Efficacy of Ancillary Cardiopulmonary Therapeutic Regimen on Tissue Perfusion, Post-operative Pain, and Pulmonary Functions During Acute Phase I of Cardiopulmonary Rehabilitation Following CABG Surgery: A Pilot study

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ABSTRACT

Background: Impaired tissue perfusion, postoperative pain discomfort, and postoperative pulmonary complications are all significant concerns that arise immediately after coronary artery bypass grafting (CABG).

Aim: This is a prospective pilot study that investigated the effects of prophylactic Non-Invasive Positive Pressure Ventilation (NIPPV) on tissue perfusion and the effect of Transcutaneous Electrical Nerve Stimulation (TENS) as combined ancillary therapy on acute postoperative pain at coughing and pulmonary functions in participants who underwent off-pump CABG surgery with good left ventricular function or mild left ventricular dysfunction.

Methods: This pilot study involved 40 participants, randomly divided into two groups: an intervention group (n = 20) receiving NIPPV (2 sessions) and TENS (6 sessions), and a control group (n = 20) receiving standard routine care. We assessed the tissue perfusion effect on each group using blood lactate and mixed central venous oxygenation (ScvO2) levels. We measured the effect of pain on each group using a Numerical Pain Rating Scale (NPRS) and measured lung function using spirometry.

Results: There are statically significant difference in post operative pain at coughing, tissue perfusion, pulmonary functions and length of intensive care stay ($p<0.001$). Compared to the control group (mean difference of ScvO2 and blood lactate at baseline, 1sthour, 8thhour and post 30 minutes of 8th hour were 59.3±3.294, 57.4±2.873, 57.3±3.556, 57.35±3.453 and 2.48±0.2308, 2.445±0.2417, 2.105 ±0.3649, 2.105±0,3649), NIPPV greatly increased blood flow to tissues (mean difference of ScvO2 and blood lactate at baseline, post 1st hour, 8th hour and post 30 minutes of 8th hour were 59.1±3.946, 64.1±5.16, 67±4.484, 66.9±4.229, $p<0.001$ and 2.51±0.3024, 2.095±0.2837, 1.705±0.2089, 1.705±0.2089, $p<0.001$). TENS greatly decreased pain at coughing (mean difference at day 0, 1st ,2nd and 5th postoperative day were 9.0500±.223, 6.25±1.25132, 4.8±1.15166, 4.4±0.50262 and enhanced the pulmonary function in the intervention group ($p<0.001$). Also, the intervention group showed a lower incidence of impaired respiratory events and shorter duration's of postoperative ICU stays compared to the control group.

Conclusion: Administration of prophylactic Non-Invasive Positive Pressure Ventilation (NIPPV) and TENS as combined ancillary therapy may improve tissue perfusion, reduce post operative pain at coughing, pulmonary complications, and decreases the length of intensive care stay in off-pump coronary artery bypass graft (CABG) patients with good left ventricular (LV) or mild left ventricular (LV) dysfunction during the acute phase I of cardio-pulmonary rehabilitation, when compared to standard treatment alone.

Keywords: Non-Invasive Positive Pressure Ventilation, Transcutaneous Nerve Stimulation, Blood Lactate, Mixed Central Venous Oxygenation, Numerical Pain Rating Scale.

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INTRODUCTION

Every year globally, coronary artery disease (CAD) claims the lives of 8.9 million people and causes 164.0 million disability-adjusted life years (DALYs) [1]. The United States completes approximately 200,000 cases of Coronary Artery Bypass Graft (CABG) surgery annually, while Western European countries have an average incidence rate of 62 cases per 100,000 inhabitants [2]. Studies have shown that CABG is the most effective therapeutic approach for patients diagnosed with CAD. This is because it has the potential to improve cardiac function, increase survival rates, and alleviate symptoms, ultimately leading to a better quality of life. Nevertheless, the sense of pain subsequent to CABG is multifaceted. The postoperative pain phenomenon attains its peak intensity within the first twenty-four hours following the procedure and subsequently decreases progressively over the following days due to intrinsic self-limiting mechanisms [3]. Postoperative pain may arise due to several variables, including anaesthesia, narcotics, mechanical breathing, surgical incisions, tissue retraction, electrocautery, and postoperative chest tube insertion. Hence, prioritizing pain management is important for patients in the critical care unit who are recovering from surgery. Inadequate pain management may result in a worse quality of life, prolonged rehabilitation, postoperative pulmonary complications (PPC) and increased health care cost [4]. The use of analgesic medications and non-pharmacological methods has advanced the pain management following surgery, yet it remains a significant issue in the postoperative phase. The International Association of Studies of Pain defines pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." Postoperative pain often results in increased morbidity rates, decreased quality of life, extended recovery periods, and higher healthcare expenses, impacting approximately 80% of patients [5,6]. In particular, after heart surgery, adequate postoperative pain management is essential. Despite an extensive amount of study on CABG surgery, postoperative pain discomfort is still a major problem [7,8]. Various studies have reported varying incidence rates of PPC. Notably, the incidence of PPC after cardiac surgery ranges from 10% to 25%. Specifically, around 2% to 5% of cardiac surgery patients are at risk of experiencing severe postoperative lung dysfunction after the procedure. An autopsy revealed that 5% to 8% of mortality after heart surgery may be associated with respiratory problems. [9,10] Atelectasis (16.6–88%) in particular basilar atelectasis is a common PPC that is detected in up to 94% of patients within 48 hours after CABG often, it happens due to reduced tidal volume following hypoventilation associated with pain. As a result, compromised gas exchange occurs due to an intrapulmonary shunt or ventilation-perfusion mismatch associated with a decrease in cardiovascular function right after the surgery. In addition, multiple studies declared that elevated blood lactate and reduced central venous oxygen saturation (ScvO2) have been associated with increased complication rates and prolonged hospitalization following cardiac surgery, resulting in higher morbidity and mortality after CABG [11-13]. However, multiple studies have demonstrated that PPC after CABG is unavoidable, leading to a higher likelihood of respiratory complications and prolonged recovery [14-16]. There is presently a dearth of research which acknowledges the relationship between postoperative pain, tissue perfusion, and pulmonary functions. However, not properly managing acute post-operative pain may lead to more impairments, which could make the cardiopulmonary rehabilitation period longer due to physical deconditioning, decreased functional capacity, decreased tissue perfusion, immobility, and muscle atrophy. In this particular instance, using validated measures and standardized modalities for tissue perfusion, post operative pain, and pulmonary function is essential to obtaining better outcomes during phase I cardio-pulmonary rehabilitation. Although extensive research work has favoured the application of Transcutaneous Electrical Nerve Stimulation (TENS) and Non-Invasive Positive Pressure Ventilation (NIPPV) in different medical conditions as a single treatment. However, its application as combined ancillary therapy on early acute medical or/ and post-surgical conditions is limited. Also, at present, there is a lack of research on the effects of early combined TENS and NIPPV on its modes, applications, and durations as an ancillary treatment on key parameters and clinical outcomes following CABG surgery. The aim of this study was to investigate the effects of NIPPV and TENS as ancillary therapies in improving tissue perfusion, reducing pain, and preventing postoperative pulmonary complications during the initial phase I of cardiopulmonary rehabilitation and clinical outcomes in patients who had undergone off-pump CABG with preserved good LV function or/and mild LV dysfunction.

MATERIALS AND METHODS

Ethics

Our research was carried out at a single centre, following a prospective randomized controlled trial design. The study took place in the cardio-thoracic intensive care unit (CTICU) between March and December 2023. All study participants gave their informed agreement by completing a consent form that complied with the ethical guidelines for research involving human subjects. This ensured that individuals were fully informed about the objectives, risks, and benefits of the study before consenting to take part. Following ethical standards and regulations this study protocol was approved by the institutional research ethics committee (IHEC-II/0327/23), and with Indian clinical trial registry (CTRI/2023/02/049983) and the study adheres to the CONSORT guidelines for reporting clinical trials, and a completed CONSORT checklist was completed and attached (supplementary file 1).

Study participants and randomization

The study included participants who underwent elective CABG and had a history of left ventricular ejection fraction greater than 40% ranging from good LV function (50-70%) to mild dysfunction (40-49%). Participants were required to be of either gender and aged between >25 and 75 at the time of the surgical procedure and all other demographic characteristics are depicted in Table 1. The exclusion criteria for this study consisted of moderate and severe left ventricular dysfunction, renal impairment, liver disease, chronic obstructive pulmonary disease (COPD), bronchial asthma, neurologic disease, hemodynamic instability, emergency CABG, more than 24 hours of invasive ventilation after CABG, uncooperative to non-invasive ventilation (NIV), blood lactate >3 before extubation. The day prior to surgery, study participants were assigned at random to either the control group or the intervention group .The randomization process utilized the software "random.org" to allocate participants to either the control or intervention group. Sealed, opaque envelopes were used for allocation concealment to prevent selection bias. To minimize performance bias and make certain the findings are unaffected by knowledge of the intervention, the participants and medical specialists working in ICU were blinded to the study. Hence, two assessors involved in the study. Assessor 1 will be trained to administering NIPPV and TENS. Assessor 2 will evaluate spirometry tests, measure pain severity, evaluate PPC, ICU, and hospital length of stay in both the control and intervention groups.

Procedures and settings

All participants in both groups underwent similar general anesthesia following a standardized protocol. Sufentanil and isoflurane were administered to maintain anesthesia while utilizing invasive ventilation in a synchronized inter-mandatory ventilation mode (SIMV). A tidal

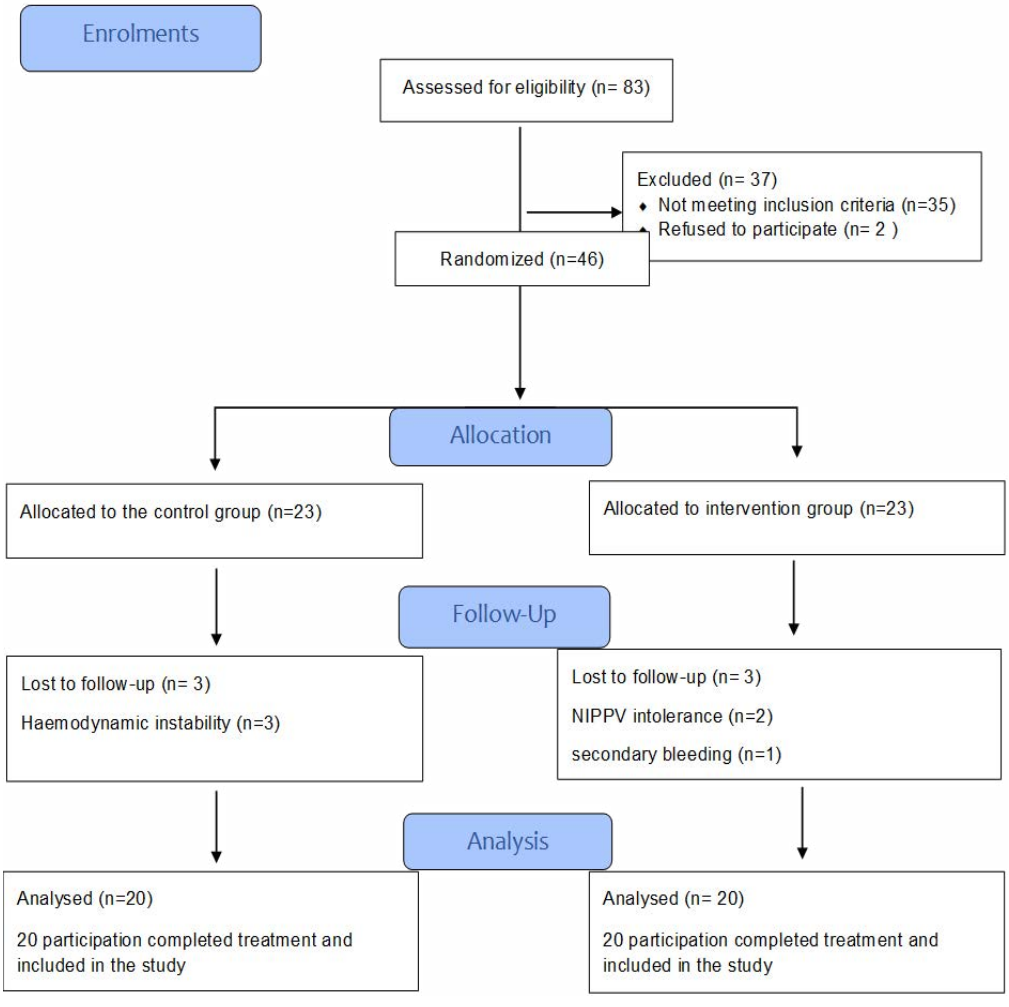
Table 1. Participant's Clinical and Demographic Characteristics

Participant's Characteristics		Frequency (n=40) Mean±SD	Control Group (n=20)	Experimental Group (n=20)	P value
Age		58.25±6.819	59.1±6.504	57.4±7.185	.438
BMI		26.64±1.806	26.83±1.797	26.46±1.843	.524
EF %		49.87±8.131	49.95±7.904	49.8±8.557	.954
Gender	Male	35(87.5)	17(85.0)	18(90.0)	.633
	Female	5(12.5)	3(15.0)	2(10.0)	
	Total	40(100.0)	20(100.0)	20(100.0)	
Smoking	Yes	11(27.5)	6(30.0)	5(25.0)	.723
	No	29(72.5)	14(70)	15(75.0)	
	Total	40(100.0)	20(100.0)	20(100.0)	
HTN	Yes	26(65.0)	14(70.0)	12(60.0)	.507
	No	14(35.0)	6(30.0)	8(40.0)	
	Total	40(100.0)	20(100.0)	20(100.0)	
DM	Yes	30(75.0)	16(80.0)	14(70.0)	.465
	No	10(25.0)	4(20.0)	6(30.0)	
	Total	40(100.0)	20(100.0)	20(100.0)	
DLD	Yes	11(27.5)	5(25.0)	6(30.0)	.723
	NO	29(72.5)	15(75.0)	14(70.0)	
	TOTAL	40(100.0)	20(100.0)	20(100.0)	

Data are shown as frequency and mean ± standard deviation, BMI=body mass index; EF, Ejection Fraction; HTN, Hypertension; DM, Diabetes Mellitus; DLD, Dyslipidemia;

Figure 1: Consort flow chart

Flowchart of consecutive CABG patients enrolled in the study.



volume of 8 mL/kg of predicted body weight, a respiratory rate of 14–16 breaths per minute with an I: E time of 1:2 to maintain PaCO2 levels between 35 and 45 mm Hg, a positive end-expiratory pressure (PEEP) of 5-7 cm H2O, and adequate FiO2 to keep oxygen saturation above 96% were the parameters for ventilation. The treatment consisted of performing a median sternotomy to access the chest, followed by the dissection of the left internal mamillary artery and saphenous veins for use as grafts. All participants underwent off-pump coronary artery bypass grafting with the assistance of an Octopus 3 suction stabilizer from Medtronic in Minneapolis, Minnesota. Throughout the procedure, the body temperature was regulated by a heated water mattress. A polyvinyl chloride drain (subxiphoid placement of 2 mediastinal drains) was inserted before closing the chest in case of an inadvertent left pleural opening. All patients were transferred to the specialized cardiothoracic surgery intensive care unit and connected to SIMV mode with same above settings mentioned. Following extubation, both group participants in the intensive care unit (ICU) received an 8 litre per minute (52%) of oxygen through a face mask, in accordance with the institutional protocol.

Interventions

NIPPV

Following extubation, the patient receives 8LPM of oxygen via a facemask. Forty-five minutes post-extubation, blood samples were taken for baseline analysis to assess the patient's blood lactate levels and central venous oxygen saturation. The ABL800 FLEX blood gas analyzer is a commonly used for obtaining measurements of blood lactate and mixed central venous oxygen saturation. At the first hour of post-extubation, participants in the intervention group received Non-Invasive Positive Pressure Ventilation (NIPPV) through an orofacial interface mask with a double limb circuit with a true exhalation valve provided with a calibrated leak. The following initial settings were used: the respiratory rate was set at 14 b/min as backup, inspiratory positive airway pressure (IPAP) of 10-12 cmH2O was initiated to overcome upper airway resistance and to reduce the work of breathing (WOB), and then adjust based on patients' comfort or clinical response. and expiratory positive airway pressure (EPAP) of 4-5 cmH2O was initiated to prevent alveoli collapse at the end of each respiratory cycle. The inspiratory pressure was set to ensure a tidal volume (VT) within the range of 6-8 mL/kg of estimated body weight and a fraction of inspired oxygen (FIO2) of 0.5 was maintained to keep SpO2 of more than 96%. The NIPPV application will be performed in the 1st hour and 8th hour (2 sessions) for durations of 45 minutes. Following the administration of NIPPV, the patients were later transitioned to 8 (52%) LPM of oxygena and the session was repeated with the same above-mentioned settings at the 8th hour of post extubation. Furthermore, a dosage of 1 gram of paracetamol was given three times a day for pain relief. Participants in the control group received continuous exposure to a 8 (52%) LPM of oxygen and pain management regimen consisting of 100 mg of tramadol hydrochloride thrice daily and 1 gram of paracetamol administered three times a day for pain relief.

TENS

The administration of Transcutaneous Electrical Nerve Stimulation (TENS) commenced immediately after the removal of the endotracheal tube and was then repeated at every 8-hour interval for a duration of 48 hours (equivalent to 2 days). We used a portable TENS device (Transcutaneous Electrical Nerve Stimulation) from KLD in Amparo, SP, Brazil to provide TENS therapy. We administered the electrical current using four self-adhesive surface electrodes, each measuring 3.5 cm. We positioned these electrodes at the subclavicular area on both sides of the incision, approximately 2-3 cm from the suture line. During the 45-minute treatment period, we maintained a constant pulse width of 150 ms and a wave frequency ranging 100 Hz. We modulate the stimulation strength based on the patient's comfort level, ensuring they experience a robust but pleasant tingling feeling. We explicitly directed participtants to initiate a request to decrease the level of stimulation intensity in instances of discomfort.

Measurements

NIPPV - (Blood lactate and ScvO2 measurements)

To assess tissue perfusion. We employed aseptic techniques to procure samples from the femoral artery catheter in order to measure arterial blood lactate levels. Furthermore, blood samples were collected from a central venous catheter to measure ScvO2 levels. Four blood samples were taken from both the control and experimental groups during the four-time-point sessions. At time point 1, participants from both groups were administered 8LPM (52%) oxygen air entrainment through a facemask immediately after extubation. Blood samples were collected from both the control and intervention groups 45 minutes post-extubation. During the 1st hour after extubation, participants in the control group were given a 8LPM (52%) oxygen air entrainment through a facemask, while the intervention group received the first session of non-invasive positive pressure ventilation (NIPPV) for 45 minutes. We obtained blood samples from both the control and experimental groups at the 45-minute mark during session 1 of NIPPV. At time point 3, specifically during the 8th hour after extubation, the control group maintained their oxygen intake at 8 LPM (52%) through a face mask, while the intervention group underwent a second 45-minute session of NIPPV. Following a 45-minute period of non-invasive positive pressure ventilation (NIPPV), blood samples were obtained from both the control and intervention groups. At time point 4, which was past thirty minutes after NIPPV session 2, we took blood samples from the both control and intervention groups.

TENS - (NPRS and spirometry measurements)

We started the TENS treatment immediately after the extubation and continued it every 8 hours for 48 hours (2 days). We will use an 11-point numeric rating scale (NRS) to evaluate pain intensity, with 0 representing no pain and 10 representing the most intense pain imaginable. The assessment will be conducted at rest, before the application of TENS, during the 24th and 48th hours, and on the 5th postoperative day. We assessed spirometry using a portable device (Micro Medical Microloop Model, Brazil). We conducted all tests in accordance with the standards of the American Thoracic Society, measuring FVC and FEV1 preoperatively and on the 1st, 3rd, and 5th postoperative days.

Statistical Analysis

The data were subjected to statistical analysis using IBM SPSS Statistics version 27. A significance level of $p < 0.05$ was employed to determine statistical significance and a 95% confidence interval was set for all analyses. The normality of distribution for the variables was assessed using the Kolmogorov-Smirnov test. The significance was determined using parametric tests once the normality test was confirmed. The clinical and demographic characteristics of the study participants and the quantitative variables were characterized by their respective measures of central tendency, specifically the mean, and measures of dispersion, specifically the standard deviation. Chi-square analysis was employed to ascertain the relationship between qualitative variables, with the results presented in terms of absolute frequencies (n) and relative frequencies (%). The application of the student's t-test has been employed to assess and compare continuous variables. A repeated

measures analysis of variance (ANOVA) to ascertain the statistical significance of both within-group and between-group comparisons.

RESULTS

The study involved 83 patients, with 37 individuals being deemed ineligible and subsequently excluded from the study. Throughout the study, a total of six patients had to be excluded for various reasons. In the control group, three patients were excluded due to hemodynamic instability. Meanwhile, in the experimental group, two patients were excluded due to intolerance to NIPPV, and one patient was excluded due to secondary bleeding from cardiac surgery. Thus, the trial was conducted with a total of 40 patients, with 20 patients in each group, as shown in the flow chart Figure 1.

Impact of NIPPV on tissue perfusion (ScvO2 and blood lactate)

Blood lactate measurement was compared to the measurements obtained at the baseline, post 1st hour, 8th hour and thirty minutes after the eighth hour of NIPPV administration, it was found that blood lactate levels had significantly decreased for both the control and intervention groups. The intervention group, however, showed the greatest stastical difference. Similarly, the ScvO2 measurements were compared to those measurements obtained at baseline, post 1st hour, post 8th hour and thirty minutes after the eighth hour of NIPPV administration, the control group showed a significant decrease in ScvO2, while the intervention group showed a significant increase in ScvO2. and it has been observed that the control group participants who engaged in spontaneous breathing experienced a significant decrease in ScvO2 ($P<0.05$) and a significant increase in lactate levels ($P<0.05$) compared to the interventional group participants who received non-invasive positive pressure ventilation (NIPPV)were shown in Table 2. The use of NIPPV led to a notable 32% reduction in blood lactate levels, along with an increase in ScvO2 by 16.9% compared to the initial measurements. On the other hand, the control group exhibited a 15.3% reduction in blood lactate levels and a 3.4% rise in ScvO2. There were no notable differences in blood lactate and Scvo2 levels between the 30-minute mark after stopping NIPPV and the 8th hour when NIPPV was given. The statistical significance of the observed difference between the groups was established through the calculation of the $P<0.05$ value.

Table 2. Effects of Non-Invasive Positive Pressure Ventilation on tissue perfusion (blood lactate and central venous oxygenation ScvO2) in patients who had cardiac surgery

Measurements	Sessions	Control group (n=20)	Experiment group (n=20)	P value
		Mean ± SD	Mean ± SD	
B. Lactate	lactate Baseline	2.48±0.2308 $	2.51±0.3024 $	.726*
	lactate post-1 Hour	2.445±0.2417 $ δ	2.095±0.2837 $ δ	0.000**
	lactate-post-8 Hour	2.105±0.3649 $ δ	1.705±0.2089 $ δ	0.000**
	lactate-After 30mins	2.105±0.3649 $ δ	1.705±0.2089 $ δ	0.000**
$ScvO_2$	ScVO2 pre-Baseline	59.3±3.294 $	59.1±3.946 $	.863*
	ScvO2 post-1 Hour	57.4±2.873 $ δ	64.1±5.16 $ δ	0.000**
	ScvO2 post-8 Hour	57.3±3.556 $ δ	67±4.484 $ δ	0.000**
	ScvO2-After 30mins	57.35±3.453 $ δ	66.9±4.229 $ δ	0.000**

B.Lactate, Blood Lactate; $ScvO_2$, Central venous oxygenation; minute ventilation; V ,Data are reported as Mean ± SD., $ = Independent sample t test used to find the comparison between control and experiment. δ= Repeated measure ANOVA is used to find the p value of Blood lactate and $ScvO_2$. *= insignificant P value, **=significant P value.

Table 3. Effects of transcutaneous electrical nerve stimulation (TENS) on pain and pulmonary functions Between the groups

Measurements	Sessions	Control group (n=20)	Intervention group (n=20)	P value
		Mean ± SD	Mean ± SD	
NPRS	NRPS-Day-0	8.8500±.489 $	9.0500±.223 $	0.105*
	NRPS-Day-1	8.1±0.96791 $ δ	6.25±1.25132 $ δ	0.000**
	NRPS-Day-2	7.35±0.98809 $ δ	4.8±1.15166 $ δ	0.000**
	NRPS-Day-5	6.3±0.47016 $ δ	4.4±0.50262 $ δ	0.000**
FVC	FVC-Baseline	2.419±0.37304 $	2.516±0.29389 $	0.367*
	FVC-Day-1	1.006±0.27329 $ δ	1.336±0.20093 $ δ	0.000**
	FVC-Day-3	1.3455±0.23529 $ δ	1.5105±0.19359 $ δ	0.000**
	FVC-Day-5	1.4885±0.23729 $ δ	1.686±0.22106 $ δ	0.000**
FEV1	FEV1-Baseline	2.081±0.39786 $	2.235±0.29832 $	0.174*
	FEV1-Day-1	0.92±0.23396 $ δ	1.1985±0.19057 $ δ	0.000**
	FEV1-Day-3	1.1725±0.22431 $ δ	1.38±0.18038 $ δ	0.000**
	FEV1-Day-5	1.303±0.21714 $ δ	1.527±0.21919 $ δ	0.000**

NPRS, Numerical pain rating scale; FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume; Data are reported as Mean ± SD., $ = Independent sample t test used to find the comparison between control and experiment. δ= Repeated measure was used to find the repeated measures of Blood lactate and ScvO2, *= insignificant P value, **=significant P value.

The Impact of TENS on Pain

As expected, cardiac surgery resulted in notable pain. However, all participants tolerated TENS well and no significant side effects were observed. The pain intensity during coughing after the surgery, before the application of TENS, was found to be similar between the groups (Mean ± SD 8.8500±.489, Mean ± SD 9.0500±.223, P = 0.105). The pain levels consistently decreased after each TENS treatment, with all participants experiencing lower pain scores subsequently on the 1st, 2nd, and 5th days compared to day 0, as indicated in Table 3.

The impact of TENS on pulmonary function

Baseline predicted pulmonary function measurements of FVC and FEV1 did not show any significant difference between two groups. However, there were notable differences were seen between the pre- and postoperative values of FVC and FEV1. In each measurement time point, there was an increase in FVC and FEV1 compared to the previous measurement. However, it is worth noting that both FVC and FEV1 showed a significant increase in the TENS group compared to the control group on day 1, day 3, and day 5 after surgery, as shown in Table 3. In addition, the experimental group showed a significant decrease in requests for chest radiographs. Analgesia in this group was managed using TENS and paracetamol at a dosage of 1 gram three times a day, with no tramadol administered. In addition, there were no significant differences observed in the duration of ICU stays and drainage secretions between the two groups.

This study examined the correlation between mild left ventricular (LV) dysfunction and blood lactate levels, as well as scov2 levels, in control and experimental subjects. The study's results indicate a potential link between mild LV dysfunction and changes in blood lactate and scov2 levels. Specifically, 7 participants in the control group showed significantly higher blood lactate levels (mean value of 2.4 mmol/L) and lower scov2 levels (mean value of 54%). These findings highlight the importance of further investigating the relationship between mild LV dysfunction and these biomarkers. In addition, it is worth noting that the control group demonstrated a statistically significant higher occurrence of atelectasis and a longer duration of stay in the CTICU, as illustrated in figure 2. Nevertheless, there were no significant differences found in the length of hospital stays between the two groups.

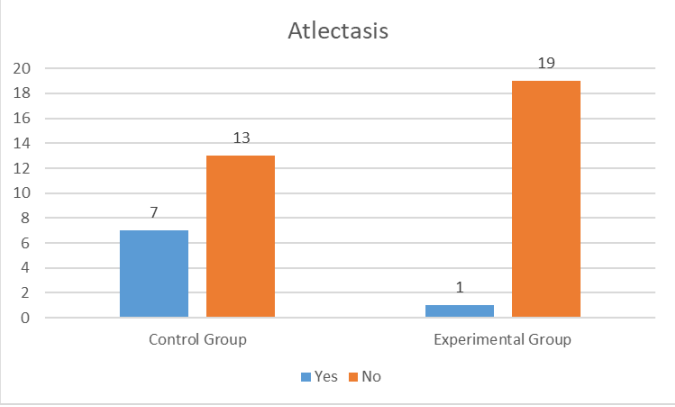


Figure 2. Depicts the incidence of Atelectasis in both control (n=20) and experimental group (n=20)

DISCUSSION

Individuals who have undergone cardiac surgery frequently encounter postoperative pain linked to reduced pulmonary and exercise capacity during the initial phase of cardiopulmonary rehabilitation, in contrast to those who have had less invasive procedures or non-cardiac interventions [17-19]. This study is the first to incorporate prophylactic NIV and TENS as an ancillary therapy in phase 1 cardio-pulmonary rehabilitation to investigate tissue perfusion, postoperative pain during coughing, and pulmonary functioning in post-CABG patients. This study evaluated the impact of TENS on pulmonary function and postoperative pain during coughing, along with NIV on tissue perfusion. The findings highlight that patient who received NIV and TENS as combined ancillary therapy experienced reduced pain discomfort during coughing, enhanced tissue perfusion, better pulmonary function and reduced pulmonary complications. Additional notable impacts of using prophylactic NIV and TENS included a decrease in the consumption of pain medication, a decreased occurrence of post-operative respiratory issues, and a diminished necessity for chest X-rays. This enables greater mobility and the removal of secretions, potentially enhancing the recovery process [20]. In the initial hours following surgery, this study observed notable fluctuations in tissue perfusion levels. Our hypothesis suggests that using prophylactic non-invasive positive pressure ventilation (NIPPV) may enhance myocardial contractility and improve cardiac functions in the current clinical setting. The NIPPV modality is frequently used to treat patients with respiratory failures, cardiogenic pulmonary edema, and exacerbations of chronic obstructive pulmonary disease (COPD). Recently, there has been an increase in the use of NIPPV for treating acute respiratory failure and preventing complications after surgery [21,22]. Furthermore, there was a rise in pain levels right after the operation; nevertheless, by postoperative days 1, 3, and 5, there was a decrease in pain levels and an upsurge in pulmonary functions, tissue perfusions. However, pain intensity displayed fluctuations within the first 48 hours post-surgery and started to decrease on the second day after the procedure [17,23]. Measuring blood lactate and ScvO2 levels is the conventional approach to assess tissue perfusions. Blood lactate concentrations have been thoroughly studied as a potential indicator of oxidative damage following postoperative reperfusion. It is important to note that these values could suggest a transition in the myocardium's metabolism from aerobic to anaerobic, not just oxidative damage. An increased occurrence of surgical complications has been associated with elevated lactate levels, known as hyperlactemia, and is commonly observed in the postoperative phase [24,25]. Polonen et. al. suggested implementing a goal-oriented treatment plan in clinical settings to achieve normal blood lactate levels in heart surgery patients, resulting in reduced hospital stays [26]. Levels of lactate exceeding 3 mmol/l demonstrated the highest sensitivity (82%) and specificity (80%) for predicting mortality [27]. Thus, a lactate threshold of less than 3 mmol/L was utilized in our investigation, and we identified the effect of NIPPV application on cardiac morphology by observing an increase in pleural pressure, which subsequently decreased transmural pressure. Consequently, this enhances cardiac performance by reducing the preload and afterload of the left ventricle, thereby optimizing perfusion to the tissues [28,29,30,31]. Evidence of TENS in pain management is a dearth. However, Studies by Stubbing et al. and Benedetti et al. found no effect of TENS on pain after thoracotomy, [32, 33] whereas other studies and in our study found significant pain relief with TENS. A possible explanation for the inconsistent result could be the different TENS settings and types of surgery utilized in this and other studies. TENS operates based on Melzack and Wall's pain gate theory mechanisms. Myelinated A fibres can effectively inhibit the pain signals from unmyelinated C fibres. Upon stimulation, these fibers block the entry of painful peripheral sensations into higher cerebral centers. The other mechanisms proposed for TENS-induced pain management include endorphin release and activation of inhibitory reflex regions in the brain stem [25]. TENS has been shown to be helpful even in patients with more severe pain when administered for 4 hours, but in our trial, conventional TENS was shown to be effective when it is applied for a short period of 45 minutes, three times a day

for 48 hours and it was noted that TENS proved to be successful in decreasing pain levels and lowering the requirement for opioids and analgesia when electrodes were positioned around the incision area [34,35]. It's interesting to understand that different studies have pointed out a significant decrease in the requirement for pain medication in patients who receive TENS treatment. Similarly, we found applications of TENS after surgery decreases the need for opioids and analgesia. According to Endorgan et al., TENS is useful in reducing the need for opioids after surgery and is successful in treating pain from a thoracotomy [36]. In similar to the statement of Sbruzzi et al., we found opioids were discovered to decrease activity, impede normal breathing recovery, and suppress coughing and airway clearance which lead to atelectasis in control group [37]. In contrast to the statement of Sezen et al, we find a significant reduction in pulmonary complications with the addition of TENS therapy [38]. As a result of CABG surgery, sternotomy pain and intercostal artery harvesting reduces FVC, thereby increased residual volume promote shallow breathing which may lead to atelectasis, a common complication of cardiac surgery, resulting from reduced functional residual capacity after increased resistance in airways, postoperative pain, and leading to hypercapnia, hypoxia, and changes in respiratory mechanics [39]. In such circumstances, Cipriano et al. reported that TENS can be beneficial on pulmonary function in cardiac surgery patients which is similar to our study [40]. McDowell et al. found that application of TENS could increase maximum expiratory pressure, which results in the removal of mucus from the lungs, more effective coughing, and increased pulmonary ventilation and reduction of atelectasis [41]. Fiorelli et al. found that the TENS group showed significantly better results in terms of measured FVC and FEV1 as a percent of predicted values before surgery and at 72, 96, and 120 Post operative hours (POHs) [42]. Another study measured FVC and FEV1 at 24, 48, and 72 POHs. The results showed a significant improvement in FVC at all three-time points. While there was no significant improvement in FEV1 at 24 POHs, it was found to be significant at 48 and 72 POHs.[43]. Likewise, in our study application of TENS significantly improved FVC and FEV1 on days 1, 3 and day 5. Hence, TENS is still a good option for pain management because of its few contraindications and low rate of adverse effects. As a result, it shows promise as a useful component of multimodal pain management to promote healing and lessen dependency on opioids and painkillers, even after discharge [23,38]. Moreover, the opioid dose, requests for chest radiographs and length of ICU stay were significantly lower in the intervention group, which may be due to fewer symptoms of atelectasis, such as low oxygen saturation and retention of lung secretions.

In addition, we found that NIPPV and TENS do not cause any adverse effects. NIPPV can effectively improve the tissue perfusion and TENS can effectively control acute sternotomy pain. However, it may not be as effective in managing severe sternotomy pain with atelectasis. Additional analgesic medication is strongly recommended for these patients instead of relying solely on TENS for pain control. Recent past studies stated that NIPPV and TENS have been found to be effective in reducing the need for opioid intake after surgery and in managing acute post-thoracotomy pain following posterolateral thoracotomy. In a similar vein, Benedetti and colleagues found that TENS effectively controls mild to moderately acute post thoracotomy pain resulting from muscle-sparing thoracotomy, median sternotomy, and video-assisted thoracoscopic surgery [33]. We affirm that NIPPV improves tissue perfusion, although diligent monitoring and patient comfort are essential to avoid barotrauma [44]. We also found that NIPPV and TENS reduce postoperative pain. Although TENS has not been shown to impede the heart rate variability whereas NIPPV impede the heart rate variability, hence, this adverse effect should be considered [28-30]. In our trial, NIPPV and TENS increased FEV1 and FVC, requiring less Opioids with no post-operative complications. We also saw no adverse effects such as nausea, vomiting, drowsiness, and haemodynamic instability. Also, our patients did not report electrode site discomfort from the adhesive or gel, however, these possible adverse effects should be acknowledged. Though it has adverse effects which needs vigilant monitoring, NIPPV and TENS are safe and straightforward to use. As for the risk/benefit ratio, chosen patients may have very low risk. We found no negative effects with NIPPV or TENS.

LIMITATIONS

There are certain limitations to our study

1. This study is a preliminary investigation (pilot study); therefore, the sample size is limited.
2. The duration of two 45-minute sessions of NIPPV administered at the first and eighth hours after extubation might not have been sufficient to accelerate the recovery of tissue perfusion after CABG surgery.
3. It is possible that the three 45-minute TENS treatment sessions conducted for two days may not provide a comprehensive evaluation of pain, unpleasantness, and spirometry.

RECOMMENDATIONS

Further investigation is warranted to assess the resilience and long-term effects of Non-Invasive Positive Pressure Ventilation (NIPPV) and Transcutaneous Electrical Nerve Stimulation (TENS) treatments as ancillary therapy in acute phase I cardio-pulmonary rehabilitation.

CONCLUSION

The Pilot study suggest that adding NIPPV (Non-Invasive Positive Pressure Ventilation) and TENS (Transcutaneous Electrical Nerve Stimulation) as combined ancillary therapy during acute phase I of cardio-pulmonary rehabilitation following CABG (coronary artery bypass graft) surgery may be extremely beneficial. The research findings demonstrated that the intervention led to a reduction in sternotomy pain discomfort, enhancement of tissue function and pulmonary functions, and a decrease in the length of stay in the critical care unit.

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