Influence of inspired nitrogen concentration during anaesthesia for coronary artery bypass grafting on postoperative atelectasis

C. J. JOYCE, A. B. BAKER AND S. CHARTRES

Summary

Pulmonary collapse is a common problem after coronary artery bypass graft surgery (CABG). If absorption atelectasis during anaesthesia is an important mechanism in the genesis of pulmonary collapse after CABG, the addition of nitrogen to the inspired gas during anaesthesia should reduce the amount of postoperative collapse. We studied 30 patients who were allocated randomly and prospectively to receive either 100 % oxygen or an oxygen–air mixture as the inspired gas during anaesthesia for CABG. Lung volumes, PaO₂, and an x-ray atelectasis score were measured before and after surgery to assess the degree of atelectasis. There were no significant differences between the two treatment groups in any of these measurements.

Key words


Atelectasis is common after coronary artery bypass graft surgery (CABG). The reduction in lung volume and changes in other indices of respiratory function are severe, and persist for up to several months after operation [1, 2]. Perioperative pulmonary collapse is a major clinical problem in this group of patients.

Alveolar atelectasis may be caused by a variety of factors including compression, loss of surfactant and absorption of gas [3]. Any of these may contribute to atelectasis during anaesthesia and the postoperative period.

During anaesthesia conditions exist that favour the development of absorption atelectasis. High inspired oxygen concentrations are administered routinely to avoid hypoxaemia. Lung volume is reduced by anaesthesia, and evidence of atelectasis after short periods of oxygen breathing has been demonstrated in normal conscious subjects under a variety of conditions that force them to breathe at low lung volume [4, 5]. Airways closure may occur during anaesthesia, particularly in middle aged or elderly patients [6].

High inspired oxygen concentrations of up to 100 % are used routinely during anaesthesia for CABG. The rate of absorption of gas from unventilated areas of lung depends on the composition of the inspired gas [7]. Breathing high inspired oxygen concentrations promotes absorption atelectasis, while the addition of nitrogen to the inspired gas retards this process. If absorption atelectasis during anaesthesia is an important mechanism in the genesis of pulmonary collapse after CABG, the use of air–oxygen mixtures for the inspired gas during anaesthesia instead of 100 % oxygen should reduce the amount of postoperative collapse.

We have tested the null hypothesis that “the amount of postoperative atelectasis that develops in patients who have undergone CABG does not depend on whether ventilation of the lungs during the operation is with 100 % oxygen or an air–oxygen mixture”.

Patients and methods

Lung volume was chosen as the main index of postoperative atelectasis. Power analysis [8] indicated that 15 subjects were required in each group. Chest x-rays and blood-gas measurements were performed routinely after cardiac surgery. Chest x-ray atelectasis scores and postoperative PaO₂ were also recorded.

The study was approved by the Ethics Committee of the Otago Area Health Board. Patients undergoing elective CABG with cardiopulmonary bypass were studied. Exclusion criteria included previous CABG, significantly reduced left ventricular function (ejection fraction < 40 %), evidence of cardiac failure on clinical examination or chest x-ray, the presence of obstructive lung disease (FEV₁/FVC ratio < 70 % in the sitting position), a history of respiratory disease, severe unstable angina or weight > 100 kg.

The day before surgery patients were assessed and a PA chest x-ray obtained. Forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured in the seated position to assess suitability for

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for inclusion in the study. Subjects included in the trial were allocated randomly and prospectively to either the “oxygen group” or the “air group”.

Arterial blood-gas tensions were measured breathing air in a standardized semi-recumbent position, with the legs horizontal and the trunk at 45° to the horizontal. Control measurements of respiratory function were made in the same position. Functional residual capacity (FRC) was measured by helium dilution. After equilibration of the helium concentration, three slow vital capacity manoeuvres were performed. Measurements of vital capacity (VC), expiratory reserve volume (ERV), tidal volume (VT) and inspiratory reserve volume (IRV) were made from the best effort of the VC manoeuvres (greatest VC), allowing total lung capacity (TLC) and residual volume (RV) to be calculated. Following this, three FVC manoeuvres were performed in the same position and FEV₁ and FVC determined.

Before each set of respiratory function tests a visual analogue pain score (VAS) was measured (before score), asking the subjects to score the pain they felt at that moment. The VAS was repeated at the end of the respiratory function tests (after score), asking the subjects to score the most pain that they felt during the tests. A “difference score” (after score − before score) was then calculated.

Patients were premedicated with lorazepam 1 mg on the night before surgery and 2.5 mg on the morning of surgery. The lungs were preoxygenated with 100% oxygen for 3 min, and anaesthesia induced with fentanyl 80 µg kg⁻¹. Pancuronium 8 mg and increments of 2 mg were given as required for neuromuscular block. Isoflurane was given as required for control of arterial pressure. Vasodilator (glyceryl trinitrate) or vasopressor–inotrope therapy (metaraminol or adrenaline) was used where clinically indicated. The lungs were ventilated with a tidal volume of 10 ml kg⁻¹, at a rate adjusted to maintain PaCO₂ at 4.7–2.3 kPa, from a circle circuit with a fresh gas flow of 6 litre min⁻¹.

After tracheal intubation, during the pre-bypass period, PaO₂ in the oxygen group was maintained at 1.0 and in the air group at 0.3 (made up from air and oxygen). During cardiopulmonary bypass the same inspired gas was continued into the circuit, without PEEP. A Medtronic Maxima membrane oxygenator with an integrated filtered hardshell reservoir was used with hypothermic cardiopulmonary bypass to 25–27°C. After bypass the oxygen group was managed in the same manner as before bypass (PaO₂ = 1.0). The air group was weaned from bypass with PaO₂ 0.5, and PaO₂ reduced to 0.4 when possible while maintaining SpO₂ > 95%. During transfer to the postoperative unit the same ventilation was maintained, and subjects in the oxygen group received PaO₂ = 1.0, while subjects in the air group received PaO₂ = 0.5. The duration of operation was recorded as the time from induction of anaesthesia to arrival in the postoperative intensive care unit. After arrival in the postoperative unit, management was identical in both groups. Until the patients were able to breathe spontaneously, the lungs were ventilated with a tidal volume of 10 ml kg⁻¹, with the rate adjusted to maintain PaCO₂ at 4.7–2.3 kPa. PaO₂ was maintained at the lowest level consistent with SpO₂ ≥ 95%. Morphine or diazepam was given i.v. as required for analgesia or sedation. If hypoxaemia developed, PaO₂ was increased. If still hypoxaemic with an PaO₂ of 60% oxygen, then PEEP was added as required. Patients received physiotherapy with intermittent positive pressure breathing. In all patients the trachea was extubated on the day of operation or on the morning of the day after operation (postoperative day 1).

Chest x-rays were performed on arrival in intensive care and on the morning of postoperative days 1 and 2. Chest x-rays were graded for atelectasis using a scoring system modified from Wilcox and colleagues [9] (0 = no atelectasis, I = plate atelectasis, II = segmental atelectasis, III = partial lobar atelectasis, IV = complete lobar atelectasis, V = complete lobar atelectasis in addition to any of the above). Separate scores were recorded for each lung. The patient, the radiographer taking the chest x-rays, the radiologist interpreting them and the nursing and medical staff providing postoperative care for the patient were unaware of the patient’s treatment group.

Arterial blood-gas tensions were measured in the late afternoon or evening of postoperative days 1, 2 and 3 while breathing PaO₂ 0.5 in the standardized semi-recumbent position after allowing at least 30 min for equilibration. After measurement of blood-gas tensions, measurements of respiratory function were made, again in the same position, using the same technique as before operation. All blood-gas sampling and respiratory function tests were performed by the same blinded investigator.

Statview for the Macintosh version 4.0 was used for all statistical analyses. Summary measures were used to analyse the serial measurements of lung function in the two treatment groups, as recommended by Matthews and colleagues [10]. For a given summary measure there is a single value for each subject, allowing comparison between the two treatment groups with simple unpaired two group statistical tests. The summary measures analysed were: (a) minimum SpO₂ recorded for each subject on any of the three postoperative measurements (PaO₂, 0.5). The results from the 30 patients who completed the full study were analysed. Comparisons between the two treatment groups were made with unpaired t tests; (b) maximum atelectasis score in the left lung and maximum atelectasis score in the right lung. The results from all patients who entered the study were analysed for these two summary measures, except for one patient who did not have a full set of x-rays and was excluded (41 patients, oxygen group n = 19, air group n = 22). Comparisons between the two treatment groups were made using the Mann–Whitney U test; (c) for each lung volume measured the summary measure analysed was the maximum volume recorded for each subject on any of the three postoperative measurements, where volume = (preoperative volume−current volume)/preoperative volume. The summary measures for the lung volumes were thus maximum δFRC, δVC, δRV, δTLC, δFEV₁ and δFVC. These analyses were performed in 30 patients who completed the full
study. Comparisons between the two treatment groups were made with unpaired t-tests.

Using data from the literature on changes in lung volume with cardiac surgery, it was decided to include 15 subjects in each of the two treatment groups. A difficulty in this type of clinical trial is that not all subjects entering the study complete it. Because of this the following method of randomization was used. Each time the treatment group for a subject was selected it was drawn randomly from a pool of “remaining treatments”. Initially there were 15 oxygen and 15 air treatments in the pool. Each time the treatment group for a subject was selected, that treatment was removed from the pool. If the subject completed the full study, the treatment for the next subject was selected from the treatments remaining in the pool. If the subject did not complete the full study, the treatment for that subject was returned to the pool, and the treatment for the next subject was selected from the treatments in the pool. For example, if there were nine oxygen and seven air treatments in the pool, the treatment for a subject was selected randomly from these treatments. If oxygen was selected and the subject completed the full study, the treatment for the next subject would be selected from the treatments remaining in the pool (eight oxygen and seven air). If however the subject did not complete the full study, the treatment for that subject (oxygen) was returned to the pool and the treatment for the next subject selected from the treatments remaining in the pool (nine oxygen and seven air). The study was continued until the pool was empty (i.e. 15 subjects in each group had completed the full study).

With the exception of the atelectasis scores, analyses were carried out in only 30 subjects who completed the full study. Analysis of atelectasis scores was carried out in all 41 subjects who had a full set of chest x-rays available. This included both subjects who completed the full study and those who did not, as a full set of chest x-rays were available for all but one of the subjects.

We found no significant difference between the treatment groups for any of the indices of atelectasis measured. The next question asked was “what difference between the mean values for the treatment groups would be detected with an acceptable type 2 error?”. Sokal and Rohlf [8] described a method for calculating the number of replications needed to detect a given “true” difference between means (equivalent to unpaired t test with two samples only). This method is readily adapted to find the true difference between the means that would be detected with a given sample size, for predetermined α and β.

Results

Of the 42 patients who entered the study, 30 completed the full set of measurements. In the 42 patients there were no statistically significant differences (P < 0.05) between the oxygen (n = 20) and air (n = 22) groups in variables assessed before entry into the study (age, height, weight, sex, smoking history, PaO2 on air, seated FEV1, seated FVC), in preoperative measurements of lung volume (FRC, VC, RV, TLC, FEV1, FVC) or in factors relating to operation (duration of operation, fluid balance on bypass, bypass time, cross-clamp time, number of grafts, internal mammary artery grafting, placement of pleural drains) (table 1). In the 30 patients who completed the full set of measurements there were also no statistically significant differences between the oxygen (n = 15) and air (n = 15) groups in these variables. Thus there is no suggestion that the oxygen and air groups were obtained from different patient populations, or that bias caused by poor matching of the subjects occurred in the two groups. Comparison of these same variables between subjects who completed the study and those who withdrew showed no statistically significant differences with the exception of the time of operation, which was significantly longer in those who withdrew. Analysis of VAS pain scores showed no significant differences (P < 0.05) between the oxygen and air groups in the “before scores”, “after scores” or “difference scores” on any of the perioperative days that lung volumes were measured. This makes it unlikely that differences in pain between the two groups biased these results.

There were no significant differences between the oxygen and air groups in any of the summary measures of PaO2, lung volumes, or radiological atelectasis scores (tables 2–4). Power analysis indicates that the study had an 80 % power to detect an effect caused by the treatment group (oxygen or air), that is as large or larger than 20 % of the maximum perioperative change in lung volume (14–22 % depending on which lung volume is considered, see table 2 for these results).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient data (mean ±SE [range]) for all those who entered the study (n = 42). There were no significant differences in these variables between the treatment groups (oxygen and air) for the 42 patients who entered the study or the 30 patients who completed the full study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>59 [55–74]</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173.8 (1.1) [157–192]</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>82.0 (1.5) [52–100]</td>
</tr>
<tr>
<td>PaO2 on air (kPa)</td>
<td>11.9 (0.2) [9.5–15.7]</td>
</tr>
<tr>
<td>Seated FEV1 (litrête)</td>
<td>3.144 (0.100) [1.843–4.656]</td>
</tr>
<tr>
<td>Seated FVC (litrête)</td>
<td>4.213 (0.127) [2.471–6.036]</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>246 (5) [160–303]</td>
</tr>
<tr>
<td>Fluid balance on bypass (ml)</td>
<td>1938 (185) [170–6000]</td>
</tr>
<tr>
<td>Bypass time (min)</td>
<td>79 (3) [26–122]</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>48 (2) [14–78]</td>
</tr>
<tr>
<td>FRC (litre)</td>
<td>2.598 (0.087) [1.252–4.531]</td>
</tr>
<tr>
<td>VC (litre)</td>
<td>4.031 (0.125) [2.371–5.638]</td>
</tr>
<tr>
<td>RV (litre)</td>
<td>2.055 (0.082) [0.961–3.900]</td>
</tr>
<tr>
<td>TLC (litre)</td>
<td>6.086 (0.156) [3.814–8.701]</td>
</tr>
<tr>
<td>FEV1 (litre)</td>
<td>2.988 (0.102) [1.632–4.473]</td>
</tr>
<tr>
<td>FVC (litre)</td>
<td>4.088 (0.134) [2.365–6.036]</td>
</tr>
<tr>
<td>No. of grafts (median [range])</td>
<td>3 (1–5)</td>
</tr>
<tr>
<td>Male sex (yes : no)</td>
<td>40 : 2</td>
</tr>
<tr>
<td>Smoked in last 12 months (yes : no)</td>
<td>7 : 35</td>
</tr>
<tr>
<td>IMA grafting (yes : no)</td>
<td>40 : 2</td>
</tr>
<tr>
<td>Pleural drain(s) (yes : no)</td>
<td>31 : 11</td>
</tr>
</tbody>
</table>
Assessing the magnitude of atelectasis after cardiac surgery is not simple. The conditions of the early postoperative period make some techniques of assessing atelectasis difficult or impractical. Clinical conditions such as cardiac failure and pleural effusion may alter measurements of respiratory function without actually causing atelectasis.

Chest computed tomography (CT) is perhaps the best method of assessing the presence and extent of pulmonary atelectasis in intact humans. It frequently detects atelectasis during anaesthesia that is not evident on chest x-ray [11]. In our study of cardiac surgical patients undergoing repeated measurements in the early postoperative period, CT was deemed to be unsuitable, because of the logistics and the risk of transferring potentially unstable patients.

Erect PA chest x-rays are relatively sensitive and specific for detecting atelectasis in physiological studies of normal patients [5]. However, atelectasis may occur with substantial decreases in lung volume, and atelectasis demonstrable on CT, in the absence of chest x-ray changes. After cardiac surgery, practical considerations limit early postoperative chest x-rays to AP sitting or supine films. The scoring system for chest x-rays used in this study has been previously used to assess atelectasis after cardiac surgery [9], although it has not been validated against a “gold standard” measurement of atelectasis such as CT or histology.

The use of lung volume measurements to study perioperative pulmonary function is well established, both in cardiac [1, 2] and non-cardiac surgery [12, 13]. In the perioperative period, lung volume is a better index of atelectasis than chest x-ray. Induction of anaesthesia is consistently accompanied by a reduction in FRC by about 20 % and the development of atelectasis on CT, but no signs of atelectasis on chest x-ray [14]. Lung volume has been used widely as an index of atelectasis in physiological studies [4, 5]. In a study of absorption collapse in healthy volunteers there was little to choose between chest x-ray, FRC and $P_{bO_2}$ for detection of minimal pulmonary collapse [5]. Lung volume is affected by a variety of processes in the postoperative period, including patient co-operation, pain, pleural effusion, haemothorax, pneumothorax,
cardiac failure and ARDS. Data on the changes in lung volume after cardiac surgery were available to us before commencing this study, allowing power analysis and calculation of the number of subjects required for this study. Because of the suitability of lung volume as an index of postoperative atelectasis, and the availability of data on which to base calculations of the required number of subjects, lung volumes were used as the primary outcome measure of this study and the size of the study designed accordingly. As chest x-rays and blood-gas tensions were performed routinely after cardiac surgery and the results available, chest x-ray atelectasis scores and postoperative $P_{A\text{O}_2}$ were also analysed.

One criticism of this study is that just less than 29% of subjects did not complete the full study and their withdrawal occurred after randomization. Subjects with more atelectasis could be more prone to withdraw from the full study, and this could mask an effect of the inspired gas on atelectasis. This is unlikely for three reasons. First, six of the 12 patients who withdrew had not withdrawn before the full set of measurements were made on postoperative day 1. There were no significant differences between $P_{A\text{O}_2}$ and lung volumes in these patients on postoperative day 1 and the same measurements in patients who completed the study. Second, patients who did not complete the full set of measurements did have a full set of chest x-rays. The maximum atelectasis scores were not significantly different between those who completed the full set of measurements and those who did not. Third, of the 12 patients who withdrew, five were in the oxygen group and seven in the air group. This suggests that bias was not introduced by patients in the oxygen group suffering from more collapse and withdrawing from the study more frequently than patients in the air group.

No previously published studies have examined the effect of inspired gas mixture on postoperative atelectasis after cardiac surgery. In recent years there has been a trend towards using air–oxygen mixtures for the inspired gas during anaesthesia on the basis that it reduces the amount of perioperative atelectasis. This is attractive on theoretical grounds, as the addition of nitrogen to the inspired gas mixture may retard absorption atelectasis [7].

Prospective randomized studies examining the effect of the inspired gas composition on postoperative collapse have been conducted by two groups. Logan, Spence and Smith found that in patients who breathed 30% oxygen during upper abdominal surgery, it made no difference to postoperative lung volume or $P_{A\text{O}_2}$ whether the balance of the inspired gas during anaesthesia was nitrogen or nitrous oxide [12]. Roberts, Parke and Sykes found that in patients who were given nitrous oxide as a component of their intraoperative inspired gas mixture during cholecystectomy, nocturnal arterial oxygen desaturation below $S_{\text{O}_2}$ of 85% was less frequent than when nitrogen was given [15]. When nitrous oxide–oxygen mixtures are breathed, alveoli are more prone to absorption atelectasis than when 100% oxygen is breathed [7] so if absorption atelectasis during surgery was an important component of perioperative pulmonary collapse more collapse would be expected when nitrous oxide was breathed rather than nitrogen. Other studies examining the effects of the inspired gas composition on postoperative atelectasis have methodological limitations and have demonstrated variable results. One study showed a protective effect of adding nitrogen to the breathing mixture [16], while others showed no difference [17], and one study found that postoperative $P_{A\text{O}_2}$ was significantly lower when nitrogen was added to the inspired gas mixture instead of nitrous oxide [18]. Overall the evidence suggests that the amount of postoperative collapse is not affected by the inspired gas composition.

Postoperative atelectasis is a common problem after cardiac surgery. The aetiology of this atelectasis is unclear, but this study demonstrates that absorption atelectasis during surgery is not an important factor.

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References


