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Neuroanesthesia Abstracts

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Chronic Subdural Hematoma Drainage under Local vs. General Anesthesia: Systematic Review and Meta-analysis

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INTRODUCTION

Chronic subdural hematoma (CSDH) is one of the most encountered conditions seen in neurosurgery. Although mainstay treatment of cSDH has been burr hole drainage, no consensus yet exists on optimal anesthesia technique for surgical treatment. Currently, the decision to use either local anesthesia (LA) or general anesthesia (GA) depends on the protocol of the hospital or the preference of the individual surgeon. The primary objective of this study is to determine whether GA or LA causes the least complications peri and postoperatively. To do this, we undertook a systematic review and meta-analysis to examine the efficacy of both anesthesia types.

METHODS

A search was conducted in MEDLINE (1946 to November 11, 2022), Embase (1974 to November 11, 2022), and PubMed (up to November 11, 2022). The inclusion criteria were 1) Studies reporting clinical outcome after chronic subdural hematoma burr-hole drainage under local anesthesia, 2) Studies published in English, 3) Studies in humans. Studies were excluded if they were 1) Non-surgical studies (review articles, technique articles, commentary) and case reports, 2) Studies without separate outcomes for chronic subdural hematoma drainage under local anesthesia. We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines to systematically screen studies. Two reviewers independently screened abstracts of the studies identified through the literature search. Relevant articles were retrieved and rescreened for eligibility based on the full-text articles. Any disagreements were resolved through discussion with a third reviewer. Data was extracted in duplicate by two reviewers. Disagreements were resolved through a third reviewer.

RESULTS

Our literature search identified 521 studies, out of which 20 were included. There were a total of 1750 patients who underwent CSDH drainage under LA. The weighted mean age of the patient was 71.0 years, and 449 (27.1%) of the patients were female. The overall complication rate was significantly lower in the LA group (odds ratio 0.44, 95% CI = 0.26 to 0.77, p = 0.004). The revision rate (odds ratio 2.71, 95% CI 0.89 to 8.25, p = 0.08) and mortality rate were not significantly different between groups (odds ratio 1.23, 95% CI 0.63 to 2.43, p = 0.55). The mean operative time was significantly shorter in the LA group (mean difference -29.28 minutes, 95% CI = -41.43 to -17.13 minutes, p <0.0001). The length of admission was also shorter in the LA group (mean difference -1.58 days, 95% CI = -2.40 to - 0.76 days, p = 0.0002).

DISCUSSION

In the present meta-analysis, it is clearly shown that LA does show benefits in lower operative time, shorter admission length, and fewer postoperative complications. This makes local anesthesia a less invasive and potentially superior alternative to general anesthesia as cSDH affects mainly the elderly, a more vulnerable population, in whom the risk of general anesthesia is not insignificant.

- 1. Markwalder T-M. Chronic subdural hematomas: a review. Journal of neurosurgery. 1981;54(5):637-45.
- 2. Mersha A, Abat S, Temesgen T, Nebyou A. Outcome of chronic subdural hematoma treated with single burr hole under local anesthesia. Ethiopian Journal of Health Sciences. 2020;30(1).

Comparison of Different Vasopressors on Spinal Cord Blood Flow

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INTRODUCTION

Acute spinal cord injuries (SCI) can have long-lasting impact on a patient's physical and psychological wellbeing and have significant personal and societal costs. Therefore, the initial management of acute SCI remains critical in neurological outcomes. The current guidelines recommend increasing spinal cord perfusion pressure (SCPP) in acute phase of SCI as measured by elevated mean arterial pressure (MAP). Yet, it is not clear whether MAP is a good surrogate for spinal cord perfusion as multiple factors such as intrathecal and epidural pressures, vessel reactivity, and autoregulation can confound the overall SCPP. Therefore, this study investigated the effects of commonly used vasopressors on spinal cord perfusion as it relates to MAP in a rodent animal model. We hypothesize that MAP will have a direct correlation to SCP, and that there is no difference between various vasopressors in augmenting SCP.

METHODS

This study was approved by the Animal Policy and Welfare Committee at our institution. Under isoflurane anesthesia, nine male Sprague-Dawley rats were surgically instrumented with arterial and intravenous lines for blood pressure measurement and intravenous delivery of phenylephrine (PE), vasopressin (VP), norepinephrine (NE) and epinephrine (EP), respectively. Given the size limitations of the artery of Adamkiewicz in this rodent model, a transonic flow probe was situated around a directly adjacent lumbar spinal artery, since collateral circulation of the spinal cord often arises from these arteries.¹ The flow probe was able to detect changes in blood flow through the artery over time. Rats were subjected to the following treatments: PE 5-10 mcg/kg/min for 30 minutes, VP 0.002-0.004u/min for 30 minutes. Spinal cord blood flow following vasopressor infusion was analyzed as a percentage of the baseline blood flow prior to the start of infusion. Data are presented as mean±SEM, with statistical significance denoted at p<0.05.

RESULTS

Data were analyzed via one-way ANOVA. The baseline MAP was 108.4 ± 9.3 mmHg; following treatment with vasopressors, the MAP was 121.1 ± 10.9 mmHg (PE), 125.1 ± 8.3 mmHg (VP), 132.7 ± 10.6 mmHg (NE) and 108.4 ± 8.1 mmHg (EPI). The heart rates were 295.4 ± 12.3 (baseline), 297.0 ± 12.4 (PE), 295.1 ± 12.2 (VP), 313.8 ± 13.3 (NE), and 321.9 ± 10.6 (EPI). The percentage of spinal cord blood flow change from baseline was $102.1\pm9.6\%$ (PE), $87.34\pm12.8\%$ (VP), $100.1\pm18.9\%$ (NE), and $279.4\pm51.7\%$ (EPI) (overall p<0.0001; post-hoc p<0.0001 for EPI). The change in spinal cord blood flow normalized to the change in MAP were as follows: 0.92 ± 0.08 (PE), 0.79 ± 0.13 (VP), 0.90 ± 0.22 (NE), and 3.1 ± 0.69 (EPI) (overall p<0.0001; post hoc p=0.0003 for EPI).

DISCUSSION

To our knowledge, this is the first study to directly measure spinal cord perfusion in response to infusion of various vasopressors. The current guideline for treatment of acute SCI is to elevate MAP >85mmHg for up to 7 days, but the literature supporting these recommendations are weak. The results of this study challenges the dogma that increase in MAP directly corresponds to increase in SCP. Moreover, epinephrine may be the best vasopressor to maintain SCP. Future studies to determine if this correlates to improved blood flow in SCI (rodent SCI model) and improved outcomes following SCI (clinical study) are warranted.

REFERENCES

1. Yoshioka K, Niinuma H, Ehara S, Nakajima T, Nakamura M, Kawazoe K. MR angiography and CT angiography of the artery of Adamkiewicz: state of the art. *Radiographics*. 2006 Oct; 26 Suppl 1:S63-73.

Development of a Machine Learning Algorithm to Predict Burst Suppression During General Anesthesia Based on EEG Features

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INTRODUCTION

Processed electroencephalogram (EEG) monitors gained significant traction in recent years to monitor the depth of anesthesia (DoA). Initially developed to assess a patient's level of consciousness during general anesthesia to avoid awareness, this technology simultaneously enables the clinician to identify burst suppression (BS) in some patients. BS is defined by the alternation of isoelectric flat EEG with bursts of slow waves with high voltages and is typically associated with excessive DoA. Recently, intra-operative BS has been associated with postoperative delirium (POD)<u>1</u>, postoperative cognitive dysfunction (POCD)<u>2</u> and mortality<u>3</u>. If BS episodes could be predicted, anesthesia may be adjusted in order to avoid them. In this project, we hypothesize that raw EEG signals can be analyzed to predict future events of BS at 2, 5, 7 and 10 minutes before its occurrence.

METHODS

Using the open-access VitalDb anesthesia database, we extracted 1369 episodes of BS and 7821 BS-free episodes from a total of 4596 patients. BS episodes were defined as more than 60 seconds of BIS suppression ratio (SR) higher than 0.1. BS-free episodes were defined as 8 minutes of BIS SR equal to 0. We divided the dataset into a training and validation cohort using a 70/30 split ratio. We trained algorithms using pre-processed 10, 20, and 30 seconds EEG segments and 2, 5, 7, and 10 minutes of prediction lag (time between the analyzed EEG segments and the start of the BS/BS-free episode). From these, we extracted 29 features in the power, entropy and spectral domains. Based on feature importance from initial training, we selected 13 features for the final algorithm.

RESULTS

Optimized Multilayer Perceptron (MLP), XGBoost and Logistic Regression (LR) were tested with each combination of EEG segment's duration and prediction lag to predict burst suppression with the highest area under the receiver operating characteristic (AUROC) value. The best results were achieved using a MLP using 30 seconds segments. The algorithm predicted BS episodes with a sensibility and specificity of 90.6% (87.6 to 94.3%), 92.1% (86.7 to 95.4%) 2 minutes before a BS episode (AUROC, 0.963 [0.960-0.967]). The algorithm predicted BS with a high sensibility and specificity (82.9% (78.3 to 88.2%), 83.0%

(79.0 to 87.0%)) up to 10 minutes before a BS episode (AUROC, 0.910 [0.903-0.913]) (Fig.1).

DISCUSSION

Our results demonstrate that using raw EEG-extracted features, deep learning algorithms can predict BS with a high sensibility and specificity up to 10 minutes in advance during general anesthesia. The development and clinical use of BS prediction algorithms could allow anesthetic treatment optimization in order to avoid them. However, the impact of this type of algorithm on patient outcomes, like POD, POCD and mortality, remains to be studied.

- Pedemonte JC et al. Electroencephalogram Burst-suppression during Cardiopulmonary Bypass in Elderly Patients Mediates Postoperative Delirium. *Anesthesiology*. 2020;133(2):280-292.
- 2. Deiner S et al.. Can intraoperative processed EEG predict postoperative cognitive dysfunction in the elderly? *Clin Ther.* 2015;**37**(12):2700-2705.
- Watson PL et al. Presence of electroencephalogram burst suppression in sedated, critically ill patients is associated with increased mortality. *Crit Care Med*. 2008;36(12):3171-3177.



Figure 1. A : ROC Curve – 30 seconds segments, 120 seconds prediction lag. **B** : ROC Curve – 30 seconds segments, 600 seconds prediction lag. **C** : Features Mean SHAP Value, MLP - 30 seconds segments, 120 seconds prediction lag. **D**: Features Mean SHAP Value, MLP - 30 seconds segments, 120 seconds prediction lag.

Dexmedetomidine Provides Optimal Conditions for Brain Mapping during Awake Craniotomy Avoiding Airway Manipulation and Maintaining Hemodynamic Stability

AUTHORS

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INTRODUCTION

Awake craniotomy has been practiced for many decades with the goal of maximal tumor excision without impacting eloquent brain function including communication and motor function. A number of anesthetic approaches have been utilized. We have recently developed an approach to anesthesia for awake craniotomy utilizing dexmedetomidine as the primary anesthetic agent. This has allowed for proceeding with awake cases without the need for airway manipulation. However, concerns about the use of dexmedetomidine include the risk of bradycardia and hypotension and the need to support hemodynamics. We report here a case series of 74 patients undergoing awake craniotomy with dexmedetomidine as the primary anesthetic agent. We hypothesize dexmedetomidine can be utilized as an anesthetic for awake craniotomy without the risk of hemodynamically significant hypotension (greater than 20% sustained reduction in SBP) or bradycardia (requiring treatment with muscarinic antagonist).

METHODS

With research ethics approval, the charts of 74 patients who underwent awake craniotomy between 2012 and 2022 were reviewed by two authors (AP, GB). A previous publication had reviewed 55 of these cases¹, in which the minimum and maximum blood pressure and heart rate (HR) were reported. In the current study, we assessed maximum and minimum systolic and dyastolic blood pressures and HR as well as inspected all anesthetic records for evidence of hypotension and bradycardia throughout the duration of the procedure. Airway instrumentation/management was defined by the use of a laryngeal mask or endotracheal tube during the procedure. We also assessed the use of vasopressors (ephedrine, phenylephrine) and glycopyrrolate/atropine. Data are presented as mean and standard deviation. Utilization of additional anesthetic and analgesic medications were assessed as well as conditions for brain mapping, degree of tumor excision, duration of surgery and post-operative disposition.

RESULTS

Patients were 38% female, mean age 46 ± 16; and BMI 27.3 ± 5.5. Length of surgery was 280 ± 73 minutes. Maximal and minimal systolic and diastolic blood pressures and HR were 152 ± 19 and 107 ± 14 mmHg; 84± 9 and 56 ± 5 mmHg; 78 ± 14 and 54 ± 10 BPM, respectively. Dexmedetomidine was the primary anesthetic in all cases. Five patients (7%) received ephedrine (10 mg); 3 patients (4%) received phenylephrine, infusions (20 mcg/minute; 30 or 120 minutes). Two patients (3%) received glycopyrrolate (0.2 mg) No patients required airway intervention. Transient focal seizures occurred in 10 patients; 5 resolved with cold saline application alone; 5 required midazolam/phenytoin/levetiracetam. Patient were discharged to the floor (7%), step down unit (92%) and ICU (1%). The Average length of stay was 4 ± 4 days. New neurological deficits were observed in 11/75 (15%) patients. Most resolved completely.

DISCUSSION

We have completed a series of 74 patients for awake craniotomy utilizing dexmedetomidine with favorable outcomes with no need for airway instrumentation. Optimal conditions for brain mapping were obtained with a low incidence of intraoperative seizures and new neurological deficits. We observed no incidence of clinically significant hypotension or bradycardia and use of vasopressors/ glycopyrrolate was minimal. We propose that the surgical stimulations and conditions associated with awake craniotomy allow for the use of dexmedetomidine as the primary anesthetic without evidence of clinically significant hypotension or bradycardia in 74 cases.

REFERENCES

 McAuliffe N, Nicholson S, Rigamonti A, Hare GMT, Cusimano M, Garavaglia M, Pshonyak I, Das S. Awake craniotomy using dexmedetomidine and scalp blocks: a retrospective cohort study. Can J Anaesth. 2018 Oct;65(10):1129-1137. PMID: 29978278

Impact of the Transcranial Doppler in Cardiac Surgery Setting: A Retrospective Analysis

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INTRODUCTION

During cardiac surgery, transcranial Doppler (TCD) represents a noninvasive modality that allows measurement of red blood cell flow velocities in the cerebral arteries, specifically the middle cerebral artery. TCD can also be used to detect and monitor embolic material in the cerebral circulation. Detection of microemboli is reported as a high intensity transient signal (HITS). Microemboli that enter the cerebral circulation appear to be one of the frequent causes of stroke or neurologic complications during bypass surgery.¹⁻³ The importance of cerebral microemboli during cardiac surgery has been linked to the increased incidence of postoperative renal failure, right ventricular dysfunction, and hemodynamic instability.^{4,5} We aimed to determine whether the embolic load is associated with hemodynamic instability during cardiopulmonary bypass (CPB) separation.

METHODS

After approval by the local research and ethics committee, a retrospective single-centre cohort study of 354 patients undergoing cardiac surgery between December 2015 and March 2020 was conducted. Automated quantification of HITS was routinely performed in all these patients. The primary endpoint was the proportion of patients presenting an unsuccessful CPB separation defined by the use of at least 1 vasopressor and at least 1 inotrope, a return on CPB or separation with the use of a mechanical circulatory support. A successful separation from CPB was defined as the use of \leq 1 vasopressor or \leq 1 inotrope to achieve CPB separation. The distribution of successful and unsuccessful CPB separation was compared between the three groups using a chi-squared test. Multivariate logistic regression was used to determine the potential association between an unsuccessful CPB separation and the number of embolic materials. Automated quantification was obtained, and patients were divided in terciles, where 117 patients had a low quantity of embolic material (L), 119 patients have a medium quantity of microemboli (M) and 118 patients who have a high quantity of embolic material (H).

RESULTS

Difficult CPB separation was observed in 35% of patients in the H group compared to 16% and 21% of patients in the M and L groups respectively (p<0.001). In the multivariate analysis, patients with high vs. medium embolic load increased their odds of having a difficult CPB weaning (OR=3.86, CI: 1.64-9,05; p=0.002). A patient with a higher quantity of cerebral

embolic material increases his chance of having a difficult CPB weaning by 386% compared to a patient in the M group. Patients in the H group tend to have more complex surgery (H: 54%; M: 26%; L: 9%, p<0.001), longer CPB time (median [IQR], H: 98[72-136]; M: 74[53-99]; L: 67[51-94], p<0.001), higher Time of Persistent Organ Dysfunction (TPOD) (median [IQR], H: 16[3-40.5]; M: 6[2-23]; L: 9[2-22.5], p<0.001) and a longer stay in the ICU (median [IQR], H: 2[1-4]; M: 2[1-3]; L: 1[1-3], p=0.022), compared to those in the M and L groups.

DISCUSSION

In cardiac surgery, a high quantity of cerebral embolic material increases the odds of having an unsuccessful CPB separation. Also, it seems to be correlated to more complex surgery, a longer CPB time, more blood lost, a higher TPOD and a longer stay in the ICU. Finally, six out of eight patients who died in this cohort were in group H.

- 1. Ackerstaff RG, Moons KG, van de Vlasakker CJ, et al. Association of intraoperative transcranial doppler monitoring variables with stroke from carotid endarterectomy. *Stroke*. 2000;31(8):1817-1823.
- Newman MF, Grocott HP, Mathew JP, et al. Report of the Substudy Assessing the Impact of Neurocognitive Function on Quality of Life 5 Years After Cardiac Surgery. *Stroke.* 2001;32(12):2874-2881.
- 3. Mark DB, Newman MF. Protecting the brain in coronary artery bypass graft surgery. *Jama.* 2002;287(11):1448-1450.
- 4. Patel N, Minhas JS, Chung EM. Intraoperative Embolization and Cognitive Decline After Cardiac Surgery: A Systematic Review. *Semin Cardiothorac Vasc Anesth.* 2016;20(3):225-231.
- 5. Sreeram GM, Grocott HP, White WD, Newman MF, Stafford-Smith M. Transcranial Doppler emboli count predicts rise in creatinine after coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth.* 2004;18(5):548-551.

Perioperative Cortical Hand Stroke Syndrome Mimicking Peripheral Neuropathy: A Case Report and Review of the Literature

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INTRODUCTION

Timely diagnosis of perioperative stroke is challenging. As a result, therapeutic interventions are infrequently offered and prognosis may be poor. Cortical hand syndrome is a rare stroke presentation resulting from infarction of the 'hand-knob,' an omega or epsilon-shaped region within the precentral gyrus¹. These patients commonly present with symptoms mimicking peripheral nerve palsies without cerebellar or pyramidal signs suggestive of a stroke. Most commonly, symptoms consist of isolated hand paresis, but concomitant sensory disturbances as well as arm and face involvement have been observed²⁻⁴. These patients tend to recover well with no or minor ongoing deficits and low recurrence risk²⁻⁵. However, this condition should not be considered benign as prognosis depends on the stroke mechanism and risk factor control. We present a case of cortical hand syndrome in a surgical patient initially diagnosed with peripheral neuropathy. There are no prior reports of cortical hand syndrome in the perioperative setting.

CASE PRESENTATION

The patient provided written informed consent for presentation of this case. A 68-year-old male with multiple stroke risk factors underwent a nephroureterectomy for urothelial carcinoma under general anesthesia and thoracic epidural analgesia. The patient noted right-hand numbness and weakness to digits 3-5 immediately after surgery and notified his bedside nurse the following day. His symptoms were initially presumed to be an ulnar neuropathy secondary to surgical positioning. As his symptoms persisted the following day, computed tomography of the head revealed an acute cortical infarct in the precentral gyrus in the region of motor innervation of the right hand consistent with cortical hand syndrome. Subsequent detailed neurologic consultation revealed 3/5 power on right wrist extension and 0/5 power on extension of the right 3rd, 4th, and 5th digits, and 4/5 power on right arm abduction, elbow flexion, and extension. The examination also revealed right-hand numbness localized to the 3rd, 4th, and 5th digits and extending to the mid-right forearm. No deficits were found on his left side, and the rest of the neurologic examination was

unremarkable. Further work-up revealed moderate (60-80%) stenosis of the left carotid artery and he underwent a successful carotid endarterectomy one week later. He was discharged with high-dose atorvastatin and low-dose acetylsalicylic acid. His symptoms had improved substantially at 3-month follow-up.

CONCLUSION

Cortical hand syndrome is a rare presentation of perioperative stroke, which may be misdiagnosed as peripheral neuropathy. However, our case presentation highlights that perioperative stroke should be considered in patients presenting with isolated neurologic deficits of the hand, particularly in those with stroke risk factors. While the prognosis of this syndrome is good, timely diagnosis is crucial to address risk factors and offer therapeutic interventions to prevent stroke recurrence.

- 1. Yousry TA, Schmid UD, Alkadhi H, Schmidt D, Peraud A, Buettner A, et al. Localization of the motor hand area to a knob on the precentral gyrus. A new landmark. Brain. 1997;120(Pt 1):141–57.
- Peters N, Müller-Schunk S, Freilinger T, Düring M, Pfefferkorn T, Dichgans M. Ischemic stroke of the cortical "hand knob" area: Stroke mechanisms and prognosis. J Neurol [Internet]. 2009 Jul 8 [cited 2022 Oct 29];256(7):1146–51. Available from: <u>https://link.springer.com/article/10.1007/s00415-009-5104-8</u>
- 3. Orosz P, Szőcs I, Rudas G, Folyovich A, Bereczki D, Vastagh I. Cortical Hand Knob Stroke: Report of 25 Cases. J Stroke Cerebrovasc Dis. 2018;27(7):1949–55.
- Zhang Z, Sun X, Liu X, Wang L, Zhu R. Clinical features, etiology, and prognosis of hand knob stroke: a case series. BMC Neurol [Internet]. 2022 Dec 1 [cited 2022 Oct 29];22(1):1–6. Available from: https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-022-02858-0
- 5. Finkelsteyn AM, Saucedo MA, Miquelini LA, Chertcoff A, Bandeo L, Pacha S, et al. Ischemic stroke of the "hand knob area": a case series and literature review. J Clin Neurosci. 2019 Jul 1;65:100–5.

Type and Pattern of Hypercapnic Stimulus Affects Success of Cerebrovascular Reactivity Measurements: A Single Centre Retrospective Analysis of 1115 Examinations

AUTHORS

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INTRODUCTION

Cerebrovascular reactivity (CVR) is a measure of the change in cerebral blood flow in response to a vasoactive challenge¹. It is a useful indicator of the cerebrovascular reserve capacity, an important predictor of the risk of stroke and cognitive decline in patients with steno occlusive disease and the ageing brain^{2,3}. A non-invasive method of measuring CVR uses precisely controlled CO₂ as vasoactive stimuli and Blood Oxygen Level Dependent (BOLD)-MRI as a surrogate of cerebral blood flow⁴. However, the inability to tolerate CO₂ can affect the success of CVR measurement⁵. The aim of this study was to determine if the type and pattern of CO₂ stimulus influence the success of CVR measurement. We hypothesize that individualized hypercapnic stimuli (resting+10mmHg) will be better tolerated by the patients than standardized stimuli (40-50 mmHg) and hence will have higher success with CVR measurements.

METHODS

After Institutional Research Ethics Board approval and informed patient consent, we analyzed the prospectively collected database of all patients who underwent a CVR study between October 2005 and May 2021. CVR measurements were performed using precise control of end-tidal PCO₂ ($P_{ET}CO_2$) as a vasoactive stimulus and BOLD MRI as a surrogate of CBF. The primary outcome was to compare the effect of two types of hypercapnic stimuli (40 mmHg to 50 mmHg vs. resting $P_{ET}CO_2 + 10$ mmHg) on the success of CVR examinations. The secondary outcome was to compare the two different patterns of stimuli; 2 square wave patterns of stimulus (2 STEP protocol) vs a square wave stimulus followed by a slow ramp stimulus (STEP + RAMP protocol). Successful CVR examinations were defined as those where: 1) patients were able to complete CVR testing, and 2) a clinically useful CVR map was generated. Differences in the outcome between the groups were compared with the Chi-Square test.

RESULTS

A total of 1115 CVR tests in 662 patients were included in the final analysis. The mean (±SD) age was 46.1 (±18.8) years, and 43% of patients were female. The study population included 491 steno-occlusive disease and 171 non-steno-occlusive disease patients. With regards to hypercapnic stimuli, 558 (50.0%) studies used 40-50 stimuli and 520 (46.6%) studies used resting + 10 stimuli. Regarding the pattern of stimuli, 663 (59.4%) studies used a 2 STEP (40-50mmHg) stimulus protocol and 415 (37.2%) used the STEP + RAMP protocol. Overall, 1012 (90.8%) examinations were successfully completed. The resting + 10 mmHg stimuli type had a higher success rate [94.4% (421/520)] compared to the 40-50 stimuli type [87.8% (489/558)] (p- < 0.001). Regarding the pattern of stimulus, the STEP + RAMP protocol had a higher success rate [95.2% (395/ 415)] compared to the 2 STEP protocol [88.4% (586/663)]. (p < 0.001) (Figure 1).

DISCUSSION

This large series single-centre study showed that CVR measurement using precisely controlled CO_2 in an MRI environment was well tolerated in 90.8% of patients with no major adverse events. However, hypercapnic stimuli type and pattern do affect the patient tolerability and hence the success of CVR measurement. Baseline (resting) +10 mmHg stimulus is better tolerated than 40 to 50 stimuli because the baseline $P_{ET}CO_2$ amongst these patients varies from 24 mmHg to 50 mmHg. The findings of our study are valuable for developing a cerebrovascular stress test that assesses the cerebrovascular reserve on an individual basis

- 1. Juttukonda MR, Donahue MJ. Neuroimaging of vascular reserve in patients with cerebrovascular diseases. NeuroImage. 2017; 17: 30828–5
- 2. Balucani C, Viticchi G, Falsetti L, Silvestrini M. Cerebral hemodynamics and cognitive performance in bilateral asymptomatic carotid stenosis. *Neurology*. 2012;79:1788-1795.
- 3. Fisher JA, Venkatraghavan L, Mikulis DJ. Magnetic Resonance Imaging-Based Cerebrovascular Reactivity and Hemodynamic Reserve. Stroke. 2018 Aug;49(8):2011-2018.
- 4. Sobczyk O, Fierstra J, Venkatraghavan L, Poublanc J, Duffin J, Fisher JA, et al. Measuring Cerebrovascular Reactivity: Sixteen Avoidable Pitfalls. Front Physiol. 2021;12:665049
- 5. Spano VR, Mandell DM, Poublanc J, Sam K, Battisti-Charbonney A, Pucci O, et al. CO2 blood oxygen level-dependent MR mapping of cerebrovascular reserve in a clinical population: safety, tolerability, and technical feasibility. Radiology. 2013;266(2):592-8.



Figure 1: Figure showing % of success with the type (A) and pattern (B) of hypercapnic stimuli. The resting + 10 mmHg stimuli type had a higher success rate [94.4% (421/520)] compared to the 40-50 stimuli type [87.8% (489/558)] (chi-square test, p-value < 0.001). (Figure A). The STEP + RAMP protocol had a higher success rate [95.2% (395/415)] compared to the 2 STEP protocol [88.4% (586/663)]

(chi-square test, p-value < 0.001) (Figure B)