], and the development of practice guidelines promoting multimodal analgesia as the top priority [1]. Pain could be considered as the cornerstone for improvement in patient suffering in ICU. However, other symptoms should be considered [2, 31] and have created more and more interest, like anxiety [26], dyspnea [32, 33], thirst [24, 34], and sleep disruption [1]. It should be noted that for the latter symptom, the intensity of "lack of rest" was measured in the present study instead of "sleep disruption" because the relaxation sessions were organized during the day and not at night.

There has been an increased interest to use non-pharmacological strategies to relieve stressful symptoms in ICU. Listening music was proved to be effective on anxiety [26] while optimizing the ventilator setting was effective on both anxiety and dyspnea [25] and should even be encouraged first before escalating analgesia sedation in mechanically ventilated patients [35, 36]. Sleep and thirst should be facilitated using a bundle of non-pharmacological techniques (e.g., earplugs, eyemask, reduction in noise, light, and care to promote sleep [1], oral swab wipes, ice-cold water sprays, lip moisturizer, mini mint ice cubs to minimize thirst [24, 34]).

The present study reports promising results regarding the use of VR to improve anxiety (both devices), pain

Table 2 Symptoms, Analgesia Nociception Index, and physiological variables recorded before and after each of the four relaxation sessions

	Type of relaxation techniques							
	Standard		**Music care®**		**VR Deepsen®**		**VR Healthy mind®**	
Symptoms								
NRS overall discomfort								
Before	4	[2;6]	4	[2;6]	5	[2;6]	4	[2;6]
After	4	[2;5]	25	[1;5]	4	[1.5;5]	2	[0;5]
p	*0.27*		*0.06*		0.21		**0.02**	
NRS pain								
Before	2	[0;5]	2	[0;5]	3	[0;5]	2.5	[0;5]
After	2	[0;5]	1	[0;5]	2	[0;4]	1	[0;4]
p	*0.7*				0.3		0.12	
NRS anxiety								
Before	2.5	[0;5]	3	[0;5]	3	[0;5]	3	[0;5]
After	2	[0;4]	2	[0;5]	1	[0;4]	1.7	[0;4]
p	*0.52*		***0.32***		0.03		0.05	
NRS thirst								
Before	6	[1;9]	6	[1;8]	5	[1;8]	4	[0;7]
After	6	[0;8]	5	[1;8]	4	[0;8]	4	[0;6]
p	*0.68*		*0.53*		0.38		0.93	
NRS Dyspnea								
Before	1.5	[0;5]	2	[0;5.5]	2	[0;5]	2	[0;4]
After	1	[0;4]	1	[0;4]	2	[0;5]	0.5	[0;4]
p	*0.89*		*0.13*		0.44		0.5	
NRS lack of rest								
Before	4	[2;6]	5	[2;7]	5	[3;8]	5	[3;8]
After	4	[1;6]	4	[0;5]	2	[1;5]	3.5	[2;5]
p	*0.49*		**0.05**		< 0.01		0.02	
ANI and physiological variables								
ANI								
Before	62	[48;85]	66	[56;82]	72	[53;80]	67	[51;80]
After	69	[51;82]	82	[65;93]	80	[70;98]	91	[70;98]
p	*0.45*		***< 0.01***		< 0.01		< 0.01	
Heart rate (/min)								
Before	89	[81;102]	88	[80;102]	87	[78;99]	88	[77;100]
After	92	[79;102]	85	[81;101]	84	[74;98]	92	[80;97]
p	*0.88*		*0.68*		0.51		0.69	
Respiratory rate (/min)								
Before	21	[18;24]	20	[17;26]	20	[17;25]	21	[16;27]
After	22	[18;27]	19	[15;24]	21	[17;26]	20	[16;24]
p	*0.74*		*0.34*		0.81		0.14	
Systolic blood pressure (mmHg)								
Before	134	[120;144]	128	[117;154]	136	[121;151]	134	[118;146]
After	133	[119;146]	127	[113;143]	137	[120;151]	131	[115;148]
p	*0.99*		*0.51*		0.86		0.82	
Diastolic blood pressure (mmHg)								
Before	72	[65;82]	71	[62;82]	70	[62;81]	73	[65;82]
After	72	[64;79]	66	[61;77]	75	[61;84]	71	[62;81]
p	*0.52*		*0.18*		0.38		0.65	

The data correspond to a rating from 0 to 10 on a numerical rating scale, where 0 is the best and 10 the worst intensity, and are expressed in median [25th–75th percentiles]. The *p* value was calculated via Mann–Whitney-Wilcoxon test for nonparametric data and via Student's *t* test for parametric data

Table 2 (continued)

The italic, bold values are for significant or trend toward significant *p* values

Table 3 Multivariate mixed-effect model—benefits of specific electronic relaxation techniques compared to standard relaxation

	Gain estimate	*p*		Gain estimate	*p*
Overall discomfort			*ANI*		
Music care®	− 0.4	*0.25*	Music care®	0.7	*0.87*
VR Deepsen®	− 0.1	*0.85*	VR Deepsen®	8.5	*0,07*
VR Healthy mind®	− 0.8	***0.01***	VR Healthy mind®	13	***0.006***
Standard	0		Standard	0	
Pain			*Heart rate*		
Music care®	− 0.3	*0.23*	Music care®	0.1	*0.39*
VR Deepsen®	− 0.3	*0.19*	VR Deepsen®	− 0.5	*0.75*
VR Healthy mind®	− 0.8	***0.001***	VR Healthy mind®	1.0	*0.47*
Standard	0		Standard	0	
Anxiety			*Systolic blood pressure*		
Music care®	− 0.1	*0.7*	Music care®	2.2	*0.7*
VR Deepsen®	− 0.9	***0.001***	VR Deepsen®	2.1	*0.5*
VR Healthy mind®	− 0.8	***0.004***	VR Healthy mind®	2.2	*0.8*
Standard	0		Standard		
Thirst			*Diastolic blood pressure*		
Music care®	0.0	*0.88*	Music care®	− 2	*0.2*
VR Deepsen®	0.0	*0.93*	VR Deepsen®	1.8	*0.2*
VR Healthy Mind®	− 0.3	*0.45*	VR Healthy Mind®	− 0.3	*0.8*
Standard	0		Standard	0	
Dyspnea			*Respiratory rate*		
Music care®	− 0.6	***0.06***	Music care®	− 1	*0.4*
VR Deepsen®	− 0.3	*0.42*	VR Deepsen®	0.5	*0.65*
VR Healthy mind®	− 0.3	*0.39*	VR Healthy mind®	− 2	*0.12*
Standard	0		Standard	0	
Lack of rest feeling					
Music care®	− 0.7	*0.26*			
VR Deepsen®	− 1.6	***0.01***			
VR Healthy mind®	− 1.2	*0.07*			
Standard	0				

This multivariable mixed model was performed to compare different electronic devices between them, dealing with multiple assessments, different orders of relaxation sessions, and significant patient characteristics. The estimate of the improvement in the self-reported assessment of symptoms' intensity, Analgesia/Nociception Index (ANI), and physiological variables was reported for each relaxation device, compared to the standard relaxation session

The italic, bold values are for significant or trend toward significant *p* values

(imagined world), or lack of rest (real world). Previous studies reported that music therapy could improve anxiety [26] and pain in ICU [12, 37]. In the present study, MUSIC-CARE© was the only device associated with a possible effect on dyspnea, with a trend toward significance (decrease of 0.6 additional point, p = 0.057, multivariate analysis, Table 3). In a larger population or in patients with higher dyspnea intensity, this technique may demonstrate significant improvement. This is consistent with a previous report by our group that observed significant improvement in ventilatory parameters with MUSIC-CARE© in intubated patients during the weaning of mechanical ventilation [12].

The present study reports that devices using both music and VR could be more effective than music therapy alone on overall discomfort and specific symptoms. Strong scientific arguments supporting the beneficial effect of VR have recently spread in medical sphere, especially for the management of mental health disorders including anxiety [38]. Results are promising

to manage pain after surgery, severe burns [39, 40], or before nociceptive procedures [41]. Hypothesis is that VR, by providing multisensory inputs, deflects attention into the virtual world and lowers the pain intensity [42]. Thus, the kind of virtual world may play a role as suggested by our results. However, patient characteristics that were not investigated in this study (preference for real or computed generated pictures for example) should be taken into account as potential bias when interpreting the results.

The present study is the first randomized study about VR evaluating the improvement in overall patient baseline comfort in a mixed medical-surgical ICU, compared to music therapy and standard relaxation. A recent review on VR in ICU reported 21 studies, mostly of them being observational, non-comparative, feasibility studies [43], whose reports are consistent with the present study with a completion rate of 74%, (95%CI 51%-96.0%). In two proof-of-concept studies designed by the same group, heart rate and blood pressure decreased in 37 patients [44], while respiratory rate and discomfort decreased in 33 patients [45]. Physiological variables did not change in the present study. This may be explained by differences in the severity of critical illness among studied populations. Usually, physiological variables may change only a little in critically ill patients compared to behavioral pain scales [46, 47] or heat rate variability devices [20]. Among RCTs, one assessed the type of computer-generated video (urban *versus* mountain world *versus* a video displayed on the bedroom-TV screen) on 45 patients, reporting a better restoration feeling with the mountain world [48], consistently with findings of the present study that highlights a different impact of VR related to device characteristics. Three RCTs included 48(24/group) [49], 100(25/group) [50], and 200(100/group) [51] post-cardiac surgery patients. VR improved significantly sleep [49] and relaxation [50] but failed to improve anxiety and pain at rest [50] or during chest drain removal [51]. In the latter study, VR was compared to nitrous oxide. Another negative RCT investigated the impact of VR on PICS in 89 patients with COVID-19 [52].

The present study presents some strengths and limitations. Strengths include the prospective recording of parameters by a research team who assured non-disturbance of care during the relaxation time, the cross-over randomized design, the multivariate analysis that was performed as a method to compare different electronic devices between them, dealing with multiple assessments, different orders of relaxation sessions, and the characteristics of patients that were diverse by nature in a mixed medical-surgical ICU population, as well as the measurement of the most common stressful symptoms [2] using validated complementary subjective and objective tools [20, 22]. Regarding the study limits, as previously discussed, a lack of power related to only moderate symptoms intensities could explain the lack of significance for some results. This study should be reproduced in patients with clinically significant symptoms (i.e., pain, anxiety, dyspnea), and calibrated on each of these stressful symptoms. However, although the absolute values of symptom improvement were rather small, it is important to note that all the results pointed in the same direction: a specific relaxation device, such as music therapy or VR, can improve self-reported patient symptoms and patient stress response. Finally, these results may be biased by the fact that much attention was paid to enrolled patients during the study: multi-daily visit, dialogue, taking into account diverse symptoms and pain, with multiple assessments by nurses and physicians, followed by frequent multidisciplinary management as basically performed for pain according to the guidelines. Also, only a selected group of ICU patients was included; specifically, they were alert and non-delirious, taken in charge in a ICU where a strategy of fast liberation from invasive mechanical ventilation was implemented [35], including a minimal use of major opioids and sedatives according to current guidelines [1, 8, 36]. Thus, further studies are needed to measure the impact of electronic devices in ICU at a large scale, in multiple centers with diverse ICU populations and cultures, and to explore all different characteristics of the devices and their impact on short and long-term outcomes. Because managing ICU patients who are often weak or tired is challenging, these findings could also promote the evaluation of these innovative devices to help managing diverse stressful symptoms in other hospital settings or at home, where they could be easier to implement that in the ICU. Finally, one important finding highlighted by the exploratory part of the study (specific symptom analysis) is that pain might not be the main stressful symptom in critical illness. Attention to pain management in ICU has been placed as the top priority in guidelines for many years but should not mask other significant stressful symptoms. Such symptoms, diverse by nature, deserve further investigations.

Conclusion

This first RCT investigating different VR devices compared to standard relaxation and to music therapy shows that VR with computer-generated pictures is the most effective to improve overall discomfort and to reduce the physiological stress response in alert and non-delirious ICU patients. Moreover, the type of virtual world and music therapy may impact the symptoms differently: beneficial effects of these new therapies depend on the device characteristics and the targeted symptoms.

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Abbreviations
ANI: Analgesia Nociception Index; CAM-ICU: Confusion assessment method for the ICU; ICU: Intensive care unit; NRS: Numeric Rating Scale; RASS: Richmond Agitation Sedation Scale; SAPS: Simplified acute physiological score; SOFA: Sequential organ failure assessment score; VR: Virtual reality.

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Author contributions
LMG and CR contributed equally to the study. GC, OG, JC, ADJ, NM, and SJ designed the trial and obtain the research funding. LMG, CR, and OG enrolled the patients, performed the research, and collected the data. NM performed an independent statistical analysis. LMG, CR, and GC drafted the manuscript. All authors reread and approved the manuscript.

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Availability of data materials
Data are protected by the Clinical Research Direction of the Montpellier University Hospitals and will be available for research upon request after approval by a French ethics committee according to the law.

Declarations

Ethics approval and consent to participate
The study was approved by an ethics committee [Comité de Protection des Personnes Sud-Méditerranée-1 (ID-RCB:2016-A00748-43)] according to French law and registered on Clinical Trials NCT04017299.

Adult consent to participate
Adult patients over 18-yo admitted to the ICU were eligible if they were alert and nondelirious, following the French validated versions of the Confusion Assessment Method for the ICU (CAM-ICU) [16, 17] and the Richmond Agitation Sedation Scale (RASS) that had to be ≥ 0 [18]. Patients were screened daily for eligibility by investigators and included in the study after written consent.

Human accordance statement
The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Competing interests
Samir Jaber reports consulting fees from Drager, Xenios, Medtronic and Fisher and Paykel. Other authors declare no conflicts of interest. The music therapy system was purchased by the hospital several years before the study. The two virtual reality systems were lent to the hospital by the manufacturers for a free test. Manufacturers gave their consent for the evaluation study but had strictly no implication on the study design, data analysis, and study reporting.

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Publisher's Note

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Virtual reality device to improve the tolerability of lumbar puncture

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ABSTRACT

Background Virtual reality is increasingly being used as an adjunct or replacement to pharmacological analgesia and sedation during medical procedures.

Methods and results We report the successful use of a virtual reality device in a highly anxious patient undergoing lumbar puncture.

Conclusion The case demonstrates how virtual reality technology may benefit patients undergoing invasive procedures such as lumbar puncture. Virtual reality may, therefore, offer an alternative or adjunct to sedation and analgesia and may reduce the amount of pharmacological therapy required.

REPORT

A 63-year-old man was referred for assessment of recurrent episodes of collapse. MRI suggested raised intracranial pressure and the patient was admitted for an elective lumbar puncture to assess cerebrospinal fluid and measure opening pressures. The patient was also under the care of the adult mental health team and was being treated for somatoform disorder with severe anxiety and depression. On admission, the patient was highly anxious about his current symptoms as well as the lumbar puncture procedure. He was identified as a potential candidate that may benefit from a virtual reality (VR) device to improve tolerability and the hospital's clinical VR team were contacted for assistance.

The VR system that was chosen was a Healthy Mind (Paris, France) Pico device with headphones. The immersive scene within the software includes a three-dimensional natural location, environment-based hypnotherapy scripts, accompanying music, relaxation features to encourage deep breathing, and distraction techniques to focus attention away from the clinical procedure. The patient was given verbal and written information about the VR device and the potential benefits it may have to him during the procedure. He was also given the opportunity to try on the VR headset and headphones before the procedure commenced and make a choice as to which immersive scene he might find the most relaxing during the procedure. The patient opted for an underwater scene (figure 1). He was informed that the clinical team would be able to communicate with him during the procedure using the text feature of the device, whereby he would receive written notifications within the immersive scene (eg, before local anaesthetic was administered). The patient was also informed that he could gain the clinical team's attention during the procedure by raising his hand.

Figure 1 Underwater immersive environment as seen by the patient

Figure 2 Patient in left lateral position using the virtual reality headset and headphones.

The lumbar puncture lasted 20 min and proceeded without complication (figure 2). The patient's well-being was checked regularly throughout the procedure, and he remained calm throughout. Approximately 10 min into the procedure, the patient fell asleep and remained so for the duration of the procedure. Verbal feedback was obtained about the patient's experience of the procedure using the VR device and he reported that

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the VR system helped him to forget what was happening and relax more.

Clinical VR is a rapidly evolving sector with benefits being applied to a wide range of settings within healthcare. It is hypothesised that VR reduces pain by providing an effective distraction away from the painful stimuli that the patient would otherwise be focused on.[1–5] This results in less attentional resources available to process nociceptive signals.[6] In addition to a reduction of subjective pain perception, VR has also been shown to reduce pain-related brain activity on functional MRI.[7 8]

The case presented here demonstrates how VR technology may benefit patients undergoing invasive procedures such as lumbar puncture. VR may, therefore, offer an alternative or adjunct to sedation and analgesia and may reduce the amount of pharmacological therapy required.

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Virtual Reality – a new addition to the anxiolytic armamentarium during implantation of cardiac devices.

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INTRODUCTION

Pacemaker implantation can be a painful and anxiety-provoking procedure[1]. Perioperative pain and anxiety impact patients' experiences and are associated with higher complication rates and prolonged recovery times.

Through distraction, virtual reality (VR) can improve the experience of patients undergoing these procedures, blunting pain perception[2]. Further, as the experience of pain is strongly influenced by psychological and environmental factors, transporting the patient from the unfamiliar environment of the operating theatre to a relaxing and meditative scene can help alleviate both anxiety and pain[3].

We conducted a pilot study to assess the effects of the use of intra-operative VR in patients undergoing pacemaker implantation.

Figure 1. Example VR Meditation Scene: Zen Garden Scene (Image: HealthyMind)

METHODS

Twenty patients undergoing elective or urgent pacemaker procedures were screened for eligibility. Two were excluded (lacking capacity, 1; visual impairment, 1), and one declined participation. The mean age was 81.5 years.

The control group (n=8) received standard care: local anaesthetic (lidocaine 1%) at the pacemaker implantation site and use of intravenous midazolam at the operator's discretion. The intervention group (n=9) received an immersive guided meditation in VR (HealthyMind) during the procedure, in addition to standard care.

The VR experience was controlled using a linked wireless tablet by the researcher, which also allowed direct communication with the patient. The patient was free to remove the headset at any time.

	Period	Control (n=8)	VR (n=9)
Anxiety			
Overall (STAI) State	Pre	87.9 (10.5)	82.8 (9.2)
Trait Anxiety Index	Post	81.9 (5.6)	80.4 (5.7)
	Change (%)	-6.0 (-7%)	-2.3 (-3%)
Pain			
Visual analogue score		3.1 (1.5)	1.9 (1.4)
Sedation			
Modified Ramsay score		2.5 (1.2)	3.2 (1.6)
Comfort			
Fell asleep, n		1 (13%)	3 (33%)
Removed headset due to discomfort, n		-	1 (11%)
Local Anaesthetic Use			
Mean dose lidocaine 1%, ml (SD)		28.5 (6.0)	28.3 (5.3)
Anxiolytic use			
Required, n		2 (25%)	1 (11%)
Mean dose midazolam, mg		1.8	1.0

Table 1. Results

RESULTS

Pain & Anxiety:

- Lower reported **pain** (visual analogue scale; 1.9 vs. 3.1);
- Post-procedure **anxiety** was similar in both groups (State-Trait Anxiety Index; 80.4 vs 81.9);

Medication use:

- No significant difference in local anaesthetic use (28.3 vs 28.5 ml of 1% lidocaine);
- Fewer patients required the anxiolytic midazolam (11% vs 25%);

Comfort:

- Three patients in the VR group (33%) fell asleep during the procedure, compared with only one in the standard care group (13%).
- One patient removed the headset during the procedure due to discomfort related to the device strap

Physiological monitoring:

- The prerequisite dysrhythmias in patients undergoing pacemaker implantation precluded any meaningful interpretation of HR and HRV-derived stress scores (Figure 2).

There were no significant procedural complications.

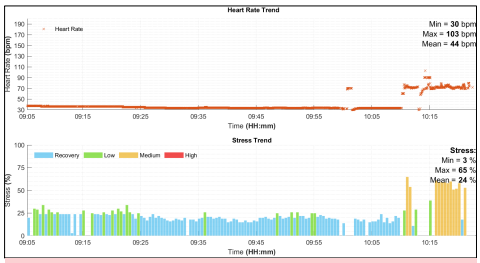

Figure 2. B-Secur HeartKey continuous heart rate and Physiological Stress score monitoring.

DISCUSSION

This pilot study showed good acceptability of VR in this demographic of patients and lower pain scores for those receiving VR anxiolysis. This work is caveated by small sample size, heterogeneous study population and multiple confounding factors. Future studies could include alternative biometrics, such as galvanic skin response, as physiological markers of pain and anxiety.

Figure 3. Patient wearing HealthyMind VR headset during procedure. (Shared with patient's consent).

CONCLUSION

The use cases for VR in healthcare are expanding, from medical simulation for clinician education and complex procedure planning to virtual rehabilitation programmes[4].

This pilot study sits alongside a growing body of evidence supporting the perioperative use of VR[5] and demonstrates that VR is a feasible intervention to reduce pain and anxiety during the implantation of cardiac devices.

In addition to good tolerability and analgesic effect, the trend toward reduced medication requirements with VR suggests that patients will avoid harm from medication side effects and recover more promptly after their procedure. Given the excellent safety profile of VR, there seems little to lose.

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