Patient-Controlled Sedation in Port Implantation (PACSPI 1) – a Feasibility Trial

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Research Article

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Abstract

Purpose: Central venous access is essential for the administration of chemotherapy and frequent blood sampling in patients with cancer. The subcutaneous venous port (SVP) is commonly used for this purpose. SVP implantation is a minor surgical procedure; however, it can provoke pain and anxiety in these vulnerable patients. The aim of this study was to determine the feasibility and safety of patient-controlled sedation (PCS) with propofol and alfentanil as an adjunct to local anesthesia during SVP implantation.

Methods: We prospectively studied 40 patients scheduled for SVP implantation between April 14, 2021, and October 15, 2021, at a 500-bed secondary level hospital in Sweden. Anesthesiologists performed SVP implantation with PCS using propofol and alfentanil. We determined pain perception (primary outcome), patient satisfaction, sedation score, and key safety measures.

Results: Of the 40 patients with cancer, 80% reported a pain score ≤3 on an 11-point numeric rating scale (NRS) during SVP implantation. Overall satisfaction with pain management and operating conditions was graded as 10 of 10 on the NRS. Four patients (10%) had bradypnea (<8 breaths/min) without oxygen desaturation to ≤90%. Rescue sedation was administered to one patient (2.5%).

Conclusion: PCS with propofol and alfentanil during SVP implantation is feasible, safe, and well accepted. Its efficacy must be evaluated in a randomized controlled trial to provide clinicians with evidence-based guidance for choosing the optimal perioperative strategy for SVP implantation.

Trial registration number at clinicaltrials.gov: NCT04631393 before study commencement.

Introduction:

In Sweden, cancer is diagnosed in more than 60,000 patients annually. A newly diagnosed cancer imposes psychological as well as physical challenges to the patients, making this group vulnerable to different aspects of their care. Many cancer patients are eligible for chemotherapy administered through a totally implanted venous access device, commonly referred to as the subcutaneous venous port (SVP). According to the Swedish Perioperative Registry, SVP implantation is one of the most common surgical procedures in Sweden [1]. However, there is no current guidance as to which procedural analgesic strategy is superior during SVP implantation. Several strategies exist (local anesthetic [LA] only, LA in combination with analgosedation or general anesthesia), and practice is likely to be based on local institutional traditions rather than evidence-based guidance. During SVP implantation using LA alone, one-fourth of patients experience severe pain and discomfort [2].

Clinician-controlled sedation (CCS) involves administration of procedural analgosedation by a trained clinician. However, it carries the risk of oversedation and generates higher costs compared to alternative sedation methods [3, 4]. Patient-controlled sedation (PCS) is an alternative sedation method to CCS, enabling patients to self-administer and self-regulate their sedation and analgesia during the procedure.

The procedural use of PCS with different sedatives and analgesics is well described and regarded as a safe alternative with a lower incidence of analgesic or sedative rescue interventions compared to CCS in a number of clinical settings [5]. Propofol and alfentanil, with their short-acting properties, ensure rapid induction and recovery, making them suitable for outpatient procedures.

In this prospective trial, we aimed to examine the safety and feasibility of PCS with propofol and alfentanil for SVP implantation using self-reported pain perception scores, overall satisfaction scores, sedation scores, and incidence of adverse events.

Methods:

Trial design and participants: The PACSPI 1 trial was a prospective feasibility study of the effects of PCS with propofol and alfentanil as an adjunct to LA during SVP implantation. Patients aged ≥18 years who were scheduled for SVP implantation between April 14, 2021, and October 15, 2021, at the Department of Anesthesia and Intensive Care at Ryhov County Hospital were eligible for inclusion. Inability to operate the PCS apparatus, inability to communicate in Scandinavian languages, the need for general anesthesia, contraindications to sedation as per anesthesiologist assessment, non-fasting state, inability to establish peripheral vein access, and pregnancy were exclusion criteria. Patients were screened for eligibility by the nursing staff upon arrival to the preoperative unit. Eligible patients were subsequently informed and included by a physician from the Department of Anesthesia and Intensive Care.

Participants were instructed on use of the PCS pump (Syramed µSP6000, Arcomed AG, Switzerland) by a nurse anesthetist. The syringe was loaded with 36 ml propofol (10 mg/ml) and 4 ml alfentanil (0.5 mg/ml). Each time the patient pressed the handheld button, an aliquot of 0.5 ml was injected (4.5 mg propofol/0.025 mg alfentanil). The injection time was set to 8 s, restricting self-administration to a maximum of 7 bolus doses per minute corresponding to 31.5 mg propofol and 0.175 mg alfentanil per minute. No lockout period was applied. Carbocaine-adrenalin (10 mg/ml) diluted with sodium bicarbonate (50 mg/ml) was injected into the operative site. Vital parameters prior to the procedure were recorded. Patients were monitored using electrocardiographyr for heartrate (HR), non-invasive blood pressure (BP), oxygen saturation (SpO_2), and respiratory rate (RR) at 5-min intervals during the procedure. Bradycardia was defined as HR <40 beats/min, tachycardia as HR >100 beats/min, hypotension as systolic BP < 90 mmHg or a decrease of >30% from baseline, hypoxia as SpO_2 <90% or a decrease of >5% from baseline, and bradypnea as RR of <8 breaths per minute. Bradypnea was treated with verbal stimulation. Oxygen desaturation was treated with increased oxygen flow rate. Supplemental oxygen via a capnograph-fitted nasal cannula was administered to all patients at 2 L/min during the procedure. The Observer`s Assessment of Alertness/Sedation score (OAA/S) [6] was used to determine the sedation level during the four procedural steps: 1) sterile swabbing, 2) injection of LA, 3) catheter tunneling, and 4) sterile drape removal. The operating anesthesiologist assessed the operating conditions on an 11-point NRS, with 10 being perfect operating conditions. Puncture attempt was defined as continuous needle advancement to establish vein puncture. An unvalidated patient perception assessment tool with seven dimensions applying the NRS was used to evaluate patient perception.

Outcomes:

The primary outcome was maximal pain perception during the procedure as assessed in the recovery unit on an 11-point NRS prior to discharge (0 = no pain; 10 = worst pain imaginable). Secondary outcomes were NRS scores for patient satisfaction with the procedure and pain management (0 = not at all satisfied, 10 = very satisfied), delivered doses of propofol and alfentanil, time consumption, operating conditions, OAA/S scores during the procedure, and adverse events (AE)

Statistical analyses:

Continuous variables are summarized using descriptive statistics: n (non-missing sample size), median, minimum, and maximum. Frequencies and percentages are reported for categorical variables. Statistical analyses were performed using SPSS version 27 (IBM, Armonk, NY, USA).

Results:

In all, 109 participants were recruited during the study period. The exclusion criteria applied to 18 patients. Of the 91 eligible patients, 51 (56%) declined to participate. The patient enrollment flowchart is illustrated in Figure 1.

Patient baseline characteristics are summarized in Table 1.

Table 1

Patient characteristics. Data are presented as number (%) or median (minimum-maximum)

Age (years)	66 (37-80)
Sex	
Female	27 (67.5)
Male	13 (32.5)
BMI (kg/m^2)	25 (19-34)
ASA class	
1	3 (7.5)
2	24 (60)
3	13 (32.5)
Treatment goal for cancer diagnosis	
Adjuvant	26 (65)
Palliative	14 (35)
Previous long-term venous access	5 (12.5)
BMI: body mass index, ASA: American Society of Anesthesiologists	

The preferred vessel for puncture was the right internal jugular vein (87.5%). Arterial puncture and hematoma each occurred in one patient. (Table 2). Ultrasound guidance was used for all procedures. The anesthesiologists' satisfaction with the operating conditions was graded as 10. The procedure characteristics are listed in Table 2.

Table 2

Sedation characteristics and adverse events. Data are presented as number (%) or median (minimum-maximum)

OAA/S score at procedural stage	
T1	5 (3-5)
T2	5 (4-5)
T3	5 (3-5)
T4	5 (1-5)
Delivered volume propofol/alfentanil (ml)	7.3 (0-27)
Delivered propofol (mg)	65.7 (0-243)
Delivered alfentanil (mg)	0.37 (0-1.36)
Rescue sedation	1 (2.5)
Hypoxia ($Sp0_2$ <90%)	0
Bradypnea (<8 breaths/min)	4 (10)
Chin lift	0
Mask ventilation	0
Tachycardia (>100 beats/min)	0
Bradycardia (<40 beats/min)	0
Hypotension (systolic pressure <90 mmHg)	0
Time in recovery (min)	45 (15-103)
OAA/S: Observer's Assessment of Alertness/Sedation score	

The median administered doses of propofol and alfentanil were 65.7 mg (0-243) and 0.37 mg (0-1.36), respectively. The median sedation score was 5 at all procedural time points. Bradypnea occurred in 4 patients (10%) and resolved by verbal stimuli. No hypoxic events were observed. One patient (2.5%) required rescue sedation. Sedation characteristics and adverse events are presented in Table 3.

Table 3

Procedure characteristics and complications. Data are presented as number (%) or median (minimum-maximum)

Waiting time in preoperative unit (min)	41 (10-215)
Vein choice	
Internal jugular	40 (100)
Laterality	
Right	35 (87.5)
Left	5 (12.5)
Ultrasound guidance	40 (100)
LA volume (ml)	30 (10-40)
Number of punctures	1 (1-6)
Arterial puncture	1 (2.5)
Hematoma	1 (2.5)
Pneumothorax	0
Assistance from colleague	1 (2.5)
Procedure aborted	0
Catheter tip position	
Lower 1/3 SVC	31 (77.5)
RA	9 (22.5)
Procedural time (min)	32 (17-84)
Operating conditions (NRS)	10 (5-10)
LA: local anesthetic, SVC: superior vena cava, RA: right atrium, NRS: numeric rating scale	

Thirty-two patients (80%) experienced pain levels of 3 or less on the NRS, with a median pain perception of 1 (0-6). Median satisfaction with pain management was 10 (6-10). The patient response regarding the importance of being in control of sedation and analgesia was 8.5 (0-10). The patients' pain perceptions and satisfaction are presented in Table 4.

Table 4

Pain perception and patient satisfaction. Data are presented as number (%) and median (minimum-maximum)

NRS score for pain perception ≤3	32 (80)
Maximal pain perception during procedure	1 (0-6)
Maximal pain perception in arm with infusion	1 (0-8)
Overall satisfaction with pain management	10 (6-10)
Overall satisfaction with care	10 (9-10)
Satisfaction with staff contact	10 (9-10)
How important is sedation?	9.5 (0-10)
How important is it to be in control of sedation?	8.5 (0-10)
NRS: numeric rating scale	

Discussion:

The main finding of this feasibility trial was that PCS was safe and generated good operating conditions during the procedures. In addition, PCS with propofol and alfentanil for SVP implantation resulted in low self-reported pain perception and high patient satisfaction. To the best of our knowledge, no prior study has examined PCS with propofol and alfentanil in the context of SVP implantation.

Safety for procedural sedation is crucial and has been addressed in several guidelines [7, 8]. The concept of PCS was first described in 1989 [9]. Since then, the use of PCS has been described in several clinical settings and with different sedative and analgesic regimens [5]. PCS with propofol is regarded as a safe technique that reduces the risk of oversedation compared to CCS [4]. PCS with propofol and alfentanil has been used for procedural sedation in gynecological and endoscopic settings. However, data regarding respiratory safety are contradictory. PCS with a combination of propofol and alfentanil was shown to facilitate completion of gynecological operative procedures compared to propofol alone; however, respiratory status was compromised. In contrast, it was found to have no respiratory adverse effects in the setting of endoscopic retrograde cholangiopancreatography [10, 11]. In the present trial, alfentanil at 0.025 mg/dose was associated with limited episodes of bradypnea in four patients, without oxygen desaturation or the need for mechanical ventilation, suggesting that it is safe regarding respiratory adverse events. No AE´s related to heart rate and blood pressure were registered.

Opioids play a crucial role in the relief of procedural pain. Preprocedural buccal administration of fentanyl as well as short-acting intravenous remifentanil has been shown to decrease patients' pain perception during SVP implantation [12, 13]. In the present trial, the overall perception of pain was low, and 80% of the patients experienced pain of 3 or less on the 11-point NRS during SVP implantation. Furthermore, the satisfaction with pain management was high. This trial suggests a somewhat lower degree of pain perception in SVP implantation with PCS than with LA only.

Interestingly, self-administered doses varied substantially, ranging from 0-27 ml, suggesting large inter-individual differences in sedative and analgesic requirements. This is consistent with previous findings in which PCS with midazolam and fentanyl were used for tunneled venous access [14]. More than a third of eligible patients declined participation, as they considered sedation for a presumably minor procedure unnecessary or wanted to drive their vehicles home after discharge. This not only generated selection bias, but might reflect patients' varying needs for sedation and analgesia, as mentioned above. The challenge lies in identifying patients according to their sedative needs before the procedure begins. As suggested earlier, the likely determinants for self-administered anxiolytics seem to be the patient's own assessment of his or her needs in a shared decision-making process [15]. A preoperative consultation might therefore suffice to clarify the patient's needs and to agree on an individualized analgesic strategy.

Patient satisfaction with care and staff contact was very high. Patient satisfaction is challenging to quantify, and patient-related experience measures (PREM) are key to providing good patient-centered clinical care and allowing comparison of clinical routines [16]. Unfortunately, no appropriate validated questionnaire for sedation in minor procedures (such as central venous access) exists, leading to the pragmatic approach of using established methods, though not validated, to facilitate comparison [14].

The present trial has limitations that must be mentioned. First, with a small sample size, rare adverse events were likely missed. However, the primary goals of the trial were to assess PCS during SVP implantation and to provide guidance for future trials. Second, the lack of a validated PREM for central venous access insertion limits proper tools for measuring patient satisfaction and comparison with other studies, which must be addressed in the future.

Conclusion:

SVP implantation is a common procedure in everyday practice; however, no evidence-based recommendations can currently be made from the existing literature regarding which perioperative analgesic and/or sedative strategies are superior for patients in need of SVP. PCS with propofol and alfentanil during SVP implantation is feasible, safe, and well accepted. Its efficacy is yet to be evaluated in a randomized controlled trial to provide evidence-based guidance for choosing the optimal perioperative strategy for SVP implantation.

Abbreviations

AE	Adverse Event
ASA	American Society of Anesthesiologists
CCS	Clinician controlled sedation
CONSORT	Consolidated Standards of Reporting Trials
GCP	Good Clinical Practice
ICH	International Council for Harmonisation
LA	Local anesthesia
NRS	Numeric rating Scale
OAA/S	Observer Assessment of Alertness/Sedation Scale
PCS	Patient-Controlled Sedation
SVP	Subcutaneous venous port

Declarations

Ethics approval:

This trial was approved by the Swedish Ethical Review Authority on July 7, 2020 (Dnr: 2020-02642). The trial was registered at clinicaltrials.gov (NCT04631393) prior to trial commencement. Printed information was provided, and written informed consent was obtained from all participants. This trial was conducted according to the standards of Good Clinical Practice (GCP) defined by the International Conference on Harmonization, ethical principles with their origin in the Declaration of Helsinki, and all applicable national and local regulations. The trial adhered to the Consolidated Standards of Reporting Trials guidelines for feasibility trials (CONSORT).

Consent to participate and publish:

Written informed consent and permission to publish was obtained from all participants included in the study.

Data availability:

The datasets generated during the current study are available from the corresponding author on reasonable request.

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Conflict of interests:

The authors have no relevant financial or non-financial interests to disclose.

Code availability:

IBM SPSS statistics 27

Author contributions:

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Stefanie Seifert and Knut Taxbro. The first draft of the manuscript was written by Stefanie Seifert, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. Årsrapport SPOR 2020. Swedish perioperative registry (2020); https://spor.se/spor/arsrapporter/.Accessed 26 November 2021
2. Taxbro K, Hammarskjöld F, Thelin B, Lewin F, Hagman H, Hanberger H, et al. (2019). Clinical impact of peripherally inserted central catheters vs implanted port catheters in patients with cancer: an open-label, randomised, two-centre trial. Br J Anaesth;122(6):734-41.http://dx.doi.org/10.1016/j.bja.2019.01.038.
3. Grossmann B, Nilsson A, Sjöberg F, Bernfort L, Nilsson L. (2020). Patient-controlled sedation with propofol for endoscopic procedures-A cost analysis. Acta Anaesthesiol Scand;64(1):53-62.http://dx.doi.org/10.1111/aas.13463.
4. Kreienbühl L, Elia N, Pfeil-Beun E, Walder B, Tramèr MR. (2018). Patient-Controlled Versus Clinician-Controlled Sedation With Propofol: Systematic Review and Meta-analysis With Trial Sequential Analyses. Anesth Analg;127(4):873-80.http://dx.doi.org/10.1213/ane.0000000000003361.
5. Grossmann B, Nilsson A, Sjöberg F, Nilsson L. (2020). Patient-controlled Sedation During Flexible Bronchoscopy: A Randomized Controlled Trial. Journal of bronchology & interventional pulmonology;27(2):77-85.http://dx.doi.org/10.1097/lbr.0000000000000610.
6. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, et al. (1990). Validity and reliability of the Observer's Assessment of Alertness/Sedation Scale: study with intravenous midazolam. J Clin Psychopharmacol;10(4):244-51.

7. (2018). Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018: A Report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology. Anesthesiology;128(3):437-79.http://dx.doi.org/10.1097/aln.0000000000002043.
8. Hinkelbein J, Lamperti M, Akeson J, Santos J, Costa J, De Robertis E, et al. (2018). European Society of Anaesthesiology and European Board of Anaesthesiology guidelines for procedural sedation and analgesia in adults. Eur J Anaesthesiol;35(1):6-24.http://dx.doi.org/10.1097/eja.0000000000000683.
9. Galletly DC, Short TG, Forrest P. (1989). Patient-administered anxiolysis--a pilot study.Anaesth Intensive Care;17(2):144-50.http://dx.doi.org/10.1177/0310057x8901700204.
10. Mazanikov M, Udd M, Kylänpää L, Mustonen H, Lindström O, Halttunen J, et al.(2012). Patient-controlled sedation for ERCP: a randomized double-blind comparison of alfentanil and remifentanil. Endoscopy;44(5):487-92.http://dx.doi.org/10.1055/s-0031-1291655.
11. Nilsson A, Nilsson L, Ustaal E, Sjöberg F. (2012). Alfentanil and patient-controlled propofol sedation - facilitate gynaecological outpatient surgery with increased risk of respiratory events. Acta Anaesthesiol Scand;56(9):1123-9.http://dx.doi.org/10.1111/j.1399-6576.2012.02749.x.
12. Bortolussi R, Zotti P, Matovic M, Morabito A, Bertuzzi C, Caserta M, et al. (2016). A phase II study on the efficacy and safety of procedural analgesia with fentanyl buccal tablet in cancer patients for the placement of indwelling central venous access systems. Support Care Cancer;24(4):1537-43.http://dx.doi.org/10.1007/s00520-015-2939-7.
13. Burlacu CL, McKeating K, McShane AJ. (2011). Remifentanil for the insertion and removal of long-term central venous access during monitored anesthesia care. J Clin Anesth;23(4):286-91.http://dx.doi.org/10.1016/j.jclinane.2010.12.007.
14. Clements W, Sneddon D, Kavnoudias H, Joseph T, Goh GS, Koukounaras J, et al. (2018). Randomized and controlled study comparing patient controlled and radiologist controlled intra-procedural conscious sedation, using midazolam and fentanyl, for patients undergoing insertion of a central venous line. J Med Imaging Radiat Oncol;62(6):781-8.http://dx.doi.org/10.1111/1754-9485.12817.
15. Chittle MD, Oklu R, Pino RM, He P, Sheridan RM, Martino J, et al. (2016). Sedation shared decision-making in ambulatory venous access device placement: Effects on patient choice, satisfaction and recovery time.Vasc Med;21(4):355-60.http://dx.doi.org/10.1177/1358863x16643602.
16. Barnett SF, Alagar RK, Grocott MP, Giannaris S, Dick JR, Moonesinghe SR.(2013). Patient-satisfaction measures in anesthesia: qualitative systematic review. Anesthesiology;119(2):452-78.http://dx.doi.org/10.1097/ALN.0b013e3182976014.

Figures

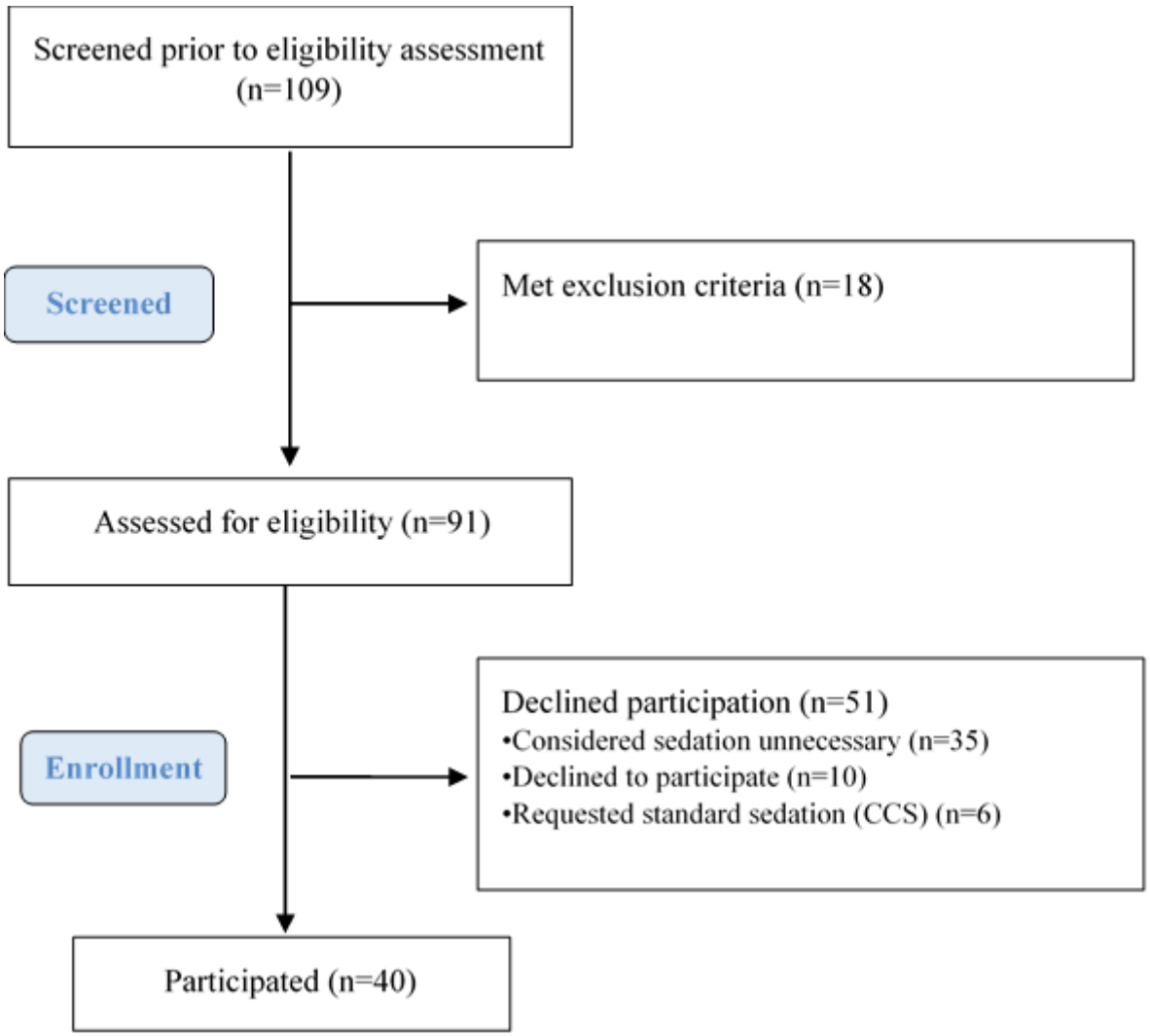

Figure 1

Study outline and flow chart