



Contents lists available at ScienceDirect

Critical Care and Resuscitation

journal homepage: www.elsevier.com/locate/ccrj

Original Article

Effect of automated titration of oxygen on time spent in a prescribed oxygen saturation range in adults in the ICU after cardiac surgery

Louis W. Kirton, MBChB ^{a, b, *}, Raulle Sol Cruz, BSN ^{a, c}, Leanlove Navarra, BSN ^{a, c}, Allie Eathorne, BSc ^a, Julie Cook, MBChB ^a, Richard Beasley, DSc ^{a, b}, Paul J. Young, MBChB, PhD ^{a, c, **}

^a Medical Research Institute of New Zealand, Wellington, New Zealand; ^b Victoria University Wellington, Wellington, New Zealand; ^c Te Whatu Ora, Capital and Coast, Wellington, New Zealand

ARTICLE INFORMATION

Article history:

Received 16 November 2023

Received in revised form

8 January 2024

Accepted 9 January 2024

Keywords:

Oxygen delivery

Intensive care

Cardiac surgery

Gas exchange

ABSTRACT

Objective: The objective of this study was to determine whether automated titration of the fraction of inspired oxygen (FiO₂) increases the time spent with oxygen saturation (SpO₂) within a predetermined target SpO₂ range compared with manually adjusted high-flow oxygen therapy in postoperative cardiac surgical patients managed in the intensive care unit (ICU).

Design: Single-centre, open-label, randomised clinical trial.

Setting: Tertiary centre ICU.

Participants: Recently extubated adults following elective cardiac surgery who required supplemental oxygen.

Interventions: Automatically adjusted FiO₂ (using an automated oxygen control system) compared with manual FiO₂ titration, until cessation of oxygen therapy, ICU discharge, or 24 h (whichever was sooner).

Main outcome measures: The primary outcome was the proportion of time receiving oxygen therapy with the SpO₂ in a SpO₂ target range of 92–96 %.

Results: Among 65 participants, the percentage of time per patient spent in the target SpO₂ range was a median of 97.7 % (interquartile range: 87.9–99.2 %) and 91.3 % (interquartile range: 77.1–96.1 %) in the automated (n = 28) and manual (n = 28) titration groups, respectively. The estimated effect of automated FiO₂, compared to manual FiO₂ titration, was to increase the percentage of time spent in the target range by a median of 4.8 percentage points (95 % confidence interval: 1.6 to 10.3 percentage points, p = 0.01).

Conclusion: In patients recently extubated after cardiac surgery, automated FiO₂ titration significantly increased time spent in a target SpO₂ range of 92–96 % compared to manual FiO₂ titration.

© 2024 The Authors. Published by Elsevier B.V. on behalf of College of Intensive Care Medicine of Australia and New Zealand. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

The recommended approach to oxygen therapy in hospitalised patients is to titrate the inspired oxygen concentration (FiO₂) to ensure that patients are maintained within a prescribed oxygen saturation (SpO₂) target range.^{1–3} This strategy minimises the chance of exposing the patient to both hypoxaemia^{1,4} and

hyperoxaemia.^{1,5,6} This targeted approach to oxygen delivery is mostly a manual task, requiring a clinician to monitor, record, and interpret pulse oximetry measurements and adjust the oxygen flow rate in response to SpO₂ measurements that fall outside the target range. In the intensive care unit (ICU), where high nurse-to-patient ratios allow for closer monitoring, more frequent oxygen titration is possible than in the ward, leading to tighter SpO₂ control. This was illustrated in a single trial that reported the median proportion of time with SpO₂ inside the prescribed target SpO₂ range was 89 % in patients receiving standard, manually adjusted, high-flow nasal oxygen therapy (HFNOT) for acute hypoxaemic respiratory failure.⁷ In contrast, SpO₂ was maintained within the target range for only 56 % of time in medical in-patients receiving HFNOT.⁸

* Corresponding author at: Medical Research Institute of New Zealand, Wellington, New Zealand. Tel.: +64 226922497.

** Corresponding author at: Te Whatu Ora, Capital and Coast, Wellington, New Zealand.

E-mail addresses: louis.kirton@mrnz.ac.nz (L.W. Kirton), Paul.Young@ccdhb.org.nz (P.J. Young).

Automated oxygen-control systems comprise a closed-loop controller that automatically adjusts the FiO_2 in response to current and predicted future SpO_2 levels. This novel oxygen delivery system results in improved adherence to a target SpO_2 range in various hospital settings.^{7,9–11} In the ICU, an automated oxygen-control system (Hamilton Medical, Bonaduz, Switzerland) delivering HFNOT resulted in an increase in time within a target SpO_2 range from 89 % to 97 %, as compared to manual oxygen titration, in patients with moderate to severe acute hypoxaemic respiratory failure.⁷ Whether similar efficacy exists with different closed-loop oxygen titration devices, in different ICU populations, is unknown.

The primary aim of this randomised clinical trial was to determine the effect of an automated closed-loop system (Fisher and Paykel Healthcare, Auckland, New Zealand) on time spent within a prescribed SpO_2 target range in ICU patients recently extubated after elective cardiac surgery. We hypothesised that the proportion of time spent within the target SpO_2 range following extubation would be greater using automated oxygen control than with manual oxygen titration.

2. Methods

2.1. Study design

This single-centre, open-label, randomised, parallel group, controlled trial evaluated the efficacy of HFNOT with an automated oxygen-control system in adults who had a postextubation oxygen requirement in a tertiary centre ICU following elective cardiac surgery. The study recruitment period was from 30 September 2021 till 19 December 2022. Ethical approval was obtained from the Northern B Health and Disability Ethics Committee (HDEC) (reference 21/NTB/103). The trial was run in accordance with Good Clinical Practice guidelines and the declaration of Helsinki. This trial was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12621000658819).

2.2. Participants

Participants were adults requiring elective cardiac surgery, identified in consultation with the Wellington Regional Hospital Cardiothoracic Surgical Unit and approached preoperatively to obtain written informed consent. Eligibility was assessed before tracheal extubation. Inclusion criteria were met if the potential participant was deemed ready for extubation, HFNOT was planned, care was delivered in the ICU following elective cardiac surgery, and participants had a documented SpO_2 target range of 92–96 %. Participants were excluded if they were aged less than 18 years; had risk factors for hypercapnic respiratory failure (chronic obstructive pulmonary disease, cystic fibrosis, bronchiectasis, chest wall deformity, or neuromuscular disease) and if an investigator considered 92–96 % to be an inappropriate SpO_2 target; had a concerning discrepancy between arterial blood oxygen saturation and SpO_2 ; were infected or colonised with drug-resistant bacteria (*Pseudomonas* species, *Burkholderia Cepacia* or mycobacteria); were being treated with palliative intent or not expected to survive until hospital discharge; had nasal trauma or recent transnasal neurosurgery; had vascular compromise prohibiting pulse oximetry use; were pregnant or breastfeeding; had cognitive impairment precluding consent; or had any other condition considered by an investigator to present a safety risk.

2.3. Protocol amendment

After 10 participants had completed the trial, six had required little or no supplemental oxygen during the study period. The trial

management committee deemed it necessary to amend the protocol to include only those with a ratio of arterial oxygen tension to inspired oxygen concentration ($\text{PaO}_2:\text{FiO}_2$) of <350 before extubation. This protocol amendment was reviewed and approved by the Northern B HDEC before being implemented.

2.4. Randomisation

Eligible participants were block randomised with variable block size, 1:1 to receive the intervention therapy (automated oxygen control) or the control therapy (manual oxygen control). The randomisation code was generated by the study statistician using a computer-generated sequence. Allocation was concealed by the Research Electronic Data Capture electronic case report form and released to investigators at time of randomisation. The nature of the intervention meant investigators and participants could not be blinded to the allocated intervention.

2.5. Procedures

Randomised participants were transferred to HFNOT using the AIRVO3 (Fisher and Paykel Healthcare) device. Optiflow (Fisher and Paykel Healthcare) nasal cannulas were fitted, and the gas flow rate was set and titrated between 25 and 70 L/min at the discretion of the treating clinician. A pulse oximeter (Nonin 7000A, Minnesota, U.S.A) was attached to an appropriate finger. The control of inspired oxygen concentration (FiO_2) was set according to the randomised treatment allocation, either using the automated setting (OptiO₂ Fisher and Paykel Healthcare), or manually by the participant's primary ICU nurse. In both study groups, an alarm was set to trigger when SpO_2 was ≤ 90 %. Nursing staff operating the AIRVO3 device were trained in its use. Participants remained on the study intervention for 24 h, until cessation of oxygen therapy, or until ICU discharge, whichever came first. At study completion, participants were returned to a respiratory support strategy deemed appropriate by the treating clinical team. All other aspects of participant care were provided by designated clinical staff in accordance with Wellington Regional Hospital ICU standard procedures.

2.6. Outcomes

The primary outcome was the proportion of time spent within the SpO_2 target range of 92–96 %, comparing automated to manually adjusted oxygen. Secondary outcomes included the proportion of time above and below the target range, length of ICU stay, and distribution of physiologic and device variables: SpO_2 , FiO_2 , respiratory rate (RR), number of FiO_2 adjustments, and total oxygen volume used; compared between automated and manual oxygen delivery strategies. In addition, the AIRVO3 RR-sensing mechanism was compared to RR measured manually by research staff.

2.7. Statistical analysis

Continuous data were summarised by mean and standard deviation, median and interquartile range (IQR) (25th to 75th percentile), and minimum to maximum. Categorical data were summarised by counts and proportions expressed as percentages.

The analysis for the primary outcome, time in range, used a Mann–Whitney U test with the Hodges–Lehmann estimator for location difference and appropriate confidence intervals (CIs). A sensitivity analysis was performed using a weighted linear model with predictor variables of baseline SpO_2 and treatment and total time measured as the weighting (due to unequal time of measurement between individuals). Given the skewed distribution, the

response variable was transformed to the log of 100 minus the time in range (i.e., the time not in range). Differences in logarithms are interpreted as the ratio of geometric means, and a value of <1 means the time not in range is lower in the first-named treatment. The distributions remained skewed when transformed for time SpO₂ below and above range. As such, these are analysed by a Mann–Whitney U test with the Hodges–Lehmann estimator for location difference and appropriate CIs.

The following variables are analysed by a t-test and by analysis of covariance with adjustment for baseline (where applicable): SpO₂ maximum, SpO₂ mean, SpO₂ minimum, RR maximum, RR mean, and RR minimum. Due to normality assumptions not being well met (checked by residual distributions and plots of residuals versus predicted values), FiO₂ maximum, FiO₂ mean, FiO₂ minimum, number of FiO₂ adjustments, total oxygen volume used, and length of stay are also analysed by a Mann–Whitney U test with the Hodges–Lehmann estimator for location difference and appropriate CIs.

Agreement between research staff and AIRVO3 RR was attained by calculation of the mean difference between the two (bias) and calculation of limits of agreement (plus or minus two paired standard deviations) and Bland–Altman plots. For the density plots, nonparametric kernel density estimates with a standardisation bandwidth of 10 were overlaid on transparent histograms. For the large data sets of one measurement per second per participant for the duration of the study, every fifth measurement was used to manage the algorithm to generate the plots. SAS version 9.4 was used.

3. Results

Key participant baseline characteristics are described in Table 1, with additional characteristics provided in the online supplement (Table S1). Fig. 1 is a Consolidated Standards of Reporting Trials diagram. Median (IQR) cardiopulmonary bypass time was longer in the manual oxygen adjustment group 159 min (122.5–234.5) than that in the automated group 129.5 min (105–190).

The percentage of time per patient spent in the target SpO₂ range was a median of 97.7 % (IQR: 87.9–99.2 %) and 91.3 % (IQR: 77.1–96.1 %) in the automated (n = 28) and manual (n = 28) titration groups, respectively (Table 2). In the automated oxygen-control group, significantly less time was spent below range, but there was no significant difference in time above range, when compared to that in the manually adjusted oxygen group (Table 2). Fig. 2 is a box and whisker plot showing how the proportion of time inside the target range was distributed in participants receiving automated and manual oxygen strategies. Fig. 3 presents individual participant density plots of the proportion of SpO₂ values at discrete levels compared between automated (blue) and manual (red) oxygenation strategies. The proportion of time within the target range analysed using a weighted linear model can be found in the online supplement (Table S2).

Over the course of the study, the mean (\pm standard deviation) FiO₂ used was 26.8 % (6.1) with automated oxygen control and 26.3 % (5.8) with manual oxygen control; the estimated difference (\pm standard deviation; p-value) was 0.07 percentage points (–2.18 to 2.76; p = 0.64). The mean number of FiO₂ adjustments in the automated group was 2.1 (2.5) per participant, compared to 11.8 (11.4) in the manual group; the estimated difference (95 % CI; p-value) was 8 (4–11; p < 0.001), and fewer adjustments were needed in the automated group.

Mean and median lengths of ICU stay were significantly shorter in the automated oxygen-control group than in the manual group (Table 3). The distribution of other physiologic and device-related variables, such as SpO₂, FiO₂, RR, and total oxygen volume used,

were not significantly different between the automated and manual oxygen-control groups.

Mean difference (95 % CI) between simultaneous RR measurements performed by manual count and by the AIRVO3 device were not significantly different: –0.63 (–1.29 to 0.03; p = 0.06) breaths per minute, and the accompanying limits of agreement were –5.08 to 3.82 (See Fig. S1).

Nine participants were withdrawn from the trial prematurely, seven from the manual oxygen group, and two from the automated oxygen group. All primary endpoint data were lost for two participants (both received manual oxygen control), so these participants could not contribute to the analysis. Eight participants meeting exclusion criteria (six with chronic obstructive pulmonary disease and two with obstructive sleep apnoea) were inadvertently enrolled in the study as these diagnoses were not apparent at the time of randomisation: their data were retained in the analysis. There were no device-related adverse events in either group (See Fig. 1).

4. Discussion

Automated HFNOT significantly increased the time spent with SpO₂ inside a prespecified target SpO₂ range compared with standard, manually adjusted oxygen, in extubated ICU patients following elective cardiac surgery. The automated oxygen-control system also significantly reduced the proportion of time spent below the SpO₂ range. These findings suggest that the AIRVO3 device with OptiO₂ improves maintenance of a target SpO₂ range compared to manually adjusted oxygen delivered in a highly monitored and controlled ICU environment. Furthermore, automated oxygen control was associated with fewer FiO₂ setting adjustments and in turn likely to have reduced clinician time spent titrating oxygen.

The efficacy of the automated oxygen-control system used in this study is comparable to other recent trials. To the knowledge of the investigators, only two other randomised controlled trials have assessed automated HFNOT in hospitalised adults, with median proportions of time in range of 96 % in a hospital acute medical ward⁹ and 97 % in an ICU.⁷ The comparator groups in each of these trials received manually adjusted HFNOT with median proportions of time in range of 71 % and 89 %. Compared to the previously conducted ICU-based study that enrolled participants with moderate to severe respiratory failure,⁷ the present study reports distinct findings in participants with a relatively low oxygen requirement (approximate mean FiO₂: 26 %). In the ICU, tighter control of SpO₂ with manually titrated oxygen could reasonably be expected in those with mild respiratory failure, compared to moderate or severe respiratory failure. However, in the present study, similar improvements in adherence to the target SpO₂ range were observed using automated oxygen titration in mild respiratory failure compared to manual oxygen titration, meaning that use of this novel technology in the ICU can now be considered similarly effective across a spectrum of respiratory failure severities.

Similar effects were observed in earlier trials, where automated oxygen-control systems were used with conventional forms of low-to medium-flow oxygen. In a trial conducted outside of the ICU low-medium-flow oxygen used for up to 3 days after abdominal or thoracic surgery resulted in a mean 94 % of time in range in the automated oxygen-control group compared to 62 % in the manual group.¹⁰ During 3 h of oxygen therapy in an emergency department, the mean time spent within range was 81 % for those receiving automated low-flow oxygen and 52 % for manual low-flow oxygen.¹¹

Across these trials, the location of patient care appears to influence the accuracy of manually adjusted oxygen, with

Table 1
Study participant characteristics.

Categorical variables				
	All participants N/56 ^a (%)	Automated N/28 ^a (%)	Manual N/28 ^a (%)	
Sex (Female)	12 (21.4)	4 (14.3)	8 (28.6)	
Ethnicity				
Asian	3 (5.4)	1 (3.6)	2 (7.1)	
European	41 (73.2)	22 (78.6)	19 (67.9)	
Māori	7 (12.5)	2 (7.1)	5 (17.9)	
Pacific	5 (8.9)	3 (10.7)	2 (7.1)	
Smoking status	N = 54	N = 26	N = 28	
Never	27 (50)	12 (46.2)	15 (53.6)	
Current	3 (5.6)	1 (3.8)	2 (7.1)	
Former	24 (44.4)	13 (50)	11 (39.3)	
Obstructive sleep apnoea	6 (10.7)	1 (3.6)	5 (17.9)	
Chronic obstructive pulmonary disease	2 (3.6)	0 (0.0)	2 (7.1)	
Operation details				
Coronary artery bypass graft	35 (62.5)	19 (67.9)	16 (57.1)	
Valve surgery	32 (57.1)	15 (53.6)	17 (60.7)	
Aortic valve surgery	19 (59.4)	9 (60)	10 (58.8)	
Mitral valve surgery	19 (59.4)	10 (66.7)	9 (52.9)	
Tricuspid valve surgery	6 (18.8)	2 (13.3)	4 (23.5)	
Pulmonary valve surgery	0 (0.0)	0 (0.0)	0 (0.0)	
Other surgery	17 (30.4)	10 (35.7)	7 (25)	
Cardiopulmonary bypass used	56 (100)	28 (100)	28 (100)	
Continuous variables				
Automated	N	Mean (\pm SD)	Median (IQR)	Min to Max
Age (yrs)	28	64.7 (10.6)	67.5 (58.4–71.8)	39.5 to 84.9
BMI (kg/m ²)	28	30 (7.4)	28.8 (25.8–31)	20.8 to 51.3
Cardiopulmonary bypass time (mins)	28	159.1 (74.9)	129.5 (105–190)	72 to 372
Respiratory rate (breaths per minute)	28	16.6 (3.7)	17 (14–19)	9 to 25
PEEP (cmH ₂ O)	28	5.4 (1.2)	5 (5–5)	5 to 10
SaO ₂ (%)	28	96.4 (1.8)	96.5 (94.9–97.5)	93.5 to 99.8
SpO ₂ (%)	28	96.4 (1.6)	96 (95–97.5)	93 to 100
FiO ₂	28	0.3 (0.1)	0.3 (0.3–0.3)	0.2 to 1
Manual	N	Mean (\pm SD)	Median (IQR)	Min to Max
Age (yrs)	28	64.1 (11.9)	65.4 (61.2–73.4)	30.9 to 80
BMI (kg/m ²)	28	30.6 (6)	29.8 (26.6–33)	20.6 to 48.3
Cardiopulmonary bypass time (mins)	28	185.7 (84)	159 (122.5–234.5)	54 to 403
Respiratory rate (breaths per minute)	28	17.8 (4.2)	18 (14.5–20.5)	9 to 26
PEEP (cmH ₂ O)	28	5.8 (1.2)	5 (5–6.5)	5 to 8
SaO ₂ (%)	28	95.1 (5.7)	96.1 (95.2–97.1)	67.5 to 99.2
SpO ₂ (%)	28	95.5 (2.4)	95.5 (94–97)	90 to 100
FiO ₂	28	0.3 (0.1)	0.3 (0.2–0.3)	0.2 to 0.4

Abbreviations: BMI = body mass index, PEEP = positive end-expiratory pressure, SaO₂ = arterial oxygen % saturation, SpO₂ = peripheral oxygen % saturation, FiO₂ = fraction of inspired oxygen, SD = standard deviation, IQR = interquartile range, Min = minimum, Max = maximum, cmH₂O = centimetres of water pressure.

^a Unless otherwise specified.

Table 2
Distribution of SpO₂ in relation to SpO₂ target range, compared between automated and manual oxygen control.

Distribution		Comparison: Automated minus manual				
Time SpO ₂ in range (%)						
	N	Mean (\pm SD)	Median (IQR)	Min to Max	Rank-based difference (95 % CI)	P
Automated	28	94 (7.5)	97.7 (87.9–99.2)	74 to 100	4.79 (1.55–10.33)	0.01
Manual	26	84 (18.9)	91.3 (77.1–96.1)	15.9 to 100		
Time SpO ₂ below range (%)						
	N	Mean (\pm SD)	Median (IQR)	Min to Max	Rank-based difference (95 % CI)	P
Automated	28	3.9 (6.7)	0.9 (0.2–3.9)	0 to 25.9	–2.40 (–4.97 to –0.24)	0.03
Manual	26	9.6 (16.9)	3.5 (2.2–9.7)	0 to 84.1		
Time SpO ₂ above range (%)						
	N	Mean (\pm SD)	Median (IQR)	Min to Max	Rank-based difference (95 % CI)	P
Automated	28	2.2 (3.7)	0.3 (0.1–2.2)	0 to 13.7	–0.38 (–1.96 to 0.16)	0.31
Manual	26	6.4 (10.8)	1.4 (0–7.9)	0 to 36.3		

Abbreviations: SpO₂ = peripheral oxygen % saturation, SD = standard deviation, IQR = interquartile range, Min = minimum, Max = maximum.

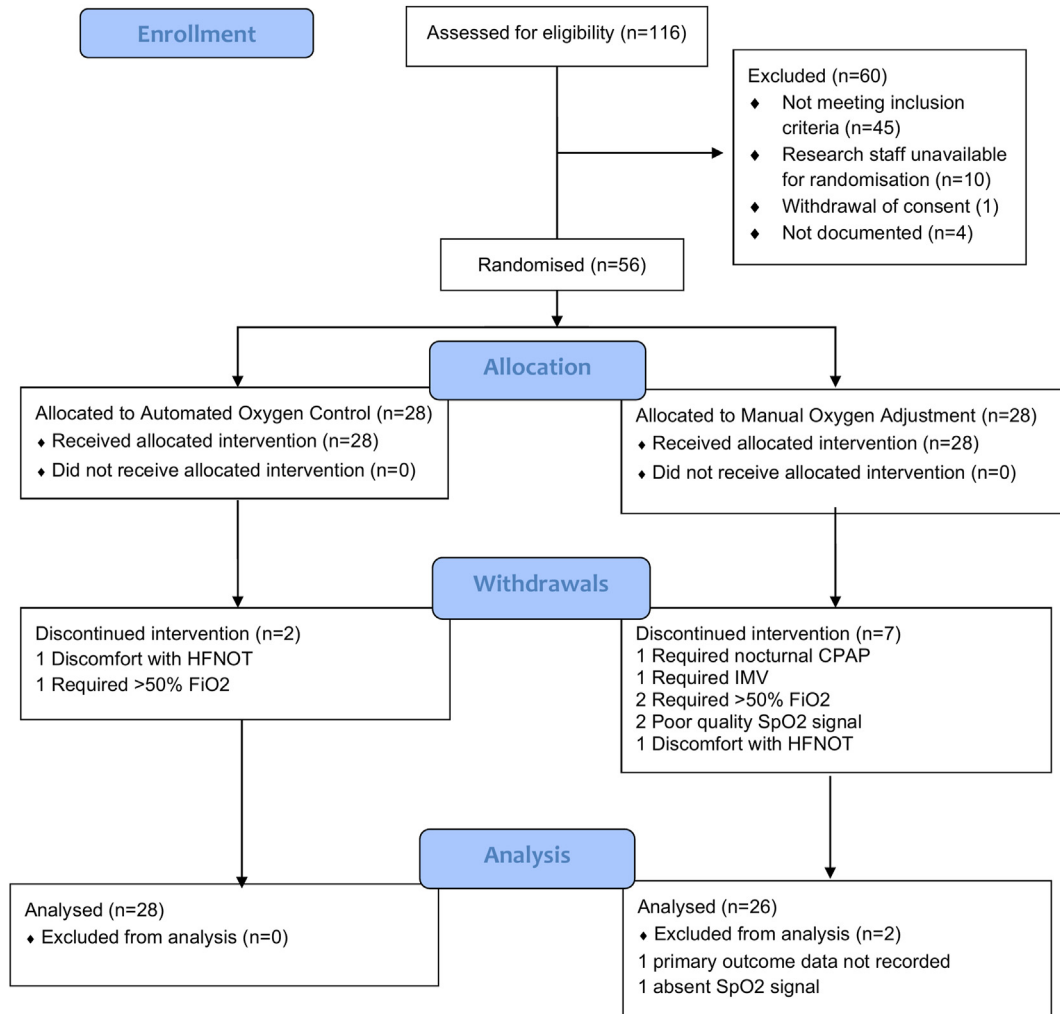


Fig. 1. CONSORT diagram. Abbreviations: CONSORT = Consolidated Standards of Reporting Trials, CPAP = continuous positive airway pressure, IMV = invasive mechanical ventilation, FiO₂ = fraction of inspired oxygen, SpO₂ = peripheral oxygen % saturation, NHF = nasal high flow.

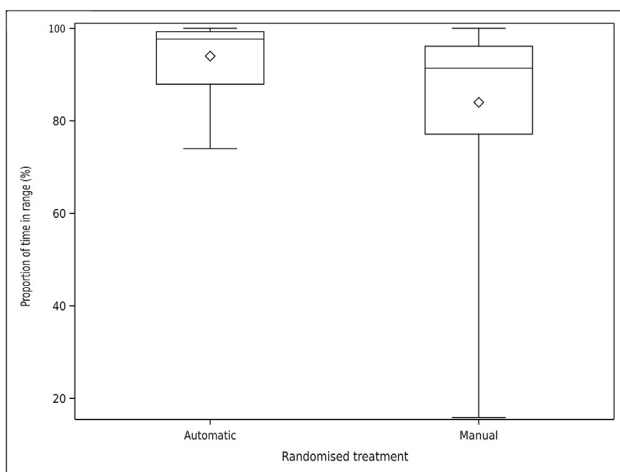


Fig. 2. Boxplot distribution of proportion of time spent within SpO₂ target range comparing automated to manual oxygen control. The horizontal lines are the 25th, 50th (median), and 75th percentiles, the \diamond symbol is the mean, and the whiskers extend from the minimum to maximum values. Abbreviations: SpO₂ = peripheral oxygen % saturation.

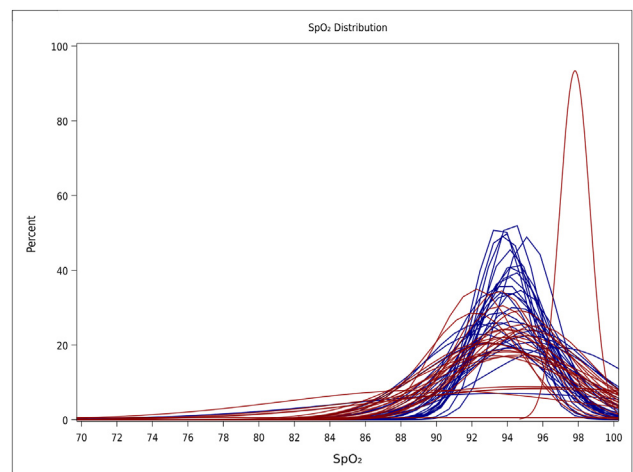


Fig. 3. SpO₂ density plot by participant. Blue plots = automated oxygen. Red plots = manual oxygen. Abbreviations: SpO₂ = peripheral oxygen % saturation.

Table 3
Distribution of ICU length of stay compared between automated and manual oxygen-control groups.

Length of stay in the ICU (hrs)	Distribution				Comparison: Automated minus manual	
	N	Mean (\pm SD)	Median (IQR)	Min to Max	Rank based difference (95 % CI)	P
Automated	28	38.8 (19.9)	35.8 (23.8–48.3)	18 to 101.7	–21.83 (–29.83 to –7.10)	0.001
Manual	28	70.7 (47.1)	51.8 (44.4–70)	21.6 to 213.3		

Abbreviations: ICU = Intensive Care Unit, SD = Standard Deviation, IQR = Inter-quartile Range, Min = Minimum, Max = Maximum.

progressively better performance from the ED, to postsurgical, to medical inpatient, to ICU care, presumably relating to closer nursing monitoring of vital signs. This observation suggests that the magnitude of the increase in the time spent in range achieved with an automated oxygen-control system is greater in non-ICU settings. Even so, any reduction in exposure to hypoxaemia is potentially desirable, and it is noteworthy that in this study, automated oxygen control reduced time below the target SpO₂ range compared to oxygen adjusted manually by highly skilled ICU nurses, providing one-to-one care, using continuous oximetry, in a clinical setting where risks of postoperative pulmonary complications and mortality are particularly high.^{12,13} Hypoxaemia has been associated with increased risk of adverse postoperative outcomes including silent myocardial ischaemia¹⁴ and cardiorespiratory arrest.¹⁵ Additionally, perioperative tissue hypoxia has been associated with increased risk of surgical site infection¹⁶ and other major postoperative complications.¹⁷ While differences in these clinically important outcomes were not assessed, the study findings reinforce that automated oxygen control represents the optimal oxygen delivery strategy for minimising the time exposed to hypoxaemia.

Median proportion of time exposed to relative hyperoxaemia (SpO₂ > 96 %, with FiO₂ \geq 21.5) was less than 1.5 % in both randomised study arms. Other trials of automated HFNOT have reported that compared to manually adjusted oxygen, the time spent exposed to SpO₂ levels that are above the target range can be significantly reduced.^{7,11,18} Albeit with a heterogenous effect depending on the underlying disease, exposure to hyperoxaemia has been associated with increased morbidity and mortality,^{5,19,20} a risk that, in this ICU-based study, appeared to be similarly mitigated when oxygen was adjusted automatically or manually.

We acknowledge several limitations. Baseline characteristics were not well balanced between the randomised groups; in particular, the cardiopulmonary bypass time was longer in the manual oxygen-control group. This likely contributed to the observed longer duration of ICU stay in the manual oxygen group; a finding that the investigators could not plausibly attribute to the use of automated oxygen control. Potential bias may have occurred due to the inability to blind investigators and patients to randomised interventions. Furthermore, six of the first 10 participants required little or no oxygen, resulting in a protocol amendment to enrich the study population with more severely hypoxaemic participants. Loss of pulse oximetry signal occurred in approximately 1 % of all SpO₂ recordings made during the study. A reliable SpO₂ signal is integral to the function of the OptiO₂ automated oxygen-control mechanism, and when the signal is lost, inaccuracies in oxygen titration may expose patients to potential risk. Device alarms warned study investigators of this problem, but alarming repetitively can become counterproductive,²¹ as was observed in two participants who were withdrawn due to clinical concern about oximetry signal interruptions.

In conclusion, the automated closed-loop oxygen control with HFNOT following extubation after major elective cardiac surgery increased time spent within a target SpO₂ range when compared to that spent with manually adjusted oxygen.

Guarantor statement

LWK takes responsibility for the content of the manuscript.

CRediT authorship contribution statement

LWK had full access to all the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis including and especially any adverse effects. RSC, LN, AE, JC, RB, and PJY contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript.

Role of the sponsor

Fisher and Paykel Healthcare awarded a research grant to fund this study, were involved in the study design, but were not involved in data collection, data analysis, data interpretation, manuscript preparation, or the decision to submit for publication.

Publications/presentations

This abstract and manuscript have not been published or presented elsewhere.

Data availability statement

Data are available on reasonable request. Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures and appendices) will be available until a minimum of 10 years after publication to researchers who provide a methodologically sound proposal that has been approved by the study steering committee and sponsor to achieve the aims outlined in the approved proposal. This is possible through a signed data access agreement and subject to approval by the principal investigator (louis.kirton@mrinz.ac.nz) and the study sponsor (james.revie@fphcare.co.nz). No other documents will be available.

Conflict of interest

PY declares that he is an Associate Editor for Critical Care and Resuscitation. PY declares that Fisher and Paykel Healthcare paid his institution for costs associated with the conduct of this research. This research was conducted during the tenure of a Clinical Practitioner Research Fellowship from the Health Research Council of New Zealand held by PY. LK declares that Fisher and Paykel Healthcare paid for travel costs to present at a national conference.

Funding

The MRINZ is supported by Independent Research Organisation funding from the Health Research Council of New Zealand.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ccrj.2024.01.001>.

References

- [1] O'Driscoll BR, Howard LS, Earis J, Mak V. BTS guideline for oxygen use in adults in healthcare and emergency settings. *Thorax* 2017 Jun;72(Suppl 1): ii1–90.
- [2] Beasley R, Chien J, Douglas J, Eastlake L, Farah C, King G, et al. Thoracic Society of Australia and New Zealand oxygen guidelines for acute oxygen use in adults: swimming between the flags. *Respirology* 2015 Nov;20(8):1182–91.
- [3] Piraino T, Madden M, Roberts KJ, Lamberti J, Ginier E, Strickland SL. AARC clinical practice guideline: management of adult patients with oxygen in the acute care setting. *Respir Care* 2022 Jan;67(1):115–28.
- [4] Beasley R, Mackle D, Young P. Oxygen: a new look at an old therapy. *J Roy Soc N Z* 2019 Apr 3;49(2):126–42.
- [5] Chu DK, Kim LHY, Young PJ, Zamiri N, Almenawer SA, Jaeschke R, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. *Lancet* 2018;391(10131): 1693–705. [https://doi.org/10.1016/S0140-6736\(18\)30479-3](https://doi.org/10.1016/S0140-6736(18)30479-3).
- [6] Siemieniuk RAC, Chu DK, Kim LHY, Güell-Rous MR, Alhazzani W, Soccal PM, et al. Oxygen therapy for acutely ill medical patients: a clinical practice guideline. *BMJ* 2018 Oct 24;k4169.
- [7] Roca O, Caritg O, Santafé M, Ramos FJ, Pacheco A, García-de-Acilu M, et al. Closed-loop oxygen control improves oxygen therapy in acute hypoxemic respiratory failure patients under high flow nasal oxygen: a randomized cross-over study (the HILOOP study). *Crit Care* 2022 Dec;26(1):108.
- [8] Harper JCP, Semprini R, Kearns NA, Hatter L, Bird GE, Braithwaite I, et al. Determination of oxygen saturation compared to a prescribed target range using continuous pulse oximetry in acutely unwell medical patients. *BMC Pulm Med* 2021 Dec;21(1):332.
- [9] Harper J, Kearns N, Bird G, Braithwaite I, Eathorne A, Shortt N, et al. Automatic versus manual oxygen titration using a novel nasal high-flow device in medical inpatients with an acute illness: a randomised controlled trial. *BMJ Open Respir Res* 2021 Aug;8(1):e000843.
- [10] L'Her E, Jaber S, Verzilli D, Jacob C, Huiban B, Futier E, et al. Automated closed-loop versus standard manual oxygen administration after major abdominal or thoracic surgery: an international multicentre randomised controlled study. *Eur Respir J* 2021 Jan;57(1):2000182.
- [11] L'Her E, Dias P, Gouillou M, Riou A, Souquiere L, Paleiron N, et al. Automatic versus manual oxygen administration in the emergency department. *Eur Respir J* 2017;50(1).
- [12] Roques F, Nashef SAM, Michel P, Gauducheau E, de Vincentiis C, Baudet E, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. *Eur J Cardio Thorac Surg* 1999;15(6):816–23.
- [13] Mazo V, Sabaté S, Canet J, Gallart L, Abreu M, Belda J, et al. Prospective external validation of a predictive score for postoperative pulmonary complications. *Anesthesiology* 2014;121(2):219–31.
- [14] Gill NP, Wright B, Reilly CS. Relationship between hypoxaemic and cardiac ischaemic events in the perioperative period. *Br J Anaesth* 1992 May;68(5): 471–3.
- [15] Truhlar A, Deakin CD, Soar J, Khalifa GEA, Alfonso A, Bierens JJLM, et al. European resuscitation Council guidelines for resuscitation 2015. *Resuscitation* 2015 Oct;95:148–201.
- [16] Govinda R, Kasuya Y, Bala E, Mahboobi R, Devarajan J, Sessler DI, et al. Early postoperative subcutaneous tissue oxygen predicts surgical site infection. *Anesth Analg* 2010 Oct;111(4):946–52.
- [17] Abdelmalak BB, Cata JP, Bonilla A, You J, Kopyeva T, Vogel JD, et al. Intraoperative tissue oxygenation and postoperative outcomes after major non-cardiac surgery: an observational study. *Br J Anaesth* 2013 Feb;110(2):241–9.
- [18] Lellouche F, Bouchard PA, Roberge M, Simard S, L'Her E, Maltais F, et al. Automated oxygen titration and weaning with FreeO2 in patients with acute exacerbation of COPD: a pilot randomized trial. *Int J COPD* 2016;11(1):1983–90.
- [19] Hafner S, Beloncle F, Koch A, Radermacher P, Asfar P. Hyperoxia in intensive care, emergency, and peri-operative medicine: dr. Jekyll or Mr. Hyde? A 2015 update. *Ann Intensive Care* 2015 Dec;5(1):42.
- [20] Robinson TD, Freiberg DB, Regnis JA, Young IH. The role of hypoventilation and ventilation-perfusion redistribution in oxygen-induced hypercapnia during acute exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161(5):1524–9.
- [21] Lewandowska K, Weisbrot M, Cieloszyk A, Mędrzycka-Dąbrowska W, Krupa S, Ozga D. Impact of alarm fatigue on the work of nurses in an intensive care environment—a systematic review. *Int J Environ Res Publ Health* 2020 Nov 13;17(22):8409.