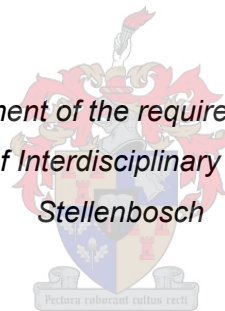


The Effects of a Lung Recruitment Manoeuvre before Extubation on Pulmonary Function after Coronary Artery Bypass Surgery

Stephanus Gerhardus Nel

*Thesis presented in partial fulfilment of the requirements for the degree of Master of
Physiotherapy in the Department of Interdisciplinary Health Sciences of the University of
Stellenbosch*



Primary supervisor: Dr SD Hanekom, the Department of Interdisciplinary Health Sciences of
the University of Stellenbosch.

Secondary supervisor: Prof André Coetzee, the Department of Anaesthesiology of the
University of Stellenbosch

March 2013

Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Date: March 2013

Abstract

Aim: The aim of this study is to determine if the addition of a pre-extubation recruitment manoeuvre to standard care is safe and will improve lung compliance and subsequent $\text{PaO}_2/\text{FiO}_2$ (PF ratio) after extubation in postoperative coronary artery bypass graft surgery patients.

Design: Prospective, triple blind, randomised, controlled trial.

Method: This study was conducted in a private hospital in the Northern suburbs of Cape Town, South Africa. All patients admitted between 03/10/2010 and 22/11/2011, for uncomplicated elective coronary artery bypass graft (CABG) surgery were eligible for inclusion into the study. Patients were randomly allocated into either the intervention group or the control group. The intervention group received a gradual build-up lung recruitment manoeuvre (RM). The primary outcome was $\text{PaO}_2/\text{FiO}_2$ (PF ratio). The secondary outcomes were safety and static lung compliance. ICU length of stay (LOS) and hospital LOS were also recorded. The pre-RM hemodynamic stability of the patient was checked before the intervention and repeated at 5 minutes after the intervention by the nursing sister. Data to calculate static lung compliance was captured at the same time. Criteria for safety and discontinuation of the RM were monitored during the intervention by the principle investigator only.

Results: Of the 69 patients eligible for the study 47 were randomly allocated into the intervention group (n=22) and control group (n=25) respectively. Groups were the same at baseline with regards to sex, pulmonary risk, sedation and surgical procedures. The RM could be completed in all patients. The prior defined criteria for discontinuation of the RM were not reached in any of the patients. No adverse effects were noted. The $\text{PaO}_2/\text{FiO}_2$ (PF ratio) decreased significantly in both groups from pre-surgery measurements compared to when measured before the RM ($p < 0.001$). There was a tendency noted for the intervention group to return to pre-surgery measurements of PF ratio within 12 hours after extubation when compared to the control group. There was no significant difference between the groups from extubation to 24 hours ($p = 0.6$). The static compliance improved at 5 minutes following the RM ($p < 0.001$) and remained improved until extubation ($p < 0.001$) for the intervention group. No difference was noted in the static compliance of the control group over the same time period. The mean hospital length of stay for the intervention group was 8.61 (95% confidence interval 7.26 to 9.96 days) and 10.08 (95% confidence interval 8.52 – 11.63 days) for the control group.

Conclusion: A gradual recruitment manoeuvre at 30cmH₂O 30minutes before extubation significantly improved static lung compliance within 5 minutes with no adverse hemodynamic side effects. There was noted maintained improved PF ratio at extubation or immediately afterwards for the intervention group and no difference in the PF ratio between the intervention group and control group.

Opsomming

Doel: Die doel van hierdie studie is om te bepaal of die toevoeging van 'n pre-ekstubasie herwinningstegniek tot standaard sorg veilig is, en of dit longvervormbaarheid en gevolglike $\text{PaO}_2/\text{FiO}_2$ (PF-verhouding) na ekstubasie in post-operatiewe kroonaaromleidingchirurgie-pasiënte sal verbeter.

Ontwerp: Prospektiewe, trippel-blinde, ewekansige, gekontroleerde proefneming.

Metode: Hierdie studie is uitgevoer in 'n privaat hospitaal in die noordelike voorstede van Kaapstad, Suid-Afrika. Alle pasiënte wat tussen 03/10/2010 en 22/11/2011 gehospitaliseer is vir ongekompliseerde elektiewe kroonaaromleidingchirurgie, kon in aanmerking kom vir die studie. Pasiënte is op ewekansige wyse ingedeel in die intervensie- en kontrolegroepe. 'n Geleidelike-opbou-van-druk-longherwinningstegniek (HT) is op die intervensiegroep toegepas. Die primêre uitkoms was die $\text{PaO}_2/\text{FiO}_2$ (PF-verhouding). Die sekondêre uitkoms was veiligheid en statiese longvervormbaarheid. ISE-verblyf en hospitaalverblyf is ook genoteer. Die navorsingsassistent het data van bestaande eenheidsdokumentasie geneem. Die pre-HT-hemodinamiese stabiliteit van die pasiënte is gemonitor voor en weer 5 minute na die intervensie. Inligting om die statiese longvervormbaarheid te bereken is terselfdertyd genoteer. Kriteria vir veiligheid en vir die staking van die HT is gemonitor tydens uitvoering deur die primêre ondersoeker en die verpleegkundige.

Resultate: Van die 69 pasiënte wat in aanmerking kon kom vir die studie is 47 op ewekansige wyse ingedeel in die intervensiegroep (n=22) en die kontrolegroep (n=25). Die groepe was dieselfde by die basislyn. Die herwinningstegniek kon volledig op alle pasiënte uitgevoer word. Die vooraf gedefinieerde kriteria vir staking van die HT is met geen pasiënte bereik nie. Geen nadelige uitwerking is genoteer nie. Die $\text{PaO}_2/\text{FiO}_2$ (PF-verhouding) het beduidend verminder in beide groepe van pre-operatiewe metings in vergelyking met meting voor die HT ($p < 0.001$). 'n Neiging is genoteer dat die intervensiegroep binne 12 uur na ekstubasie tot pre-chirurgie PF-metings teruggekeer het. Daar was geen merkbare verskil tussen die groepe vanaf ekstubasie tot 24 uur ($p = 0.6$) nie. Die statiese vervormbaarheid het verbeter teen 5 minute na HT ($p < 0.001$) en het verbeter gebly tot ekstubasie ($p < 0.001$) vir die intervensiegroep. Daar was geen verskil in die statiese vervormbaarheid van die kontrolegroep nie. Die gemiddelde hospitaalverblyf vir die intervensiegroep was 8.61 (95% betroubaarheidsinterval 7.26 tot 9.96 dae) en 10.08 (95% betroubaarheidsinterval 8.52 – 11.63 dae) vir die kontrolegroep.

Gevolgtrekking: 'n Geleidelike herwinningstegniek teen 30cmH₂O 30 minute voor ekstubasie het statiese longvormbaarheid beduidend verbeter binne 5 minute, met geen nadelige hemodinamiese newe-effekte nie. Daar was geen verskil in die oksigenasie-indeks tussen die intervensie- en kontrolegroep na ekstubasie nie.

Acknowledgements

The author would like to express his gratitude and appreciation by acknowledging the following people for their support and encouragement during the completion of this thesis:

Study leaders

Dr SD Hanekom from the Department of Interdisciplinary Health Sciences and Prof André Coetzee from the Department of Anaesthesiology of the University of Stellenbosch.

Statistician

Prof Martin Kidd at the Centrum for Statistic Consultation at the University of Stellenbosch

Staff of the hospital

The staff of the intensive care unit for their kind assistance

Research assistant

Mr Shaun Maart

Administration assistant

Mrs Yolandé de Lange

Colleagues

Mr Stuart Lee

The patients

For participating in this study

Table of Contents

Declaration	ii
Abstract	iii
Opsomming	v
Acknowledgements	vii
List of Tables	x
List of Figures	x
List of Addenda	x
Addenda Related to Methodology	x
Addenda Related to Results	xi
Glossary of Terms	xii
Outline of Thesis	xv
Chapter 1: Introduction	16
1.1 Pulmonary Dysfunction	16
1.2 Atelectasis	17
1.3 Physiotherapy Interventions	17
1.4 Recruitment Manoeuvres	18
1.5 Significance of this Study	19
Chapter 2: Research Manuscript	21
2.1 Background	21
2.2 Methods	22
2.2.1 <i>Trial design</i>	22
2.2.2 <i>Research setting</i>	22
2.2.3 <i>Ethical considerations</i>	23
2.2.4 <i>Research team</i>	23
2.2.5 <i>Sample</i>	23
2.2.6 <i>Randomisation</i>	23
2.2.7 <i>Intervention</i>	24

2.2.8	<i>Sham intervention</i>	25
2.2.9	<i>Safety</i>	25
2.2.10	<i>Outcomes measured</i>	25
2.2.11	<i>Data collection</i>	25
2.2.12	<i>Controlling for contamination of the blinding process</i>	26
2.2.13	<i>Data processing and statistical analysis</i>	26
2.3	Results	27
2.3.1	<i>Safety</i>	28
2.3.2	<i>Sedation</i>	29
2.3.3	<i>Static lung compliance</i>	29
2.3.4	<i>Oxygenation</i>	30
2.3.5	<i>Length of stay</i>	30
2.4	Discussion	30
2.5	Conclusion	33
	Chapter 3: General Discussion	34
3.1	The role of recruitment manoeuvres to decrease atelectasis	34
3.2	Physiotherapy Management	35
3.3	Risk Assessment	36
3.4	Research in the private setting in South Africa	36
3.5	Limitations	37
3.6	Recommendations	37
3.7	Conclusion	38
	Addenda Related to Methodology	43
	Addenda Related to Results	59

List of Tables

Table 2.1: Baseline data	28
---------------------------------	----

List of Figures

Figure 2.1: A graphic representation of the recruitment manoeuvre	24
Figure 2.2: CONSORT flow diagram showing inclusion and allocation of study participants	27
Figure 2.3: Static lung compliance over time (GROUP A = INTERVENTION; GROUP B = CONTROL)	29
Figure 2.4: Oxygenation index over time (PATIENT GROUP A = intervention and PATIENT GROUP B = control)	30

List of Addenda

ADDENDA RELATED TO METHODOLOGY

Addendum A: Ethical approval	44
Addendum B: Participant information leaflet and consent form	46
Addendum C: Figure A.1 - A timeline indication of arterial blood gas (ABG) measurements from extubation	54
Addendum D: Figure A.2 - A timeline indication of pre- and post-RM measurements of PEEP, plateau pressure and tidal volume (used to calculate static lung compliance)	55
Addendum E: Data sheets for recruitment contra-indication, recruitment discontinuation, recruitment interruption, ventilator settings and vital signs	56
Addendum F: Data sheets for arterial blood gas analyses and static compliance measurements	57
Addendum G: Data sheets for length of stay, pre-operative information and pulmonary risk score	58

ADDENDA RELATED TO RESULTS

Addendum H:	Figure A.3 - Systolic blood pressure (SYS) from 3hours pre RM to more than 5min after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)	60
Addendum I:	Figure A.4 - Mean arterial pressure (MAP) from 3hours pre RM to more than 5 minutes after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)	61
Addendum J:	Figure A.5 - Heart rate (HR) from 3 hours pre RM to more than 5 minutes after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)	62
Addendum K:	Figure A.6 - Saturation (SATS) from 3 hours pre RM to more than 5 minutes after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)	63
Addendum L:	Figure A.7 - Richmond Agitation-Sedation (RASS) scale for intervention group (Lightly sedated = -2; Drowsy = -1; Alert and Calm = 0)	64
Addendum M:	Figure A.8 - Static lung compliance over time for low and high risk patients	65
Addendum N:	Figure A.9 - PaO ₂ /FiO ₂ over time for low and high risk patients	66

Glossary of Terms

Acute respiratory failure is a sudden and life-threatening deterioration in the gas exchange function of the lung (1).

Arterial blood gas analysis (ABG) is a measurement used to directly assess the gas exchange function of the lung using the partial pressure of oxygen in arterial blood (PaO_2) and carbon dioxide (PaCO_2) together with pH (1).

Atelectasis is described as the loss of air in a portion of lung tissue, occurring as a result of changes in transpulmonary distending pressure or by obstruction of one or more airways, allowing distal gas to be absorbed (2).

Atelectotrauma is a well-recognised mechanism contributing to development of acute lung injury because of the cyclic “opening-closing” of unstable lung units (3).

Cardiac rehabilitation is a widely accepted form of management for patients with cardiac disease. It attempts to enable patients to regain full physical, psychological and social status and to promote and undertake secondary prevention for optimum long-term prognosis (4).

Chronic obstructive pulmonary disease (COPD) represents two diseases including: chronic bronchitis and emphysema and the chest radiograph may indicate hyperinflation (2).

Coronary artery bypass graft (CABG) is a standard form of revascularisation of coronary arteries in patients with atherosclerotic coronary disease (4).

Haemodynamic stability indicates the effect of increased intrathoracic pressure across compliant lungs on the reduction in venous return which could affect the stroke volume of the heart (5).

Impaired oxygenation is defined by $\text{PaO}_2 < 11 \text{ kPa}$ on $\text{FiO}_2 \geq 0.4$ (40%) (5).

Inspiratory pressure is the application of a constant pressure or a constant flow to generate inspiration during mechanical ventilation (4).

Lung compliance is defined as “the change in lung volume per unit change in transmural pressure gradient (in other words between the alveolus and pleural space)” (6).

Oxygen therapy is oxygen delivered by means of a facemask or nasal cannulae (4).

PaO₂ is the partial pressure of oxygen in arterial blood and normally ranges from 85 to 100 mmHg (10 to 13 kPa) for young adults and falls steadily with age, reaching approximately 85 mmHg for those aged 60 years (7).

PaO₂/FiO₂ (PF ratio) is the ratio between is the partial pressure of oxygen in arterial blood (PaO₂) and the inspired fraction of oxygen (FiO₂) (7).

Phase one cardiac rehabilitation is in hospital activity. The gradual mobilisation of cardiac patients following an acute heart attack or CABG initiated by nursing or physiotherapy staff on acute units as part of overall patient care (4).

Plateau pressure is the pressure required to maintain a delivered tidal volume in a patient's lung during no gas flow (2).

Pneumonia is infection of the lower respiratory tract or lung parenchyma (1).

Positive end-expiratory pressure (PEEP) exaggerates the inspiratory effects of positive-pressure ventilation and also maintains increased intrapleural pressure throughout expiration (2).

Postoperative pulmonary complications (PPC) are defined as “any pulmonary dysfunction occurring in the postoperative period that produces identifiable disease that is clinically significant and that adversely affects clinical course” (8).

Postoperative pulmonary dysfunctions refers to expected alterations in pulmonary function such as increased work of breathing, shallow respiration, ineffective cough, and hypoxemia(9).

Recruitment manoeuvre is a technique to reopen collapsed functional lung units. The pressure required for reopening closed units is high and is unlikely during normal breathing. In the presence of pathological lung collapse, a sustained inflation may well cause re-expansion and increased compliance (6).

Richmond Agitation-Sedation Scale (RASS) is an observer-based sedation scale developed for the ICU setting that uses a single number to describe distinct behaviours such as the level of consciousness, agitation, interaction, and calmness (10).

Saturation measured with pulse oximetry in the ICU is the functional saturation of haemoglobin with oxygen in tissues such as skin, muscle and bone (11).

Static compliance is the lung volume change per unit of pressure during a period of no gas flow (2).

Tidal volume is a static volume reflecting the volume of air inspired and expired with each breath during quiet breathing (4).

Outline of Thesis

The following thesis will be presented in a '**masters by publication**' format.

CHAPTER 1:

An introduction to the study, a literature overview and significance of the study.

CHAPTER 2:

A randomised, double blind, controlled trial to determine if the addition of a pre-extubation recruitment manoeuvre to standard care is safe and will improve lung compliance and subsequent PaO₂/FiO₂ after extubation in postoperative coronary artery bypass graft surgery patients.

CHAPTER 3:

A general discussion of results and clinical implications.

REFERENCES

ADDENDA RELATED TO METHODOLOGY

ADDENDA RELATED TO RESULTS

Chapter 1:

INTRODUCTION

This study reports on the effects, safety and influence on PaO₂/FiO₂ of a pre-extubation recruitment manoeuvre (RM) after extubation in a cardiac surgery population. The effect on lung mechanics was investigated by measuring static lung compliance five minutes after the RM and as late as possible before extubation. The safety in relation to haemodynamic stability and patient comfort was monitored during and after the RM. The study was performed at a private hospital in the northern suburbs of Cape Town, South Africa.

1.1 PULMONARY DYSFUNCTION

Cardiac surgery results in major changes in the structure and function of the respiratory system (12). Atelectasis with increased shunting and decreased compliance occurs immediately upon the induction of general anaesthesia (13). During uneventful anaesthesia prior to any surgery being carried out up to 20% of the lung is consolidated and collapsed at its base, as seen on computed tomography (CT) (14). Atelectasis can persist for several days in the postoperative period. In addition, the opening of the chest cavity with the manipulation of its contents directly affects lung structure resulting in further dysfunction (13,15). Impaired lung function tests may also persist for 3.5 to 4 months post cardiac surgery (16,17). Dysfunction of the lung however only becomes a pulmonary complication when the clinical course is adversely affected (8).

The notion that pulmonary dysfunction and pulmonary complications are two separate concepts has been described by Wynne et al (9). Postoperative pulmonary complications are defined as “any pulmonary dysfunction occurring in the postoperative period that produces identifiable disease that is clinically significant and that adversely affects clinical course” (8). Postoperative pulmonary complications are an umbrella term, which incorporates a variety of unassociated pulmonary dysfunctions. There is to date no consensus regarding the pathologies included as post-operative pulmonary complications. The incidence of reported postoperative pulmonary complications after cardiac surgery varies between 1% and 74%. This includes atelectasis, pleural effusions, pneumonia, acute lung injury, pulmonary embolism, respiratory muscle dysfunction due to phrenic nerve injury and pneumothorax. Atelectasis (63%-74%), pleural effusions (40%-50%), and pneumonia (2%-22%) are the most common complications (12). This reported variation could be explained by the conditions excluded, or included, in the group of pulmonary complications.

1.2 ATELECTASIS

Atelectasis is a visible dysfunction in 90% of all anaesthetised patients. However radiographic evidence of atelectasis does not adversely affect the post-operative clinical course in the majority of patients (8). However atelectasis can be a focus of infection, which may contribute to pulmonary complications. A reduction in atelectasis has been shown to decrease bacterial growth and translocation of pneumonia in an animal model (18). Improving lung compliance with surfactant and open lung ventilation could thus in theory reduce the risk of pneumonia and subsequent sepsis in ventilated patients.

Atelectasis also contributes to impaired arterial oxygenation. Seventy four percent of impaired arterial oxygenation can be explained by atelectasis and airway closure during general anaesthesia (19). Impaired oxygenation in patients after cardiac surgery may also be an identifiable dysfunction that is clinically significant. Current consensus regarding implementation of early mobilisation of patients following surgery requires sufficient pulmonary reserve (20). $\text{PaO}_2/\text{FiO}_2$ (PF ratio) reflects underlying pulmonary reserve (21) and failure to reach a predefined PF ratio could delay the implementation of early mobilisation. Early mobilisation as part of a short-term supervised physiotherapy exercise protocol during phase one cardiac rehabilitation improves cardiac autonomic regulation at the time of discharge (22). A physiotherapy-supervised, moderate intensity walking programme in the inpatient phase following coronary artery bypass graft (CABG) improves walking capacity at discharge from hospital (22). Furthermore, a high frequency exercise programme leads to earlier performance of functional milestones and yields more satisfaction after uncomplicated CABG surgery which should lead to an earlier discharge (23). Thus interventions to reduce postoperative atelectasis and impaired oxygenation after CABG surgery might improve the chances of early mobilisation and positively affect the clinical course of the patient.

1.3 PHYSIOTHERAPY INTERVENTIONS

The prevention of postoperative pulmonary complications has long been the focus of physiotherapy research. This includes preoperative and postoperative intervention strategies. Research to date are inconclusive due to small sample sizes and variations in the interventions investigated (12,24,25). The implementation of combined interventions such as positioning, manual hyperinflation (bagging), endotracheal suctioning, thoracic expansion exercises and upper limb exercises during the postoperative intubation phase, have not resulted in improve clinical outcomes after cardiac surgery (26). Blattner reported improvements in static lung compliance and oxygenation immediately after manual hyperinflation in cardiac surgery patients. Although these physiological improvements

decreased the time to extubation, it did not affect clinical outcomes. No effects on pulmonary complications or length of hospital stay were reported (27).

During the preoperative phase the focus has been on risk screening, inspiratory muscle training (IMT) and education. Hulzebos et al developed a preoperative risk screening model, which include six clinical factors that can be determined easily before surgery (28). This model is sensitive to identify patients at risk of developing postoperative pulmonary complications after cardiac surgery. They are: age ≥ 70 years, productive cough, diabetes mellitus, a history of cigarette smoking. Protective factors are predicted inspiratory vital capacity of $>75\%$ and a predicted maximal expiratory pressure of $>75\%$. A three-week preoperative IMT programme has been shown to reduce the incidence of clinically significant postoperative pulmonary complications (PPC) (29). The PPC was determined using the operational definition of Kroenke et al (30) (see ADDENDUM O), in patients identified to be at a high risk of developing these complications and undergoing CABG surgery. In addition the authors reported a significant reduction in the postoperative hospital length of stay compared to the control group ($p=0.02$). Preoperative physiotherapy (involving incentive spirometry and education on deep breathing exercises, assisted coughing and early mobilisation) after off-pump CABG surgery has been linked to a lower incidence of atelectasis (17% vs 36%). This difference is considered to be both significant and clinically relevant (31).

During the postoperative phase after extubation the focus has been mainly on interventions such as early mobilisation. In prospective studies on clinical outcome following pleurotomy during cardiac surgery, one of the findings was that despite the high rate of atelectasis, the incidence of clinically significant pulmonary complications were relatively low (6,32). The researchers attributed these findings to early mobilisation and effective pain control. Other postoperative interventions, which have been described to prevent pulmonary dysfunction and possible complications, are instruction on postoperative deep breathing and coughing exercises. Deep breathing exercises reduce atelectasis, as seen on CT scan, by up to 50% after CABG surgery (33).

1.4 RECRUITMENT MANOEUVRES

During the intubation phase several medical interventions, to prevent and reduce atelectasis, have been described. These include the maintenance or restoration of respiratory muscle tone, minimisation of pulmonary gas resorption, the use of positive end- expiratory pressure (PEEP), and recruitment manoeuvres (RMs) (13,34). Lung RMs with sustained inflations has been shown to improve oxygenation in selected patients with respiratory failure (34).

Inflations to pressures of 40 cmH₂O sustained for 7 to 15 seconds is needed for optimal re-expansion of atelectatic lung tissue (4). In cardiac surgery patients' lung recruitment (two 20 second inflations to 45 cmH₂O) improved oxygenation for three hours (35). The use of continuous positive airway pressure to 40 cmH₂O for 30 seconds decreased atelectasis and caused increased oxygenation for between 1 and 4 hours but not after extubation (36). RMs can be effective in improving oxygenation, but often for a limited period. The improved oxygenation lasted for a limited time period in most of the studies, between 30 minutes and 4 hours (35-38). After the cessation of positive airway pressure on extubation, the effect seems to be lost.

The effect of sustained inflation on the haemodynamic stability of cardiac surgery patients has been under investigation. RMs at 40 cmH₂O for 10 seconds and 20 seconds markedly reduced cardiac output in haemodynamically stable patients after cardiac surgery (38). Cardiac output ($p < 0.001$) and mean arterial blood pressure ($p < 0.003$) also decreased significantly during sustained pulmonary hyperinflation when performing an RM at an airway pressure of 40 cmH₂O and held for 15 seconds (37). In this study the negative effects on central haemodynamics were similar both before and after sternal closure during cardiac surgery. In further studies it was suggested that to minimise the negative circulatory and lung mechanic side effects, a slow moderate pressure RM should be used (39). The authors found in an animal model of acute lung injury that a slow lower pressure RM achieved similar improvements in lung volume, compliance and gas exchange compared to higher pressure recruitment manoeuvres. The slow lower pressure manoeuvre however caused less circulatory depression. It also had less negative side effects on lung mechanics such as over distension of already open lung units. The gradual and combined increases of PEEP and inspiratory pressure (IP) resulted in greater haemodynamic stability compared to CPAP as recruitment mode in cardiac surgery patients (36). Pressures between 30 to 35 cmH₂O are thus sufficient to improve oxygenation without causing the adverse effects (3).

In the above-mentioned studies, RMs were performed either directly after surgery or, at best, on arrival in the ICU (3,35-38). The patients were generally extubated 6 hours or more after the RM. None of the studies reviewed used an RM shortly before extubation when the patients are more alert.

1.5 SIGNIFICANCE OF THIS STUDY

Besides the effect of cardiac surgery on the structure and function of the respiratory system, the postoperative period has further challenges, such as pain and mechanical ventilation. Given that many patients undergoing cardiac surgery have underlying lung disease or a

history of smoking, it is remarkable that more patients do not suffer pulmonary complications after cardiac surgery (12). In 2609 consecutive patients who underwent cardiac surgery with cardio pulmonary bypass, 7.5% had respiratory complications that led either to death (21%) or a hospital length of stay of more than 10 days (64.3%) (40). As previously discussed, this can partly be attributed to early mobilisation (6,32). Furthermore preoperative education and inspiratory muscle training, as well as postoperative breathing exercises have also been proven to prevent complications and limit dysfunction (29,31,33).

Finding effective and safe techniques during the postoperative intubation phase to improve outcome, seems to be the next step. The reversal of atelectasis, which is the most common pulmonary dysfunction after surgery and anaesthesia, should be the aim of this technique. Furthermore, atelectasis is the major cause of impaired oxygenation. RMs have shown on CT scan to improve atelectasis and even completely reopen previously collapsed lung tissue (4). The RMs also improved PF ratio and subsequent oxygenation, although mostly for a limited time period.

The aim of this study is to determine if the addition of a pre-extubation RM to standard care will decrease atelectasis (reflected by improved static lung compliance) and subsequent $\text{PaO}_2/\text{FiO}_2$ (PF ratio) after extubation in postoperative CABG surgery patients. Additionally this study will provide information on the safety of this manoeuvre and if more alert postoperative patients will tolerate such interventions.

Chapter 2:

RESEARCH MANUSCRIPT

This chapter was prepared as a manuscript for submission to *Journal of Cardiothoracic Surgery* under the title **“A Pre-extubation Recruitment Manoeuvre to 30 cmH₂O is Well Tolerated by Patients, Safe for Mean Arterial Pressure and Improves Lung Compliance, but Not Oxygenation, in a Cardiac Surgery Population”**.

2.1 BACKGROUND

Cardiac surgery results in major changes in the structure and function of the respiratory system (12). Atelectasis with decreased lung compliance forms immediately upon the induction of general anaesthesia (13). In addition, the opening of the chest cavity with the manipulation of its contents directly affects lung structure causing dysfunction (13,15). Impaired lung function tests may persist for 3.5 to 4 months post cardiac surgery (16,33). Dysfunction of the lung however only becomes a pulmonary complication when the clinical course is adversely affected (8).

Atelectasis promotes pulmonary complications in two ways. Firstly, atelectasis can be a focus of infection that may contribute to pulmonary complication (34). Secondly, atelectasis may hinder early mobilisation by contributing to impaired oxygenation. Seventy four percent of impaired arterial oxygenation can be explained by atelectasis and airway closure during general anaesthesia (19). Impaired oxygenation in patients after cardiac surgery may also be an identifiable dysfunction that is clinically significant. Current consensus requires sufficient pulmonary reserve in order to mobilise patients early following surgery (20). Failure to reach a predefined PaO₂/FiO₂ (PF ratio) could delay the implementation of early mobilisation. The PF ratio reflects underlying pulmonary reserve (41). Early mobilisation has been shown to improve autonomic cardiac regulation (22) and walking capacity at discharge from hospital (42), and should lead to an earlier discharge after cardiac surgery (23).

Lung RMs with sustained inflations have been shown to improve oxygenation in selected patients with respiratory failure (34). Inflation to pressures of 40 cmH₂O sustained for 7 to 15 seconds is needed for optimal re-expansion of atelectatic lung tissue (4). However, in postoperative cardiac surgery patients RMs have been shown to significantly reduce cardiac output and mean arterial blood pressure (37,38). In recent years research has focused on the identification of the optimal RMs in the cardiac surgery population with the goal of balancing optimal re-expansion without adversely affecting the haemodynamic stability (43).

The gradual and combined increases of positive end-expiratory pressure (PEEP) and inspiratory pressure (IP) resulted in greater haemodynamic stability compared to continuous positive airway pressure (CPAP) as recruitment mode (44). Pressures between 30 to 35 cmH₂O are sufficient to improve oxygenation (3). The improved oxygenation lasted for a limited time period in most of the studies: between 30 minutes and 4 hours (35-38). After the cessation of positive airways pressure on extubation, the effect seems to be lost.

In the above-mentioned studies, RMs were performed either directly after surgery or, at best, on arrival in the ICU (3,35-38). The patients were generally extubated 6 hours or more after the RM. None of the studies reviewed used an RM shortly before extubation when the patients are more alert. The aim of this study is to determine if the addition of a pre-extubation RM to standard care is safe and will improve lung compliance and PaO₂/FiO₂ (PF ratio) after extubation in postoperative coronary artery bypass graft surgery patients (CABG).

2.2 METHODS

2.2.1 Trial design

Prospective, triple blind randomised controlled trial design.

2.2.2 Research setting

This study was conducted at a private hospital in the Northern suburbs of Cape Town, South Africa. Amongst the services is a dedicated cardiac surgery unit with two cardiothoracic surgeons. Patients admitted to the facility for coronary artery bypass graft (CABG) surgery follow a standard care pathway which includes admission one day before surgery for preoperative evaluation by the surgeon and anaesthetist. Arterial blood gas (ABG) analysis and fraction of inspired oxygen concentration (FiO₂) are documented as part of standard care. This includes baseline measurements in theatre and before induction of anaesthesia. After surgery the patients are admitted to a level one open intensive care unit (ICU) with a 1:1 patient-nurse ratio. The aforementioned measures are repeated, and documented by the nurse, two hourly from arrival in the ICU, and six hourly after extubation while the arterial canula is still in situ. The blood pressure of the patients is monitored and documented hourly from ICU arrival to discharge from the ICU. The Richmond Agitation-Sedation Scale (RASS) is used to rate the patients' sedation level. This scale was proven to be a reliable and valid observer-based sedation scale (10). Patients are under the care of the anaesthetist in the ICU who follows a standard protocol for fluid, sedation and ventilation management. Ventilator settings (mode, PEEP, tidal volume, respiratory rate) are documented hourly until extubation. All patients are managed by one physiotherapy practice until discharge.

2.2.3 Ethical considerations

The Committee for Human Research at Stellenbosch University approved the proposal (nr. N07/07/159). Permission and final ethical approval was obtained from the hospitals governing institution. The principal investigator obtained informed written patient consent preoperatively.

2.2.4 Research team

The research team consisted of a principal investigator, research assistant and an administrative assistant. The principal investigator performed the intervention. The research assistant (a basic trained physiotherapist), blinded to the intervention, documented pre- and post-RM measurements. The administrative assistant was responsible for subject randomisation and data entry.

2.2.5 Sample

All patients admitted between 03/10/2010 and 22/11/2011, for uncomplicated elective CABG surgery was eligible for inclusion into the study. Pre- and postoperative exclusion criteria were applicable. Patients were excluded preoperatively if they needed valve replacement in addition to CABG surgery, had previous cardiac surgery or had chronic obstructive pulmonary disease (COPD) with bullae (defined by lung function testing and assessment by a pulmonologist). Patients were excluded postoperatively for the following reasons:

- Intra-operative pulmonary trauma and/or excessive bleeding (>100ml/h)
- No arterial line in situ for regular ABG analysis (in case of accidental removal)
- Intra-aortic balloon pump (IABP) in situ
- Decreased arterial systolic pressure (<80 mmHg) and/or mean arterial pressure (< 60 mmHg) in the 3 hours prior to extubation
- Intubation time more than 14 hours

Sample size calculation was performed using a desired statistical power of 0.8. For a difference in the PF ratio of 10, and an alpha value of 0.05, it was found that a sample size of 36 patients per group was necessary to establish statistical significance (20).

2.2.6 Randomisation

After reaching predefined extubation criteria the patients were randomly allocated into two groups by the administrative assistant using a randomisation table.

2.2.7 Intervention

The Dräger Savina 2 ventilator was switched from synchronised intermittent mandatory ventilation (SIMV) to bi-level positive airway pressure (BIPAP) and the inspiratory pressure alarm set to 40 cmH₂O. The researcher then administered the gradual build up recruitment manoeuvre (RM) (see figure 2.1). The ventilator was then switched back to SIMV and other pre-RM settings. This was repeated after a 15 minute interval.

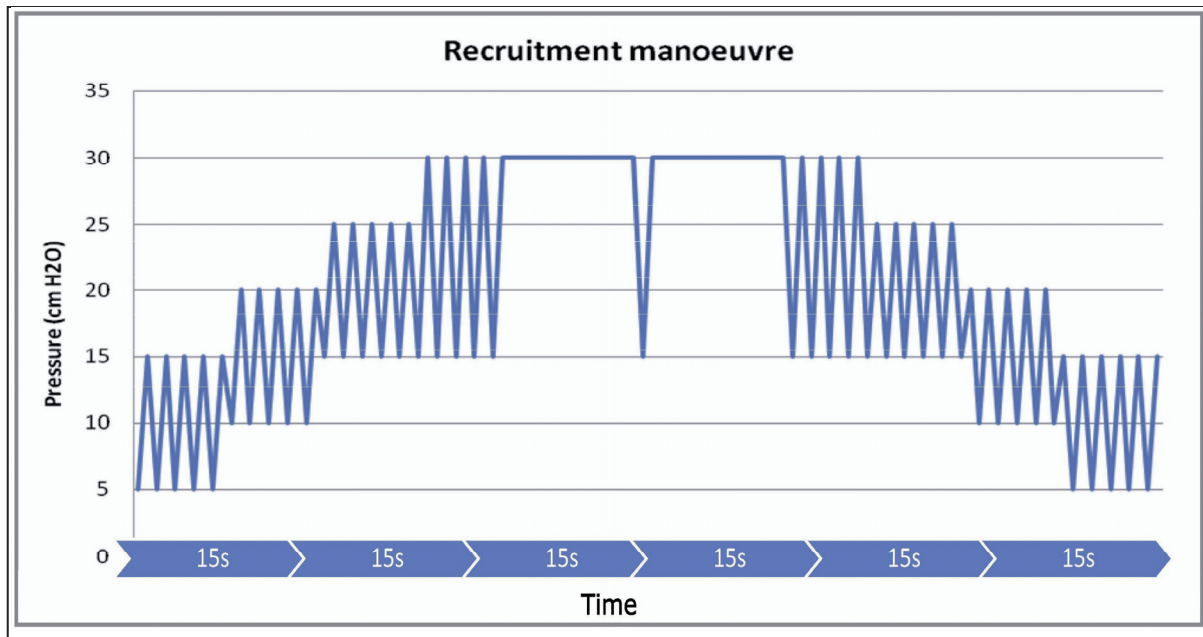


Figure 2.1: A graphic representation of the recruitment manoeuvre

The lines indicate the patient's breaths between positive end-expiratory pressure (PEEP) and peak inspiratory pressure (IP). Initially a gradual incremental increase of PEEP every 5 breaths were done. When a PEEP of 15 cmH₂O was reached the IP was incrementally increased to 15 cmH₂O above PEEP. After 5 breaths at 30cmH₂O, two consecutive inspiratory holds of 15 seconds each was applied. After another 5 breaths the IP and PEEP was decreased incrementally every 5 breaths back to pre-RM settings.

2.2.8 Sham intervention

The principal investigator spent the same amount of time at the control patients' bedsides (behind closed curtains) without performing an intervention. This was done as a sham intervention to blind the research assistant to the intervention.

2.2.9 Safety

Criteria for discontinuation of the RM (the clinical guidelines for physiotherapists during hyperinflation to ensure cardiovascular and pulmonary stability was used) (45):

- Cardiac arrhythmias specifically rapid arterial fibrillations or frequent ventricular extra systole's present
- Heart rate < 70 or > 130 beats per minute
- Observe arterial oxygen saturation (a decreasing more than 5% as a crude guideline)
- Systolic arterial pressure dropping below 80 mmHg and/or MAP dropping below 60 mmHg
- Visible discomfort or pain reaction

Patients were monitored during the intervention by the principal investigator. Changes were documented on a priori data sheet (see ADDENDUM E).

2.2.10 Outcomes measured

The primary outcome was the $\text{PaO}_2/\text{FiO}_2$ (PF ratio). Static lung compliance (compliance = V_t (median)/(plateau pressure (median) – PEEP) was a secondary outcome. The best reading of five consecutive ventilated breaths was used to determine the median of V_t and plateau pressure. Further secondary outcomes were safety (defined as a drop in blood pressure below predetermined safe values), and patient comfort (defined as a noticeable discomfort and/or an inability to maintain the sustained inflation). ICU length of stay (LOS) and hospital LOS were also recorded.

2.2.11 Data collection

The research assistant extracted the following data from existing unit documentation:

- Arterial oxygen concentration (PaO₂)
- FiO₂ values
- Hemodynamic stability
- Ventilator settings

Values for systolic (SYS), diastolic (DYS), and mean arterial blood pressure (MAP) as well as heart rate (HR), central venous pressure (CVP) and saturation (SATS) were documented by the research assistant (blinded to the intervention) on a prepared sheet. This was taken from the monitor before the intervention and 5 minutes after the intervention.

The ICU arrival measurements of PEEP, plateau pressure and tidal volume were documented from the ventilator and used to calculate the static lung compliance. The median of 5 measurements was used for each of the values. Pre-RM measurements for these values were done 30 minutes before extubation and repeated post-RM after 5 minutes and again just before extubation. The research assistant documented this on a prepared sheet.

Information for baseline characteristics, surgical procedure, clinical course and pulmonary risk score were extracted from patient records and documented by the researcher on a prepared sheet.

2.2.12 Controlling for contamination of the blinding process

A computer generated randomisation table concealed from the principal investigator was used for allocation of patients to intervention and control groups. The control group received a sham RM to keep the research assistant blinded to the intervention. The groups were referred to as A and B to conceal the intervention and control allocations from the administrative assistant.

2.2.13 Data processing and statistical analysis

The information was captured by the administrative assistant from the data sheets and randomly checked by the researcher. The summary statistics for descriptive purposes included the means and standard deviations when data was normally distributed, and the medians and interquartile ranges for skewed data. The groups were compared over time using repeated measures anova. A 5% significance level was used as a guideline for

determining significant differences. Analyses were done using intention to treat. Data was analysed in consultation with a statistician using Statssoft

2.3 RESULTS

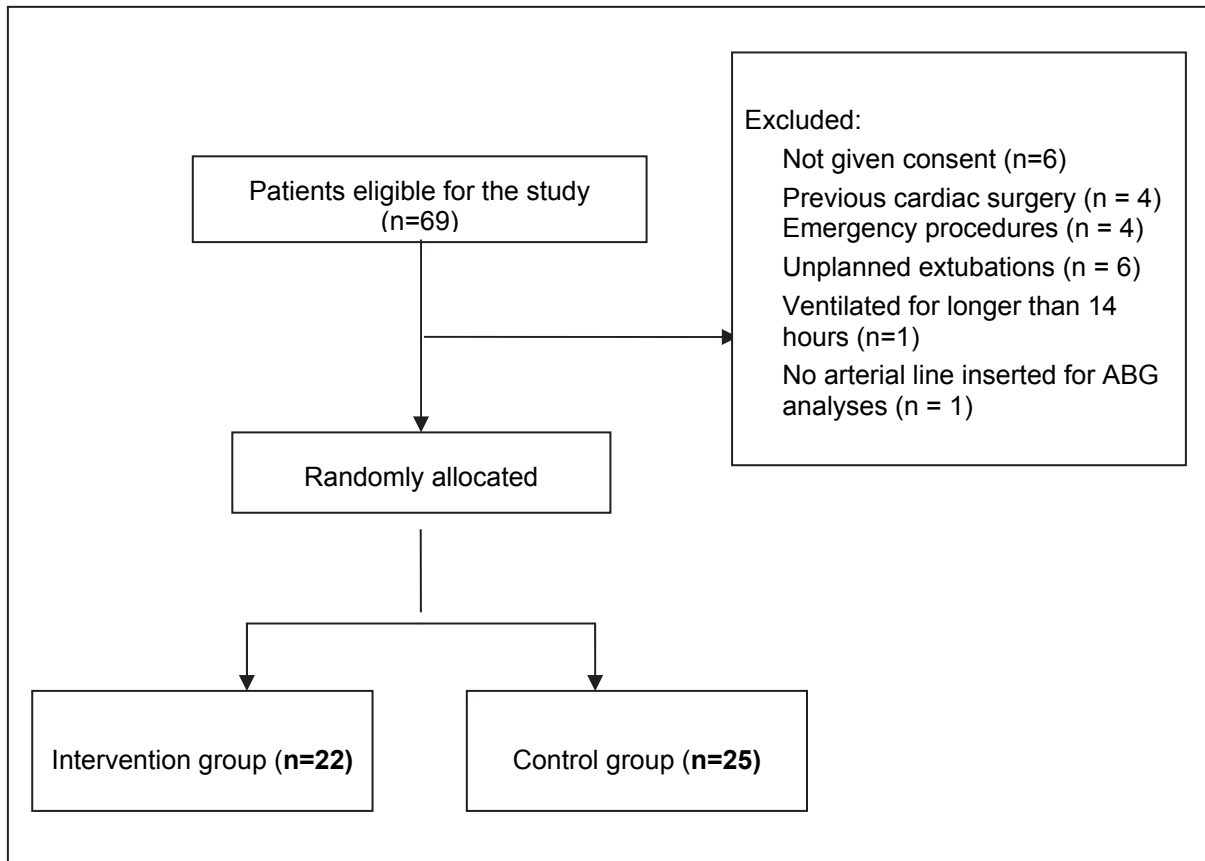


Figure 2.2: CONSORT flow diagram showing inclusion and allocation of study participants

Of the 69 patients eligible for the study, 47 were randomly allocated into the intervention group (n=22) and control group (n=25). The groups were similar at baseline for the characteristics tabulated in table 2.1. At the time of the RM, sedation was already discontinued. There was no difference between the groups for observed sedation (RASS scale) or the surgical procedures.

Table 2.1: Baseline data

Characteristics		Intervention	Control	p value
Sex (Male) n (%)		19 (86.36%)	20 (80.00%)	0.56
Age > 70 years n (%)		16 (72.73%)	21 (84.00%)	0.35
Cough and expectoration n (%)		0	1	
Diabetes Mellitus n (%)		7 (31.82%)	5 (20.00%)	0.35
Smoker n (%)		6 (27.27%)	3 (12.00%)	0.18
COPD (on medication) n (%)		1	0	
BMI ≥ 27 n (%)		13 (59.09%)	20 (80.00%)	0.12
Pulmonary risk score ≥ 2 n (%)		12 (54.55%)	10 (40.00%)	0.32
Richmond Agitation-Sedation Scale (RASS)	-3 n (%)	0	2 (8.00%)	
	-2 n (%)	11 (50.00%)	11 (44.00%)	
	-1 n (%)	8 (36.36%)	8 (32.00%)	0.56
	0 n (%)	3 (13.64%)	3 (12.00%)	
	1 n (%)	0	1 (1.00%)	
Surgical procedures				
On cardiopulmonary bypass n (%)		7 (31.82%)	12 (48.00%)	0.26
Pleural involvement n (%)		15 (68.18%)	14 (56.00%)	0.39
Duration of CPB* (min)	Mean	23.6	38.2	0.35
	(SD)	(38.68)	(40.98)	
Duration of surgery (min)	Mean	238.7	237.5	0.68
	(SD)	(49.77)	(51.83)	
Duration of sedation (hours)	Mean	13.0	20.2	0.92
	(SD)	(6.35)	(27.49)	

*CPB = cardiopulmonary bypass

2.3.1 Safety

The RM could be completed in all patients. The *a priori* defined criteria for discontinuation of the RM were not reached in any of the patients. No adverse effects were noted.

The systolic blood pressure (SYS) and mean arterial pressure (MAP) was never below the predetermined safe value of 80mmHg and 60mmHg respectively from 3 hours pre-RM up to 5 minutes after the RM. There was no difference between the groups pre- and post-RM ($p=0.57$ & $p=0.44$) for these values (see ADDENDUM H & I).

There was no difference in the heart rate ($p=0.53$) or saturation ($p=0.9$) levels for the duration of the intervention between the groups. The saturation levels never dropped more than the *a priori* defined 5%.

2.3.2 Sedation

Patients' sedation levels (RASS) at the time of the RM did not impact on the completion of the RM. Discomfort was noted in one patient. This patient was rated as lightly sedated. Three patients interrupted the procedure during either or both the inspiratory hold phases by coughing. Each of these patients was from the three different sedation level groups.

2.3.3 Static lung compliance

The static lung compliance of both groups was similar ($p=0.81$) on admission to the ICU. It remained at these levels when measured pre-RM ($p=0.78$). The static lung compliance of the intervention group improved significantly ($p<0.001$) 5 minutes after the RM with 8.14 ml/cmH₂O (confidence interval 11.89 to 4.41). This remained significantly higher until extubation ($p<0.001$). There was no difference noted in the static lung compliance of the control group over the same time period ($p=0.55$). For the the intervention group it was 8.87 ml/cmH₂O (confidence interval of 2.28 to 15.46) greater than the control group when measured pre-extubation ($p=0.009$). The static lung compliance was not affected by a high preoperative risk for developing postoperative pulmonary complications ($p=0.62$; see ADDENDUM M).

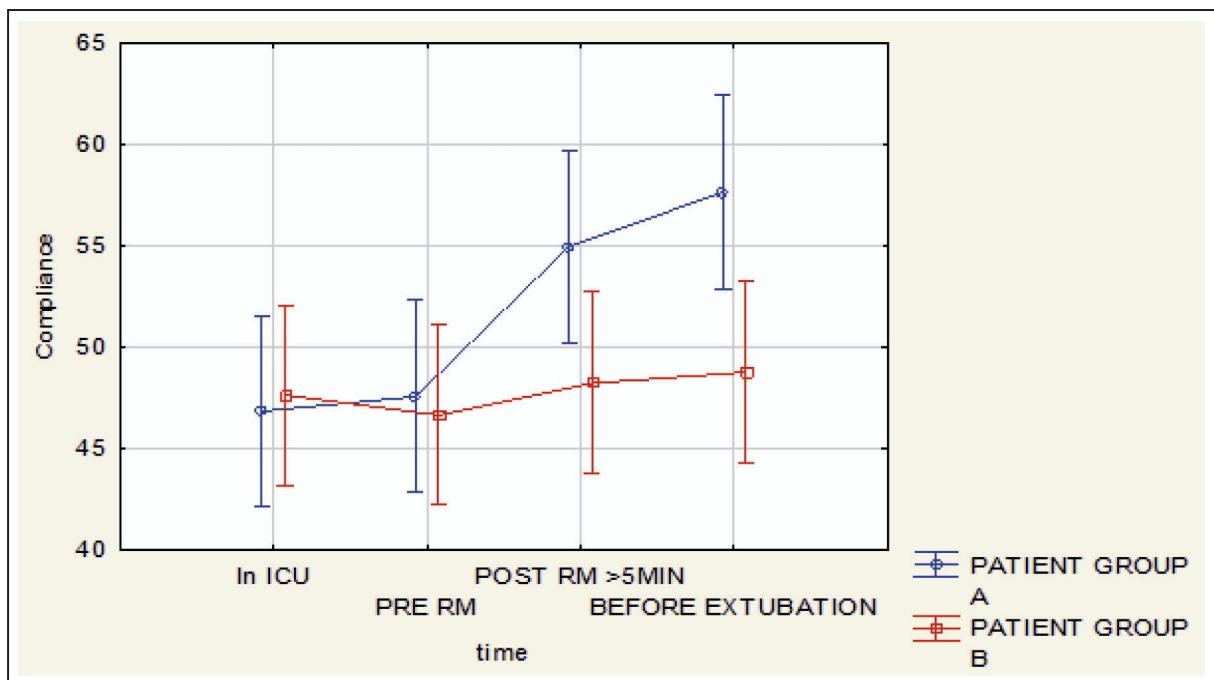


Figure 2.3: Static lung compliance over time (GROUP A = INTERVENTION; GROUP B = CONTROL); means; $p=0.0006$; type III decomposition; vertical bars denote 0.95 confidence intervals.

2.3.4 Oxygenation

The PF ratio decreased in both groups from pre-surgery compared to that before the RM ($p < 0.001$). There was no significant difference in PF ratio between the groups after extubation. A pre-operative pulmonary risk score of ≥ 2 (high risk) had no significant effect on the PF ratio ($p = 0.10$) post-extubation (see ADDENDUM N).

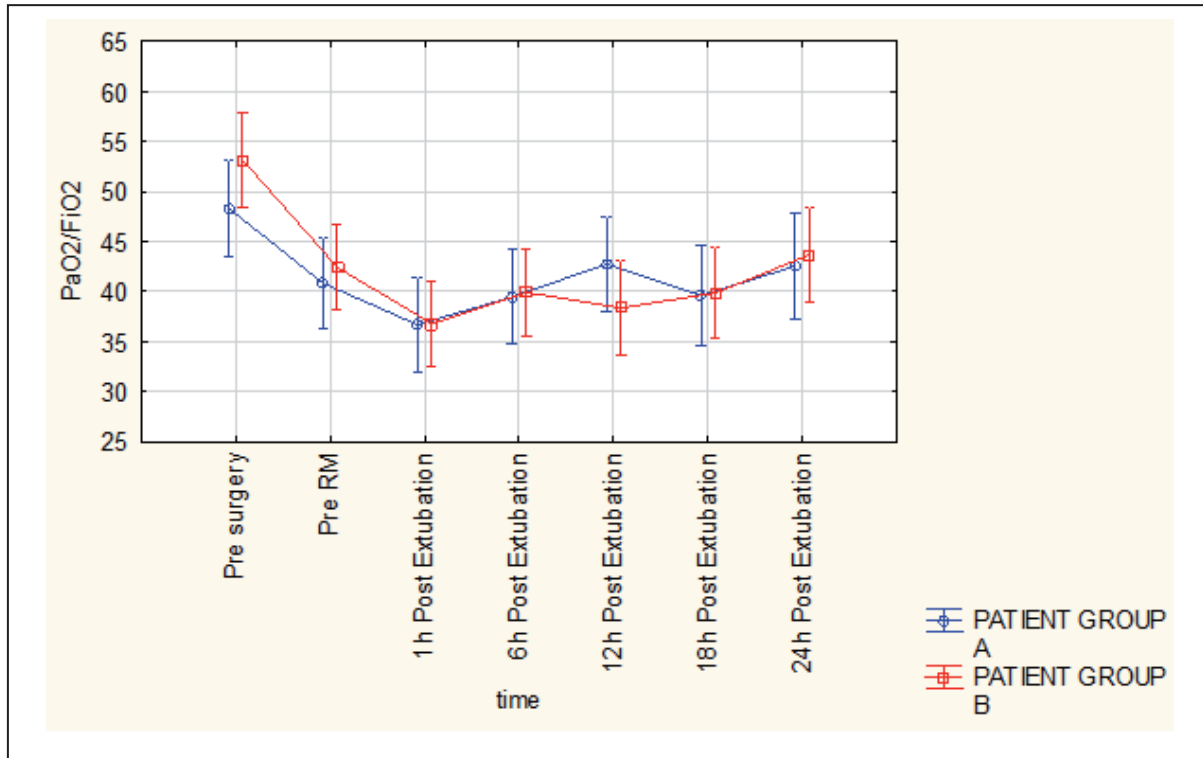


Figure 2.4: Oxygenation index over time (PATIENT GROUP A = intervention and PATIENT GROUP B = control); means; $p = 0.60320$; type III decomposition; vertical bars denote 0.95 confidence intervals.

2.3.5 Length of stay

The mean hospital LOS for the intervention group was 8.61 (95% confidence interval 7.26 to 9.96) days. For the control group it was 10.08 (95% confidence interval 8.52 – 11.63) days. This shows a moderate clinical significant effect (Cohen's $d = 0.48$). This potentially important finding did not reach statistical significance in this sample ($p = 0.12$).

2.4 DISCUSSION

This is the first study describing the effect of a pre-extubation recruitment manoeuvre (RM) on static lung compliance and post-extubation oxygenation in cardiac surgery patients. We found that the RM was well tolerated in more alert patients with no adverse effects on

systolic blood pressure, mean arterial pressure, heart rate or saturation. In addition this RM improved the pre-extubation static lung compliance of cardiac surgery patients. This however did not translate into improved oxygenation after extubation.

The RM we used was a combination of previously described manoeuvres. It included a gradual build-up of positive end-expiratory pressure (PEEP) and inspiratory pressure (IP) with two consecutive sustained inflations for 15 seconds each. A gradual build-up manoeuvre, to pressures of 30 cmH₂O, was used to prevent possible adverse alterations in hemodynamic stability (36) reported in previous studies using continuous positive airway pressure based manoeuvres at 40 cmH₂O (37,38). Less sedated patients also tolerated our manoeuvre well. Furthermore, the use of sustained inflations was used to prevent possible lung injury, such as atelectotrauma. Atelectotrauma is a well-recognised mechanism contributing to the development of acute lung injury in ventilated patients (46,47). The cyclic “opening-closing” of unstable lung units create a shear stress that cause distortion of the cell membranes. Manual hyperinflation is a technique used by physiotherapists to help clear airway secretions and reduce acute atelectasis. It has been shown recently to improve static compliance and oxygenation immediately after cardiac surgery (27). However, this technique consists of a series of larger than normal tidal volumes (to airway pressures of 40 cmH₂O) combined with an inspiratory pause (two seconds) and a rapid release of a resuscitation bag (48). The assumption could be made that a RM with sustained inflations might cause less atelectotrauma than manual hyperinflation with repetitive breaths. A RM should thus rather be used to improve lung compliance.

Given that decreased compliance may be causally related to atelectasis and decreased oxygenation (49,50), one would expect more compliant lungs to have less atelectasis and a subsequent improved PF ratio. We were unable to confirm the relationship between improved lung compliance and PF ratio following extubation. There are four possible reasons for this. Firstly, this may be due to the timing of the RM, secondly to the insufficient power of this study, thirdly due to insufficient carry-over of improved compliance after the loss of positive airway pressure on extubation and fourthly due to inaccuracies in the calculation of the PF ratio.

The timing of the RM could be important. It is standard practice that during the transfer from the theatre to the ICU patients receives manual ventilation with high fractions of oxygen and no PEEP. In our study the recurrence of atelectasis as a result of standard practice could have predisposed our patients to lung injury before our RM was performed. This observation is confirmed by Minkovich et al (3) who described similar management when patients were transferred from theatre to ICU. The researchers hypothesised that the high fractions of

oxygen inspiration and no PEEP may have predisposed their patients to the recurrence of atelectasis. For this reason a RM was repeated on ICU arrival. Repeating a RM on arrival in the ICU might have caused sustained alveolar recruitment. The authors suggest that patients in the intervention group developed less atelectasis with less atelectotrauma and subsequent lung injury, and thus faster lung recovery after extubation.

The second reason for our inability to confirm the relationship between improved lung compliance and PF ratio following extubation could be that the study was insufficiently powered. During planning of the sample size it was calculated that for a clinically significant improvement of 10 units of the PF ratio, a sample of 36 patients per group should be sufficient. An interim analysis of the data of the first 25 patients did not support our hypothesis related to the PF ratio. However it was important to confirm that the RM did improve compliance and was safe. Thus it was decided in consultation with the statistician to recruit only another 25 patients. In a post HOC analysis it was determined that 102 patients per group was needed.

Thirdly, the loss of positive airway pressure on extubation may cause collapse of unstable alveolar units and deterioration in oxygenation (50). Similar results have been reported in previous clinical trials that found no benefit in terms of PF ratio of an RM beyond tracheal extubation (35,36). Minkovich et al (3) also found no initial improvement of PF ratios immediately following extubation. When measured 24 hours after extubation however, they found significantly higher PF ratios in the intervention group when compared to the control. Our study failed to support this.

Lastly, the data used to calculate the PF ratio after extubation might be another reason for our findings. The tendency of the intervention group to recover to baseline levels at 12 hours did not reach significant levels. This potential was not continued at 18 and 24 hours after extubation. In this study the arterial blood gas (ABG) analysis and inspired oxygen concentration (FiO_2), documented as part of standard care, were used. Up to 12 hours post extubation the oxygen therapy is relatively well controlled by the nurse when patients are less active. Thus, a more true reflection of FiO_2 on the patient care chart when the ABG analysis was done. However after the first 12 hours post extubation patients are usually more active and tend to be less compliant with their oxygen therapy. Although this was not measured, the assumption might be made that the documented FiO_2 was inaccurate for the related PaO_2 used to calculate the PF ratio.

A further possible reason for our results is the fact that 30cmH₂O was insufficient pressure to completely reverse the atelectasis. Rothen et al showed that inflation pressure to 40cmH₂O is

needed for optimal re-expansion of atelectic lung tissue. Furthermore it might be that the lung compliance was already sufficient before the RM due to good respiratory management (optimal PEEP during ventilation). This might have had the effect on the PF-ratio that was intended by the RM. The length of stay (LOS) outcome provided a finding of potential clinical importance, given the cost of hospital stay. Although the hospital LOS was 1.5 days lower for the intervention group. From the available data however it was not statistically significant ($p = 0.12$).

Another interesting finding was that there was no relationship between patients at high risk for developing postoperative pulmonary complications and decreased compliance or PF ratio. Taking into account the relationship between atelectasis with subsequent decreased lung compliance and postoperative pulmonary complications, one would expect to find a relationship between high risk patients and decreased compliance. The sample size however is too small for the group to be further divided.

In the future this study might be repeated on a high-risk population only. A better PF ratio after extubation might be achieved by the addition of an RM at ICU arrival or by using higher pressures for the RM. The ABG analyses should also be done under more accurately controlled circumstances for inspired oxygen concentration (FiO_2).

2.5 CONCLUSION

A gradual recruitment manoeuvre at 30cmH₂O 30 minutes before extubation significantly improved static lung compliance within 5 minutes with no adverse side effects on arterial blood pressure. It was also well tolerated by the patients. This however did not translate into improved oxygenation after extubation.

Chapter 3:

GENERAL DISCUSSION

The aim of this study was to determine whether the addition of a pre-extubation recruitment manoeuvre (RM) to standard care is safe and will improve lung compliance and subsequent $\text{PaO}_2/\text{FiO}_2$ (PF ratio) after extubation in postoperative coronary artery bypass graft (CABG) surgery patients.

3.1 THE ROLE OF RECRUITMENT MANOEUVRES TO DECREASE ATELECTASIS

In various studies with diverse study subjects, RMs have been shown to improve lung compliance, improve oxygenation and even completely re-expand atelectatic lung tissue (4,34-36,39). The effect of these RMs were studied in experimental animal model studies, patients with respiratory failure, patients under general anaesthesia and postoperative cardiac surgery patients. Two outcomes commonly reported were: haemodynamic stability and the effectiveness of the manoeuvre to reopen collapsed alveoli. The factors which influenced these outcomes were the pressures and duration of sustained inflation. In cardiac surgery patients, a gradual increase in pressure to 40 cmH_2O (with no sustained inflation) had consistent results in ensuring haemodynamic stability during and after the RM (3,35-38,44). Studies using constant positive airway pressure (to between 30 and 45 cmH_2O) with sustained inflations (5 to 35 seconds) showed mixed results concerning haemodynamic stability (3,35,37,38,44). All manoeuvres were applied in theatre with an open or closed chest and some were repeated on ICU arrival.

The RM we described in Chapter 2 of this thesis used a gradual increase of positive end-expiratory pressure (PEEP) and inspiratory pressure (IP) to a relatively low pressure of 30 cmH_2O . These pressures were maintained for two breaths with duration of 15 seconds for each breath. The decrease in pressure between the breaths was not lower than the set PEEP of 15 cmH_2O . We found that this technique was effective in improving static lung compliance. The improved static lung compliance was accomplished while still being safe. No negative haemodynamic side effects were noted on systolic, diastolic and mean arterial blood pressure. Heart rate and oxygen saturation were also not affected. The RM was also tolerated well by the patients shortly before extubation, when they were less sedated. We postulated that the improved static compliance of the lung is due to the reopening of collapsed alveoli. Performing the RM shortly before extubation could facilitate carry-over of the effect after extubation. Furthermore, more awake patients could possibly participate during the manoeuvre to promote a more lasting effect.

We also predicted that the improved lung compliance would impact the PF ratio for the following reasons:

- Improved compliance should lead to a decrease in atelectasis given the causal relationship between compliance and atelectasis.
- Decreased atelectasis with less shunting should improve the lungs ability to oxygenate the arterial blood.

The question still remains then why the improved static lung compliance did not lead to improved PF ratio after extubation.

3.2 PHYSIOTHERAPY MANAGEMENT

Oxygenation and underlying pulmonary reserve can be measured using the PF ratio in the clinical setting. This ratio takes into account the patient's partial arterial partial pressure of oxygen (PaO_2) and fractional inspired oxygen concentration (FiO_2). A normal functioning lung of a young adult provides a PaO_2 of 13 kPa which falls gradually to 10 kPa at the age of 60 (7). This relates to a PF ratio of 48 when breathing room air ($10\text{kPa}/0.21$). If this ratio drops to 40 or less it may indicate insufficient pulmonary reserve for mobilisation (41). The implementation of early mobilisation of patients following surgery could thus be directly related to the PF ratio of the patient (20).

Early mobilisation as part of phase one cardiac rehabilitation has been shown to improve heart function, patient experience and hospital length of stay (22,23,42). Failure to reach a predefined PF ratio could delay the implementation of early mobilisation. Our intervention group recovered to a PF ratio of more than 40 at 12 hours. The control group however only reached levels greater than 40 after 24 hours. Thus the intervention group was ready for early mobilisation before the control group. We did not measure the time to early mobility as it was not part of the outcome of this thesis. However, based on earlier studies (mentioned in the beginning of the paragraph), if implemented, this might have positively influenced the clinical course in terms of ICU and hospital length of stay. The aforementioned hypothesis is strengthened by the findings of our study. The hospital length of stay of the intervention group was 1.5 days shorter than the control group. This clinically important finding did not reach statistical significance in this sample. These findings will need to be confirmed in a sufficiently powered clinical trial.

The findings of our study indicate that a pre-extubation RM has the potential to impact the clinical course of the patient. Optimising the pre-extubation physiotherapy management of the post CABG surgery patient could form a link between existing pre- and postoperative

care of this population. Preoperatively, risk screening and inspiratory muscle training have been linked to improved clinical outcomes (decreased hospital length of stay and less postoperative pulmonary complications) (29). Postoperatively, phase one cardiac rehabilitation has been linked to improved clinical, physiological and patient-centred outcomes (improved heart function, decreased hospital length of stay and improved patient experience) (22,23,42). Furthermore, preoperative education and postoperative breathing exercises have been associated with improved physiological outcome (decreased atelectasis) (31,33).

3.3 RISK ASSESSMENT

In recent years the prediction of postoperative pulmonary complications, on the basis of preoperative risk factors in patients who had undergone (CABG) surgery, has been promoted (29). In our study, however, there was no relation found between preoperative risk and the static lung compliance or PF ratio. The pulmonary dysfunction caused by CABG surgery was thus similar in both high and low risk patients. Thus, an RM could potentially be used to treat lung dysfunction regardless of the risk for developing postoperative complications.

3.4 RESEARCH IN THE PRIVATE SETTING IN SOUTH AFRICA

The research team's experiences regarding certain aspects of the research process are worth mentioning. An interesting and somewhat unexpected observation was the relatively low exclusion rate due to patients refusing to participate in the trial (n = 6; 8.7%). Given the perceived high risk of having open heart surgery, one would expect patients to be more reluctant to consent to a clinical trial. Furthermore, these patients were undergoing elective surgery in a private setting. One of the possible reasons for the relative good participation is the multidisciplinary approach employed at this hospital which aided the research process. The anaesthetists, surgeons and nurses involved were willing and available to explain any queries from the patients. Additionally, there was good communication and teamwork between doctors, nurses and physiotherapists. This teamwork enabled us to effectively complete the trial.

Another noteworthy observation was the length of time it took to acquire ethical approval from the governing private institution. After the Committee for Human Research at Stellenbosch University approved the proposal, permission was obtained from the hospital ethical committee on 06/04/2008. Further final approval was then requested from the

hospital's governing body and only granted on 18/07/2010. This delayed the initiation of data collection by more than 2 years.

3.5 LIMITATIONS

The current study displayed a number of limitations which influence the internal and external validity of the results. The study was conducted with minimum influence on standard protocol and procedures. The post-extubation values for partial arterial oxygenation (PaO_2) and inspired oxygen concentration (FiO_2) were retrieved from existing ICU documentation and arterial blood gas (ABG) analysis was performed as part of standard care. There was no control over the true inspired oxygen concentration for the corresponding ABG. After 12 hours, the patients are more active and less compliant with oxygen therapy. This could have had a major influence on the calculation of the PF ratio.

Furthermore, the study was conducted at a single centre. The small sample size is another limitation. An interim analysis of the data of the first 25 patients did not support our hypothesis related to the PF ratio. However, it was important to confirm that the RM did improve compliance. Hospital length of stay was not a primary or secondary outcome of the study. Thus it was decided in consultation with the statistician not to recruit a larger sample. This decision to not recruit further patients for the study was supported by an unforeseen change in standard care for regular ABG analysis. This would have resulted in substantial financial had we continued with recruitment and privately fund the ABG analysis needed for the study.

3.6 RECOMMENDATIONS

The preliminary results from our intervention trial warrant further investigation. To improve the internal validity of the study it is recommended that:

- For a more accurate calculation of the PF ratio, the ABG analysis should be done under circumstances where the oxygen therapy and relative oxygen concentration is controlled.
- To limit the recurrence of alveolar atelectasis and subsequent lung injury, an additional RM on ICU arrival be performed.
- Length of stay in the ICU and hospital should be a primary outcome and the study should be powered accordingly.

To improve external validity:

- The study should be conducted at multiple centres.
- The standard practice of post surgery patient care should be described.

3.7 CONCLUSION

Optimising pulmonary function in post cardiac surgery patients remains challenging. Physiotherapy is effective in the preoperative phase and the postoperative phase after extubation. This thesis describes a RM which can safely be used by physiotherapists in the postoperative CABG patient population to optimise alveolar recruitment just before extubation. Further investigation is needed to identify means of prolonging this effect in the post-extubation phase. This pre-extubation intervention has the potential to assist physiotherapists in optimising post cardiac surgery rehabilitation.

REFERENCES

- (1) Goldstein R, O'Connell J, Karlinsky J. A practical approach to pulmonary medicine. Philadelphia: Lippincott-Raven; 1997.
- (2) Wilkins RL, Sheldon RL, Krider SJ. Clinical assesment in respiratory care. 5th ed. Philidelphia: Elsevier; 2005.
- (3) Minkovich L, Djaiani G, Katznelson R, Day F, Fedorko L, Tan J, et al. Effects of alveolar recruitment on arterial oxygenation in patients after cardiac surgery: a prospective, randomized, controlled clinical trial. *J Cardiothorac Vasc Anesth* 2007 Jun;21(3):375-378.
- (4) Rothen HU, Neumann P, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G. Dynamics of re-expansion of atelectasis during general anaesthesia. *Br J Anaesth* 1999 Apr;82(4):551-556.
- (5) Singer M, Webb A. Oxford handbook of critical care. 3rd ed. New Yok: Oxford; 2009.
- (6) Lim E, Callaghan C, Motaleb-Zadeh R, Wallard M, Misra N, Ali A, et al. A prospective study on clinical outcome following pleurotomy during cardiac surgery. *Thorac Cardiovasc Surg* 2002 Oct;50(5):287-291.
- (7) West JB. Respiratory physiology : the essentials. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2004.
- (8) O'Donohue WJ,Jr. Postoperative pulmonary complications. When are preventive and therapeutic measures necessary? *Postgrad Med* 1992 Feb 15;91(3):167-70, 173-5.
- (9) Wynne R, Botti M. Postoperative pulmonary dysfunction in adults after cardiac surgery with cardiopulmonary bypass: clinical significance and implications for practice. *Am J Crit Care* 2004 Sep;13(5):384-393.
- (10) Arevalo JJ, Brinkkemper T, van der Heide A, Rietjens JA, Ribbe M, Deliens L, et al. Palliative sedation: reliability and validity of sedation scales. *J Pain Symptom Manage* 2012 Nov;44(5):704-714.
- (11) Barrash PG, Dullen BF, Stoelting RK, Cahalan MK. Clinical Anesthesia. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009.
- (12) Weissman C. Pulmonary complications after cardiac surgery. *Semin Cardiothorac Vasc Anesth* 2004 Sep;8(3):185-211.
- (13) Hedenstierna G, Rothen HU. Atelectasis formation during anesthesia: causes and measures to prevent it. *J Clin Monit Comput* 2000;16(5-6):329-335.
- (14) Hedenstierna G, Edmark L. Mechanisms of atelectasis in the perioperative period. *Best Pract Res Clin Anaesthesiol* 2010 Jun;24(2):157-169.
- (15) Hedenstierna G, Tenling A. The lung during and after thoracic anaesthesia. *Curr Opin Anaesthesiol* 2005 Feb;18(1):23-28.
- (16) Shenkman Z, Shir Y, Weiss YG, Bleiberg B, Gross D. The effects of cardiac surgery on early and late pulmonary functions. *Acta Anaesthesiol Scand* 1997 Oct;41(9):1193-1199.

- (17) Westerdahl E, Lindmark B, Bryngelsson I, Tenling A. Pulmonary function 4 months after coronary artery bypass graft surgery. *Respir Med* 2003 Apr;97(4):317-322.
- (18) van Kaam AH, Lachmann RA, Herting E, De Jaegere A, van Iwaarden F, Noorduyt LA, et al. Reducing atelectasis attenuates bacterial growth and translocation in experimental pneumonia. *Am J Respir Crit Care Med* 2004 May 1;169(9):1046-1053.
- (19) Rothen HU, Sporre B, Engberg G, Wegenius G, Hedenstierna G. Airway closure, atelectasis and gas exchange during general anaesthesia. *Br J Anaesth* 1998 Nov;81(5):681-686.
- (20) Hanekom SD, Brooks D, Denehy L, Fagevik-Olsen M, Hardcastle TC, Manie S, et al. Reaching consensus on the physiotherapeutic management of patients following upper abdominal surgery: a pragmatic approach to interpret equivocal evidence. *BMC Med Inform Decis Mak* 2012 Feb 6;12:5.
- (21) Stiller K, Phillips A. Safety aspects of mobilising acutely ill inpatients. *Physiotherapy Theory and Practice* 2003;19:239-257.
- (22) Mendes RG, Simoes RP, De Souza Melo Costa F, Pantoni CB, Di Thommazo L, Luzzi S, et al. Short-term supervised inpatient physiotherapy exercise protocol improves cardiac autonomic function after coronary artery bypass graft surgery--a randomised controlled trial. *Disabil Rehabil* 2010;32(16):1320-1327.
- (23) van der Peijl ID, Vliet Vlieland TP, Versteegh MI, Lok JJ, Munneke M, Dion RA. Exercise therapy after coronary artery bypass graft surgery: a randomized comparison of a high and low frequency exercise therapy program. *Ann Thorac Surg* 2004 May;77(5):1535-1541.
- (24) Freitas ER, Soares BG, Cardoso JR, Atallah AN. Incentive spirometry for preventing pulmonary complications after coronary artery bypass graft. *Cochrane Database Syst Rev* 2007 Jul 18;(3)(3):CD004466.
- (25) Pasquina P, Tramer MR, Walder B. Prophylactic respiratory physiotherapy after cardiac surgery: systematic review. *BMJ* 2003 Dec 13;327(7428):1379.
- (26) Patman S, Sanderson D, Blackmore M. Physiotherapy following cardiac surgery: is it necessary during the intubation period? *Aust J Physiother* 2001;47(1):7-16.
- (27) Blattner C, Guaragna JC, Saadi E. Oxygenation and static compliance is improved immediately after early manual hyperinflation following myocardial revascularisation: a randomised controlled trial. *Aust J Physiother* 2008;54(3):173-178.
- (28) Hulzebos EH, Van Meeteren NL, De Bie RA, Dagnelie PC, Helders PJ. Prediction of postoperative pulmonary complications on the basis of preoperative risk factors in patients who had undergone coronary artery bypass graft surgery. *Phys Ther* 2003 Jan;83(1):8-16.
- (29) Hulzebos EH, Helders PJ, Favie NJ, de Bie RA, Brutel de la Riviere A, van Meeteren NL. Fewer lung complications following inspiratory muscle training in patients undergoing coronary bypass surgery: a randomized trial. *Ned Tijdschr Geneesk* 2007 Nov 10;151(45):2505-2511.

- (30) Kroenke K, Lawrence VA, Theroux JF, Tuley MR, Hilsenbeck S. Postoperative complications after thoracic and major abdominal surgery in patients with and without obstructive lung disease. *Chest* 1993 Nov;104(5):1445-1451.
- (31) Yanez-Brage I, Pita-Fernandez S, Juffe-Stein A, Martinez-Gonzalez U, Pertega-Diaz S, Mauleon-Garcia A. Respiratory physiotherapy and incidence of pulmonary complications in off-pump coronary artery bypass graft surgery: an observational follow-up study. *BMC Pulm Med* 2009 Jul 28;9:36.
- (32) Johnson D, Hurst T, Thomson D, Mycyk T, Burbridge B, To T, et al. Respiratory function after cardiac surgery. *J Cardiothorac Vasc Anesth* 1996 Aug;10(5):571-577.
- (33) Westerdahl E, Lindmark B, Eriksson T, Friberg O, Hedenstierna G, Tenling A. Deep-breathing exercises reduce atelectasis and improve pulmonary function after coronary artery bypass surgery. *Chest* 2005 Nov;128(5):3482-3488.
- (34) Lapinsky SE, Aubin M, Mehta S, Boiteau P, Slutsky AS. Safety and efficacy of a sustained inflation for alveolar recruitment in adults with respiratory failure. *Intensive Care Med* 1999 Nov;25(11):1297-1301.
- (35) Dyhr T, Laursen N, Larsson A. Effects of lung recruitment maneuver and positive end-expiratory pressure on lung volume, respiratory mechanics and alveolar gas mixing in patients ventilated after cardiac surgery. *Acta Anaesthesiol Scand* 2002 Jul;46(6):717-725.
- (36) Celebi S, Koner O, Menda F, Korkut K, Suzer K, Cakar N. The pulmonary and hemodynamic effects of two different recruitment maneuvers after cardiac surgery. *Anesth Analg* 2007 Feb;104(2):384-390.
- (37) Nielsen J, Nygard E, Kjaergaard J, Tingleff J, Larsson A. Hemodynamic effect of sustained pulmonary hyperinflation in patients after cardiac surgery: open vs. closed chest. *Acta Anaesthesiol Scand* 2007 Jan;51(1):74-81.
- (38) Nielsen J, Ostergaard M, Kjaergaard J, Tingleff J, Berthelsen PG, Nygard E, et al. Lung recruitment maneuver depresses central hemodynamics in patients following cardiac surgery. *Intensive Care Med* 2005 Sep;31(9):1189-1194.
- (39) Odenstedt H, Lindgren S, Olegard C, Erlandsson K, Lethvall S, Aneman A, et al. Slow moderate pressure recruitment maneuver minimizes negative circulatory and lung mechanic side effects: evaluation of recruitment maneuvers using electric impedance tomography. *Intensive Care Med* 2005 Dec;31(12):1706-1714.
- (40) Welsby IJ, Bennett-Guerrero E, Atwell D, White WD, Newman MF, Smith PK, et al. The association of complication type with mortality and prolonged stay after cardiac surgery with cardiopulmonary bypass. *Anesth Analg* 2002 May;94(5):1072-1078.
- (41) Kathy Stiller and Anna Phillips. Safety aspects of mobilising acutely ill inpatients. *Physiotherapy Theory and Practice* 2003;19:239-257.
- (42) Hirschhorn AD, Richards D, Mungovan SF, Morris NR, Adams L. Supervised moderate intensity exercise improves distance walked at hospital discharge following coronary artery bypass graft surgery--a randomised controlled trial. *Heart Lung Circ* 2008 Apr;17(2):129-138.

- (43) Padovani C, Cavenaghi OM. Alveolar recruitment in patients in the immediate postoperative period of cardiac surgery. *Rev Bras Cir Cardiovasc* 2011 Jan-Mar;26(1):116-121.
- (44) Claxton BA, Morgan P, McKeague H, Mulpur A, Berridge J. Alveolar recruitment strategy improves arterial oxygenation after cardiopulmonary bypass. *Anaesthesia* 2003 Feb;58(2):111-116.
- (45) Hanekom S, Berney S, Morrow B, Ntoumenopoulos G, Paratz J, Patman S, et al. The validation of a clinical algorithm for the prevention and management of pulmonary dysfunction in intubated adults--a synthesis of evidence and expert opinion. *J Eval Clin Pract* 2011 Aug;17(4):801-810.
- (46) Pinhu L, Whitehead T, Evans T, Griffiths M. Ventilator-associated lung injury. *Lancet* 2003 Jan 25;361(9354):332-340.
- (47) Suh GY, Koh Y, Chung MP, An CH, Kim H, Jang WY, et al. Repeated derecruitments accentuate lung injury during mechanical ventilation. *Crit Care Med* 2002 Aug;30(8):1848-1853.
- (48) Hodgson C, Denehy L, Ntoumenopoulos G, Santamaria J, Carroll S. An investigation of the early effects of manual lung hyperinflation in critically ill patients. *Anaesth Intensive Care* 2000 Jun;28(3):255-261.
- (49) Cakmakkaya OS, Kaya G, Altintas F, Hayirlioglu M, Ekici B. Restoration of pulmonary compliance after laparoscopic surgery using a simple alveolar recruitment maneuver. *J Clin Anesth* 2009 Sep;21(6):422-426.
- (50) Magnusson L, Spahn DR. New concepts of atelectasis during general anaesthesia. *Br J Anaesth* 2003 Jul;91(1):61-72.

ADDENDA RELATED TO METHODOLOGY

ADDENDUM A



Netcare Management (Pty) Limited

Tel: + 27 (0)11 301 0000
Fax: Corporate +27 (0)11 301 0499
76 Maude Street, Corner West Street, Sandton, South Africa
Private Bag X34, Benmore, 2010, South Africa

18th July 2010

Mr SG Nel
PO Box 944
Bellville
7535

E mail: nc@woelly.co.za (0832549124)

Dear Mr Nel

THE EFFECTS OF A LUNG RECRUITMENT MANOEUVRE BEFORE EXTUBATION ON PULMONARY FUNCTION AFTER CORONARY ARTERY BYPASS SURGERY - N07/07/159

It is with pleasure that we inform you that your application to conduct research on; The effects of a lung recruitment manoeuvre before extubation on pulmonary function after Coronary Artery Bypass surgery - N07/07/159, at Netcare Kuilsriver Hospital has been successful, subject to the following:

- i) All information with regards to Netcare will be treated as confidential.
- ii) Netcare's name will not be mentioned without written consent from the Academic Board of Netcare.
- iii) Where Netcare's name is mentioned, the research will not be published without written consent from the Academic Board of Netcare.
- iv) A copy of the research will be provided to Netcare once it is finally approved by the tertiary institution, or once complete.
- v) All legal requirements with regards to patient rights and confidentiality will be complied with.

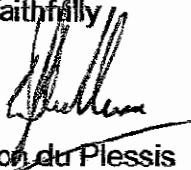
Directors: E J Brannigan, M S F da Costa, I M Davis, J du Plessis, V Firman, R H Friedland, V L J Lithakaryane, M B Nkosi, C Pailman, P Warriner

Company Secretary: L Kok Reg. No. 1995/012717/07

- vi) I will provide a copy of insurance stating the necessary indemnity cover. This cover provided to the researcher must protect both the staff and the hospital facility from potential liability
- vii) Netcare will receive a progress report by 30th September annually irrespective of the date of approval from Netcare Research Committee

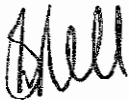
We wish you success in your research.

Yours faithfully



Prof Dion du Plessis

Full member: Research Committee & Medical Practitioner evaluating research applications as per Management and Governance Policy



Shannon Nell

Chairperson: Research Committee

Network Healthcare Holdings Limited (Netcare)

ADDENDUM B

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

The effects of a lung recruitment manoeuvre before extubation on pulmonary function after coronary artery bypass surgery.

REFERENCE NUMBER:

PRINCIPAL INVESTIGATOR: Stephan Nel

ADDRESS: Kuilsrivier Hospital
Van Riebeeck str
Kuilsrivier

CONTACT NUMBER: 021 900 6244

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Committee for Human Research at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?

- ❖ All the patients receiving heart bypass surgery at Kuilsrivier Hospital will be asked to be part of this study.
- ❖ A normal side effect of any person under general anesthesia is atelectasis or the collapse of the small lung sacs, which may decrease your lung function. This effect is more pronounced with someone having chest surgery. The aim of the study is to determine if a specific technique of inflating your lungs after your operation will improve the function of your lungs.
- ❖ After your operation, while the ventilator is still helping you to breath, your anesthetist will decide if it is safe to include you in the study and you will then be randomly selected into a group receiving this specific treatment or not.
- ❖ If you were selected into the treatment group, your lungs will be inflated to its optimal size by increasing the pressure at which the ventilator is pushing air into your lungs. You will be requested to hold your breath for 15 seconds for two consecutive breaths. This will be repeated after 15 min. We will do this procedure just before the anaesthetist removes the tube.
- ❖ From clinical experience previous patients did not report this technique to be painful.
- ❖ We will then compare your blood oxygen levels taken before the operation to those taken after the operation.
- ❖ The intervention to be used is not new but we still need to determine and document the effectiveness of this intervention in preventing lung problems after heart surgery.
- ❖ These test procedures will be done as per routine post-operative care.

Why have you been invited to participate?

- ❖ The study will be on patients at this hospital having heart bypass surgery, which is not an emergency operation.

What will your responsibilities be?

- ❖ The post operative care that you will receive is standard. These tests will be performed in the hospital at no extra cost.

Will you benefit from taking part in this research?

- ❖ You may not specifically benefit from this research, but if we can prove that this treatment is as effective we may be a step closer to preventing lung complications after heart surgery.

Are there any risks involved in your taking part in this research?

- ❖ There are no foreseeable risks involved and all procedures are standard and all necessary precautions will be taken. Your nursing sister and doctor will be present and available in case of any complications.

If you do not agree to take part, what alternatives do you have?

- ❖ You will receive the same treatment as everybody else, which is optimal care before and after the operation.

Who will have access to your medical records?

- ❖ Your doctors, physiotherapists and the researchers will have access to your medical records. All information collected will be treated as confidential and protected. If it is used in a publication or thesis, your identity will remain anonymous.

What will happen in the unlikely event of some form of injury occurring as a direct result of your taking part in this research study?

- ❖ The study intervention and measurements will take place while you are still in the ICU with specifically trained staff on 24h duty. Your doctor will be available in case of any complications. This is part of the standard care.

Will you be paid to take part in this study and are there any costs involved?

- ❖ No you will not be paid to take part in the study. There will be no costs involved for you, if you do take part.

Is there anything else that you should know or do?

- ❖ You can contact Stephan Nel at tel 021 900 6244 if you have any further queries or encounter any problems.
- ❖ You can contact the Committee for Human Research at 021 938 9207 if you have any concerns or complaints that have not been adequately addressed by your researcher.
- ❖ You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I agree to take part in a research study entitled: The effects of a lung recruitment manoeuvre before extubation on pulmonary function after coronary artery bypass surgery.

I declare that:

- ❖ I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- ❖ I have had a chance to ask questions and all my questions have been adequately answered.
- ❖ I understand that taking part in this study is **voluntary** and I have not been pressurized to take part.
- ❖ I may choose to leave the study at any time and will not be penalized or prejudiced in any way.
- ❖ I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interest, or if I do not follow the study plan, as agreed to.

Signed at (*place*) on (*date*) 20....

.....
Signature of participant

.....
Signature of witness

Declaration by investigator

I **Stephan Nel** declare that:

1. I explained the information in this document to
2. I encouraged him/her to ask questions and took adequate time to answer them.
3. I am satisfied that he/she adequately understands all aspects of the research, as discussed above
4. I did/did not use a interpreter.

Signed at (*place*) on (*date*) 20....

.....
Signature of investigator

.....
Signature of witness

Declaration by interpreter

I (*name*) declare that:

❖ I assisted the investigator (*name*) to explain the information in this document to (*name of participant*) using the language medium of Afrikaans/Xhosa.

- ❖ We encouraged him/her to ask questions and took adequate time to answer them.
- ❖ I conveyed a factually correct version of what was related to me.
- ❖ I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*) on (*date*) 20....

.....
Signature of interpreter

.....
Signature of witness

DEELNEMERINLIGTINGSBLAD EN -TOESTEMMINGSVORM

TITEL VAN DIE NAVORSINGSPROJEK:

Die effek van 'n long herwinnings prosedure voor ekstubasie op pulmonêre funksie na 'n hart omleidings operasie.

VERWYSINGSNOMMER:

HOOFNAVORSER: Stephan Nel

ADRES: Kuilsrivier Hospital
Van Riebeeckstr
Kuilsrivier

KONTAKNOMMER: 021 900 6244

U word genooi om deel te neem aan 'n navorsingsprojek. Lees asseblief hierdie inligtingsblad op u tyd deur aangesien die detail van die navorsingsprojek daarin verduidelik word. Indien daar enige deel van die navorsingsprojek is wat u nie ten volle verstaan nie, is u welkom om die navorsingspersoneel of dokter daarvoor uit te vra. Dit is baie belangrik dat u ten volle moet verstaan wat die navorsingsprojek behels en hoe u daarby betrokke kan wees. U deelname is ook **volkome vrywillig** en dit staan u vry om deelname te weier. U sal op geen wyse hoegenaamd negatief beïnvloed word indien u sou weier om deel te neem nie. U mag ook te eniger tyd aan die navorsingsprojek onttrek, selfs al het u ingestem om deel te neem.

Hierdie navorsingsprojek is deur die **Komitee vir Mensnavorsing van die Universiteit Stellenbosch** goedgekeur en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki en die Etiese Riglyne vir Navorsing van die Mediese Navorsingsraad (MNR).

Wat behels hierdie navorsingsprojek?

- ❖ Alle pasiënte wat hart omleidings ontvang by Kuilsrivier Hospitaal sal gevra word om deel te wees van die projek.
- ❖ Enige persoon wat algemene narkose kry se klein longsakkies val effens plat. Hierdie normale newe-effek kan 'n negatiewe invloed hê op jou longe se funksie. Hierdie effek is selfs meer uitgesproke in iemand wat borskas chirurgie ondergaan. Die doel van ons projek is om te bepaal of 'n spesifieke tegniek om jou longe op te blaas die funksie daarvan na die operasie sal verbeter.
- ❖ Na jou operasie, terwyl die ventilator jou nog help asemhaal sal jou narkotiseur besluit of dit veilig is om hierdie tegniek op jou te doen. Jy sal dan dmv loting in 'n groep ingedeel word wat die tegniek kry of nie en dus deel word van die studie.
- ❖ As jy in die tegniekgroep ingedeel is gaan jou longe na hul optimale grootte opgeblaas word deur die druk waarmee die ventilator lug inblaas te verhoog. Jy moet dan probeer om jou asem twee maal in 'n ry vir 15 sekondes op te hou. Ons gaan dit 15 min later weer herhaal. Dit gebeur net voor die narkotiseur die asemhalings pyp uit jou keel verwyder.
- ❖ Volgens kliniese ervaring het vorige pasiënte geen melding van pyn gemaak agv hierdie tegniek.
- ❖ Hierna gaan ons 'n vergelyking maak tussen jou long funksie toetse en bloedsuurstof vlakke wat voor die operasie geneem is met die wat na die operasie geneem is.
- ❖ Hierdie tegniek word alreeds deur ons gebruik, maar ons wil graag bepaal en dokumenteer of dit wel effektief is om long komplikasies na hart chirurgie te verminder.
- ❖ Alle toets presedures is volgens standaard post operatiewe sorg.

Waarom is u genooi om deel te neem?

- ❖ Hierdie projek sluit alle pasiënte in wat 'n hartomleiding by hierdie hospitaal kry behalwe as dit 'n noodoperasie is.

Wat sal u verantwoordelikhede wees?

- ❖ Die post operatiewe sorg wat u sal ontvang is standaard. Alle toetse voor en na die operasie word in die hospitaal gedoen teen geen ekstra koste.

Sal u voordeel trek deur deel te neem aan hierdie navorsingsprojek?

- ❖ Jy mag dalk nie direk voordeel trek uit hierdie studie nie, maar as ons kan bewys dat die tegniek effektief is mag ons dalk nader wees aan die optimale manier om long komplikasies te voorkom na hart operasies.

Is daar enige risiko's verbonde aan u deelname aan hierdie navorsingsprojek?

- ❖ Die risiko's verbonde is deel van die standaard prosedure en al die nodige voorsorg word getref. U verpleegsuster en dokters sal altyd teenwoordig en beskikbaar wees indien daar enige komplikasies sou wees.

Watter alternatiewe is daar indien u nie instem om deel te neem nie?

- ❖ U sal optimale sorg voor en na u operasie ontvang soos enigiemand anders wat hierdie operasie kry.

Wie sal toegang hê tot u mediese rekords?

- ❖ U dokters, fisioterapeute en die navorsers sal toegang hê tot u mediese rekords. Alle informasie sal konfidentiële hanteer word en u identiteit sal beskerm word indien dit gebruik sou word in 'n tesis of publikasie.

Wat sal gebeur in die onwaarskynlike geval van 'n besering wat mag voorkom as gevolg van u deelname aan hierdie navorsingsprojek?

- ❖ Die tegniek en metings word gedoen terwyl u nog in die ISE is met spesifiek opgeleide personeel 24 h op diens. U dokters is beskikbaar in die geval van enige komplikasies.

Sal u betaal word vir deelname aan die navorsingsprojek en is daar enige koste verbonde aan deelname?

- ❖ U sal nie betaal word vir deelname aan die navorsingsprojek nie. Deelname aan die navorsingsprojek sal u niks kos nie.

Is daar enigiets anders wat u moet weet of doen?

- ❖ U kan Stephan Nel kontak by tel 021 900 6244 indien u enige verdere vrae het of enige probleme ondervind.
- ❖ U kan die Komitee vir Mensnavorsing kontak by 021 938 9207 indien u enige bekommernis of klagte het wat nie bevredigend deur u studie leier hanteer is nie.
- ❖ U sal 'n afskrif van hierdie inligtings- en toestemmingsvorm ontvang vir u eie rekords.

Verklaring deur deelnemer

Met die ondertekening van hierdie dokument onderneem ek,, om deel te neem aan 'n navorsingsprojek getiteld **Die effek van 'n long herwinnings prosedure voor ekstubasie op pulmonêre funksie na 'n hart omleidings operasie.**

Ek verklaar dat:

- Ek hierdie inligtings- en toestemmingsvorm gelees het of aan my laat voorlees het en dat dit in 'n taal geskryf is waarin ek vaardig en gemaklik mee is.
- Ek geleentheid gehad het om vrae te stel en dat al my vrae bevredigend beantwoord is.
- Ek verstaan dat deelname aan hierdie navorsingsprojek **vrywillig** is en dat daar geen druk op my geplaas is om deel te neem nie.
- Ek te eniger tyd aan die navorsingsprojek mag onttrek en dat ek nie op enige wyse daardeur benadeel sal word nie.
- Ek gevra mag word om van die navorsingsprojek te onttrek voordat dit afgehandel is indien die studiedokter of navorser van oordeel is dat dit in my beste belang is, of indien ek nie die ooreengekome navorsingsplan volg nie.

Geteken te (*plek*) op (*datum*) 20....

.....
Handtekening van deelnemer

.....
Handtekening van getuie

Verklaring deur navorsers

Ek **Stephan Nel** verklaar dat:

- Ek die inligting in hierdie dokument verduidelik het aan
- Ek hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.
- Ek tevrede is dat hy/sy al die aspekte van die navorsingsprojek soos hierbo bespreek, voldoende verstaan.
- Ek 'n tolk gebruik het/nie 'n tolk gebruik het nie. (*Indien 'n tolk gebruik is, moet die tolk die onderstaande verklaring teken.*)

Geteken te (*plek*) op (*datum*) 20.....

.....
Handtekening van navorsers

.....
Handtekening van getuie

Verklaring deur tolk

Ek (*naam*) verklaar dat:

- Ek die navorsers (*naam*) bygestaan het om die inligting in hierdie dokument in Afrikaans/Xhosa aan (*naam van deelnemer*) te verduidelik.
- Ons hom/haar aangemoedig het om vrae te vra en voldoende tyd gebruik het om dit te beantwoord.
- Ek 'n feitelik korrekte weergawe oorgedra het van wat aan my vertel is.
- Ek tevrede is dat die deelnemer die inhoud van hierdie dokument ten volle verstaan en dat al sy/haar vrae bevredigend beantwoord is.

Geteken te (*plek*) op (*datum*) 20.....

.....
Handtekening van tolk

.....
Handtekening van getuie

ADDENDUM C

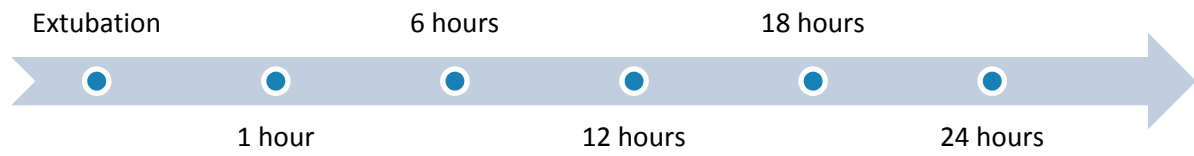


Figure A.1: A timeline indication of arterial blood gas (ABG) measurements from extubation.

ADDENDUM D

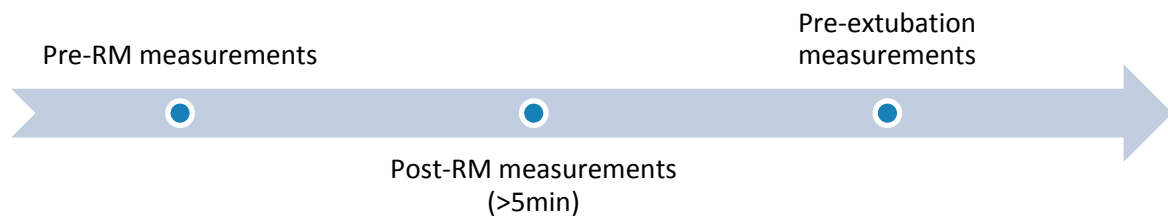


Figure A.2: A timeline indication of pre- and post-RM measurements of PEEP, plateau pressure and tidal volume (used to calculate static lung compliance).

ADDENDUM E

RECRUITMENT CONTRA-INDICATED <i>*during the last 3h</i>				
Intra-operative Pulmonary Trauma and/or Bleeding (>100ml/h)	YES	NO		
Arterial Systolic Pressure < 80 and/or MAP < 60 mmHg*	YES	NO		
COPD with bullae	YES	NO		
IABP	YES	NO		
1 > Ventilated > 14h	YES	NO		
RAS Score				
RECRUITMENT DISCONTINUED	RM1		RM2	
Abnormal ECG	YES	NO	YES	NO
Specify: _____ Time to recover _____ min	min		min	
Decreased Saturation (drop > 5%)	YES	NO	YES	NO
_____ Time to recover _____ min	min		min	
Arterial Systolic Pressure < 80 and/or MAP < 60 mmHg	YES	NO	YES	NO
_____ Time to recover _____ min	min		min	
Reaction of pain and/or discomfort	YES	NO	YES	NO
_____ Time to recover _____ min	min		min	
RECRUITMENT INTERRUPTED (airway pressure above the limit)	RM1		RM2	
During first 15 sec hold	YES	NO	YES	NO
During second 15 sec hold	YES	NO	YES	NO

VITAL SIGNS					
TIME	3h PRE-RM :	2h PRE-RM :	1h PRE-RM :	PRE-RM :	POST-RM >5min :
SYS					
MAP					
DIAS					
HR					
CVP					
SATS					

VENTILATOR SETTINGS			
TIME	ICU :	PRE-RM :	POST-RM :
Mode			
FiO ₂			
Rate (set)			
Rate (pt)			
Vt (set)			
PEEP			

ADDENDUM F

ARTERIAL BLOOD GAS ANALYSES																
Time:	Pre Surgery :	ICU :	Pre RM :	1h Post Extubation :	6h Post Extubation :	12h Post Extubation :	18h Post Extubation :	24h Post Extubation :								
PH																
pCO ₂																
pO ₂																
BICARB																
BE																
Sats																
Hb																
HCT																
FiO ₂	Additional Oxygen – MASK(m); NASAL CANULA(n/c); ROOM AIR(r/a)															
	m	n/c	r/a	m	n/c	r/a	m	n/c	r/a	m	n/c	r/a	m	n/c	r/a	
PaO ₂ /FiO ₂																

OBJECTIVE DATA CAPTURED

TIME	IN ICU :				PRE RM :				POST RM (> 5 min) :				BEFORE EXTUBATION :			
PEEP																
Vt (pt)																
Plateau Press																

Compliance = Vt_(median) / (Plateau Pressure_(median) – PEEP)

TIME	IN ICU :				PRE RM :				POST RM (> 5 min) :				BEFORE EXTUBATION :			
Vt (median)																
Plateau Pressure (median)																
Compliance																

ADDENDUM G

LENGTH OF STAY		
Admitted to hospital	Date:	Time:
In theatre	Date:	Time:
Connected to ventilator (ICU)	Date:	Time:
Sedation stopped	Date:	Time:
Recruitment	RM 1	Time:
	RM 2	Time:
Extubation	Date:	Time:
Physio initiated	Date:	Time:
ICU discharge/ Deceased	Date:	Time:
Hospital Discharge/ Deceased	Date:	Time:

PRE-OPERATIVE			
Informed consent	YES	NO	
Gender	MALE	FEMALE	
Type of surgery	Sternotomy	Thoracotomy	
Duration of CPB: min		Duration of surgery: min	
PULMONARY RISK SCORE			Score
Age(> 70 = 1 point)= yrs			
Cough and expectoration			
Diabetes mellitus			
Smoker			
COPD - pulmonary medication used			
BMI > 27.0	kg	cm	
Total			

ADDENDA RELATED TO RESULTS

ADDENDUM H

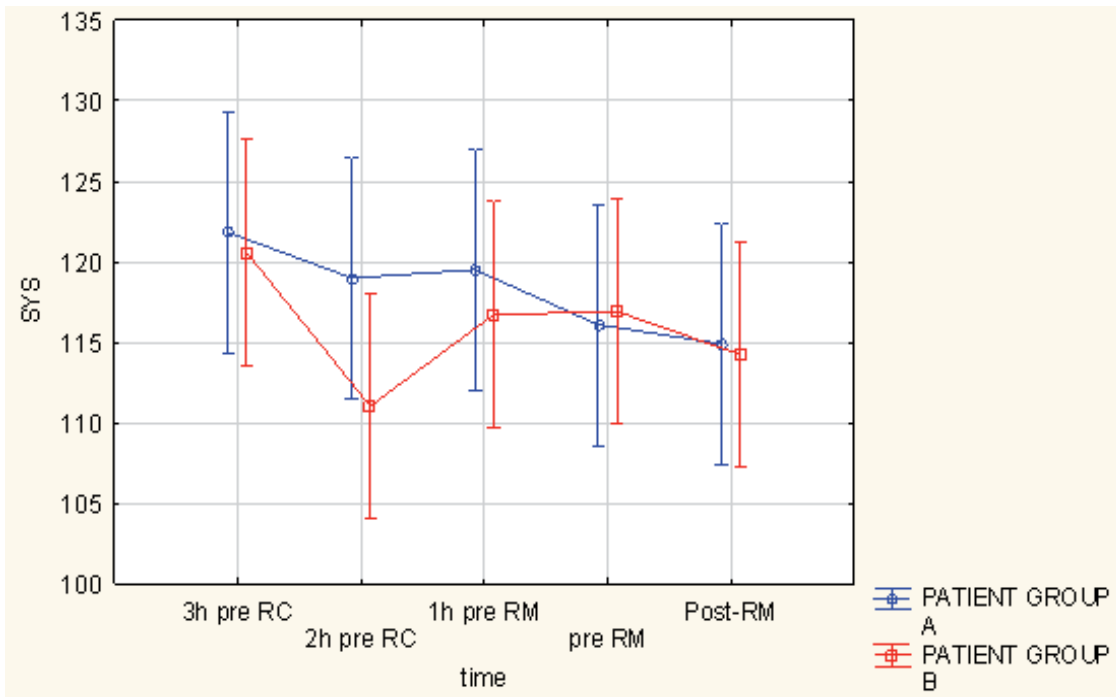


Figure A.3: Systolic blood pressure (SYS) from 3hours pre RM to more than 5min after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)

ADDENDUM I

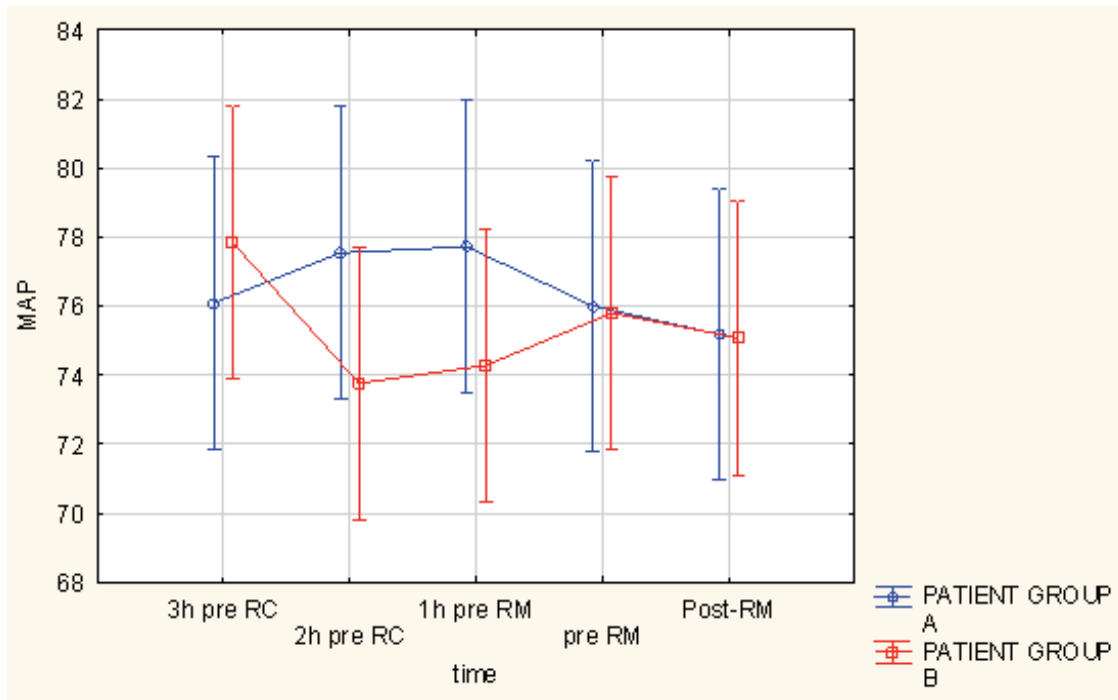


Figure A.4: Mean arterial pressure (MAP) from 3hours pre RM to more than 5 minutes after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)

ADDENDUM J

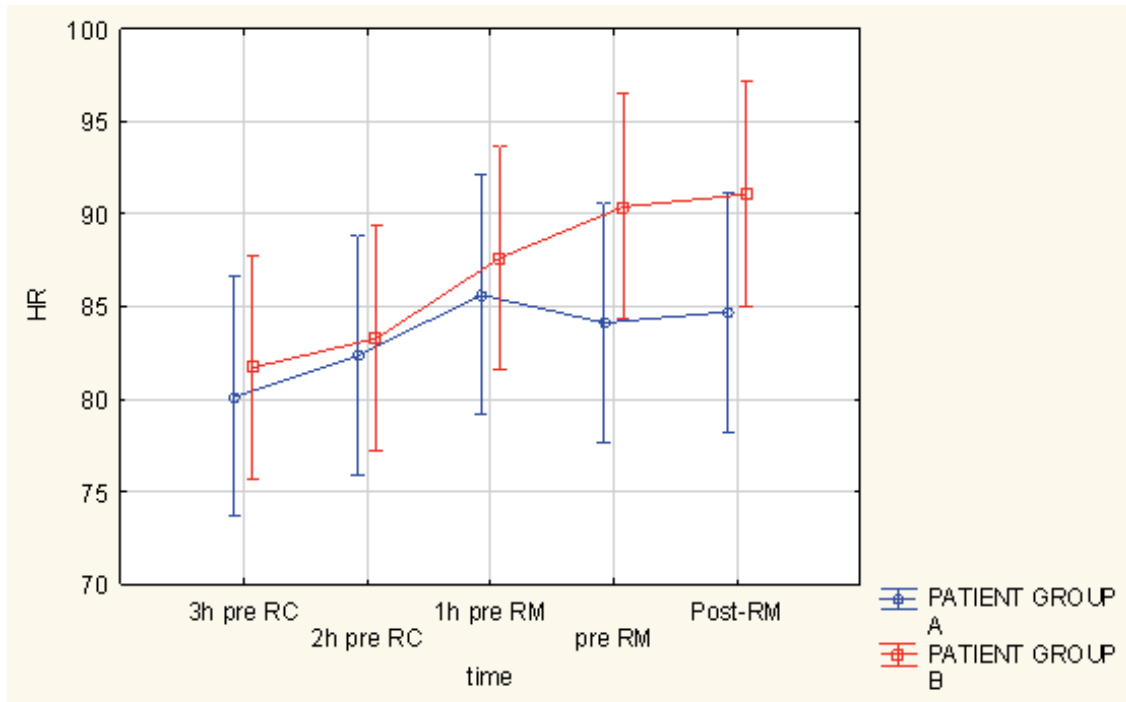


Figure A.5: Heart rate (HR) from 3 hours pre RM to more than 5 minutes after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)

ADDENDUM K

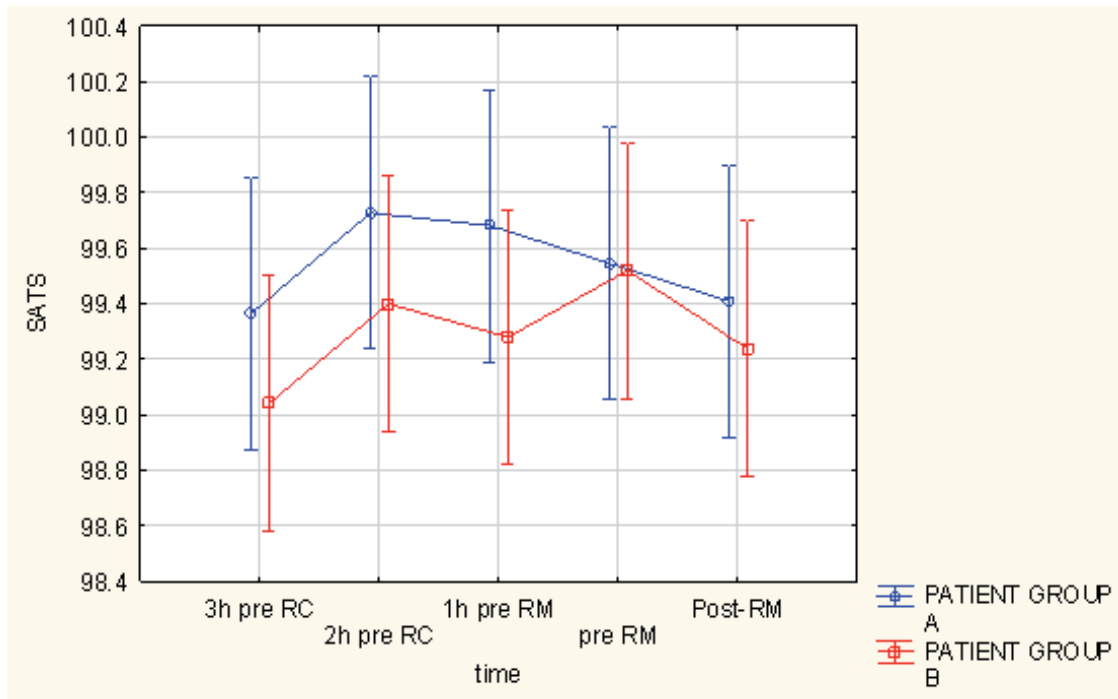


Figure A.6: Saturation (SATS) from 3 hours pre RM to more than 5 minutes after the RM (GROUP A = INTERVENTION; GROUP B = CONTROL)

ADDENDUM L

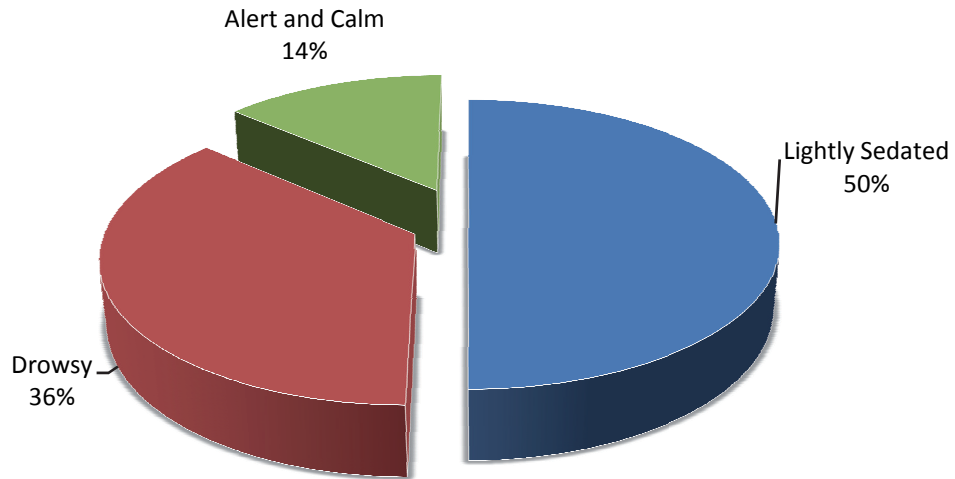


Figure A.7: Richmond Agitation-Sedation (RASS) scale for intervention group (Lightly sedated = -2; Drowsy = -1; Alert and Calm = 0)

ADDENDUM M

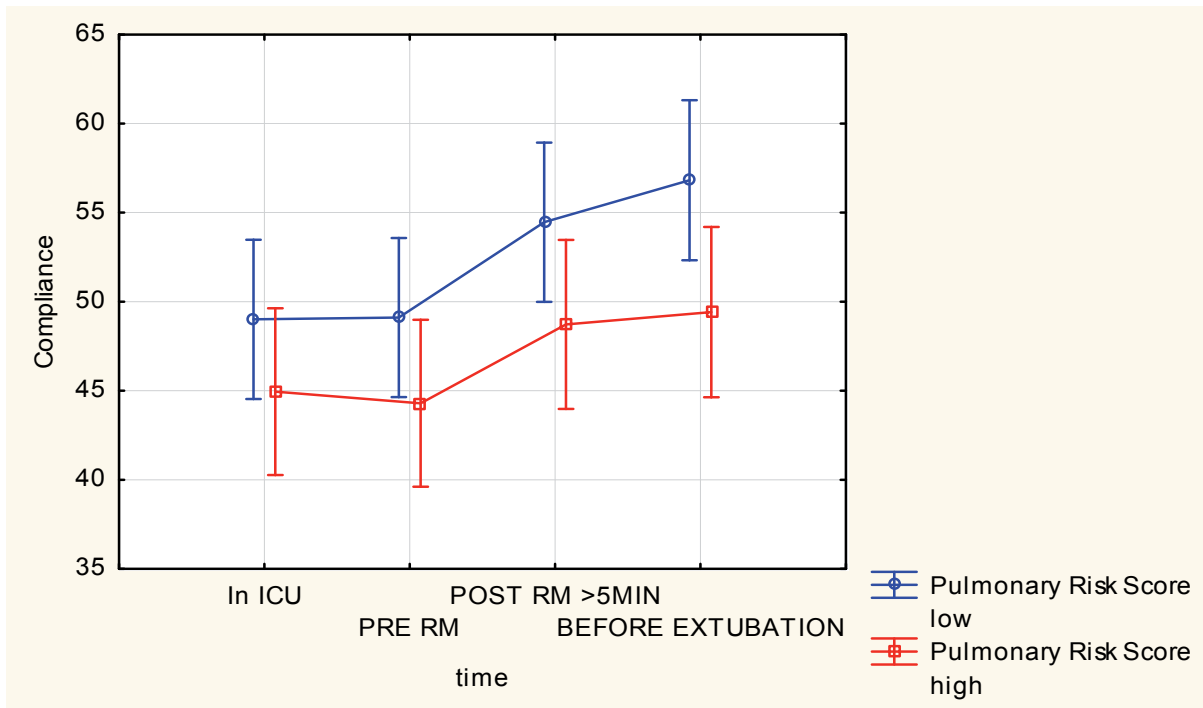


Figure A.8: Static lung compliance over time for low and high risk patients.

ADDENDUM N

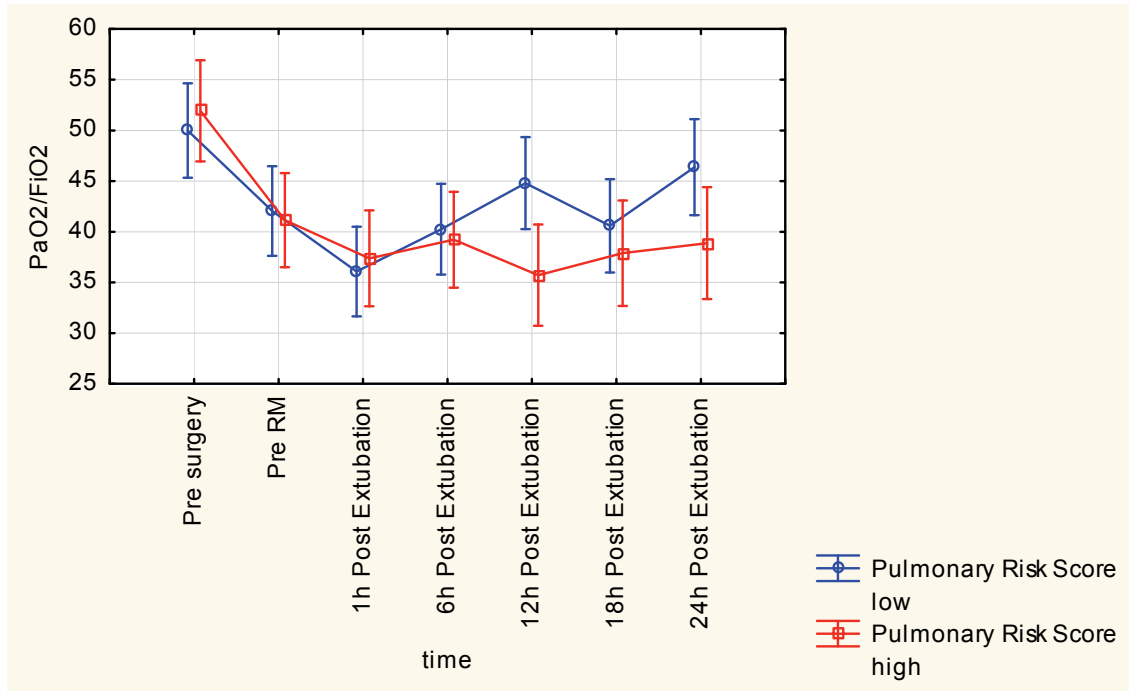


Figure A.9: PaO₂/FiO₂ over time for low and high risk patients.

ADDENDUM O

Operational Definitions of Postoperative Pulmonary Complications*

Grade 1

- Cough, dry
- Microatelectasis: abnormal lung findings and temperature $>37.5^{\circ}\text{C}$ without other documented cause; results of chest radiograph either normal or unavailable
- Dyspnea, not due to other documented cause

Grade 2

- Cough, productive, not due to other documented cause
- Bronchospasm: new wheezing or preexistent wheezing resulting in change therapy
- Hypoxemia: alveolar-arterial gradient >29 and symptoms of dyspnea or wheezing
- Atelectasis: radiological confirmation plus either temperature $>37.5^{\circ}\text{C}$ or abnormal lung findings
- Hypercarbia, transient, requiring treatment, such as naloxone or increased manual or mechanical ventilation
- Adverse reaction to pulmonary medication

Grade 3

- Pleural effusion, resulting in thoracentesis
- Pneumonia, suspected: radiological evidence without bacteriological confirmation
- Pneumonia, proved: radiological evidence and documentation of pathological organism by Gram stain or culture
- Pneumothorax
- Reintubation postoperative or intubation, period of ventilator dependence does not exceed 48 hours

Grade 4

- Ventilatory failure: postoperative ventilator dependence exceeding 48 hours, or reintubation with subsequent period of ventilator dependence exceeding 48 hours

*Source: Kroenke et al.