Original Article

The respiratory and hemodynamic effects of alveolar recruitment in cirrhotic patients undergoing liver resection surgery: A randomized controlled trial

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Abstract

Background and Aims: Extensive surgical retraction combined with general anesthesia increase alveolar collapse. The primary aim of our study was to investigate the effect of alveolar recruitment maneuver (ARM) on arterial oxygenation tension (PaO_2). The secondary aim was to observe its effect on hemodynamics parameters in hepatic patients during liver resection, to investigate its impact on blood loss, postoperative pulmonary complications (PPC), remnant liver function tests, and on the outcome.
Material and Methods: Adult patients scheduled for liver resection were randomized into two groups: ARM ($n = 21$) and control (C) ($n = 21$). Stepwise ARM was initiated after intubation and was repeated post-retraction. Pressure-control ventilation mode was adjusted to deliver a tidal volume (V_t) of 6 mL/kg and an inspiratory-to-expiratory time (*I:E*) ratio of 1:2 with an optimal positive end-expiratory pressure (PEEP) for the ARM group. In the C group, a fixed PEEP (5 cmH_2O) was applied. Invasive intra-arterial blood pressure (IBP), central venous pressure (CVP), electrical cardiometry (EC), alanine transaminase (ALT, U/L), and aspartate aminotransferase (AST, U/L) blood levels were monitored.
Results: ARM increased PEEP, dynamic compliances, and arterial oxygenation, but reduced ventilator driving pressure compared to group C ($P < 0.01$). IBP, cardiac output (CO), and stroke volume variation were not affected by the higher PEEP in the ARM group ($P > 0.05$) but the CVP increased significantly ($P = 0.001$). Blood loss was not different between the ARM and C groups (1700 (1150–2000) mL vs 1110 (900–2400) mL, respectively and $P = 0.57$). ARM reduced postoperative oxygen desaturation; however, it did not affect the increase in remnant liver enzymes and was comparable to group C (ALT, $P = 0.54$, AST, $P = 0.41$).
Conclusions: ARM improved intraoperative lung mechanics and reduced oxygen desaturation episodes in recovery, but not PPC or ICU stay. ARM was tolerated with minimal cardiac and systemic hemodynamic effects.

Keywords: Blood loss, cardiac, cirrhosis, hepatectomy, liver, lung, recruitment

Introduction

Hepatic resection for malignant foci is increasingly performed in Egypt due to hepatitis C (genotype 4).[1] Anesthesia and surgical challenges increase among cirrhotic liver tissues.[2,3] General anesthesia (GA) reduces the lung functional residual capacity and induces peripheral atelectasis. This is magnified by the extensive abdominal surgical retractors required

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to expose liver segments.[4,5] The alveolar recruitment maneuver (ARM) helps to re-expand these peripherally collapsed alveoli and maintain their re-expansion with optimal positive end-expiratory pressure (PEEP).[6] Most of the available research data in this field are for patients with healthy livers, but only a few have investigated the perioperative respiratory and hemodynamic effects in hepatic patients.[7]

The primary aim of this trial was to investigate the effect of ARM on arterial oxygenation tension (PaO_2), and the secondary aim was to investigate the effects of ARM on both systemic hemodynamics and electrical cardiometry (EC) parameters, blood loss, postoperative pulmonary complications (PPC), remnant liver functions, and on the outcome.

Material and Methods

A randomized controlled trial was approved by the local research and ethics committee of the Anesthesia Department at the Faculty of Medicine, Menoufia University, Egypt (IRB, 04-2017). The trial was registered at the Pan African Clinical Trial registry (PACTR201708002139426) (www.pactr.org). Adult hepatitis C patients (Child classification A) with cirrhosis scheduled for elective liver resection were included. Exclusion criteria included patients with pulmonary disease, rupture hepatocellular carcinoma or inoperable tumors, BMI >40 kg/m^2, laparoscopic hepatic resection, and refusal to participate. Patients were randomized into two groups. In the control group (C) (n = 21), mechanical ventilation was initiated using the pressure control ventilation (PCV) mode. Ventilators were adjusted to deliver a V_t of 6 mL/kg with an *I:E* ratio of 1:2 and PEEP of 5 cmH_2O. In the ARM group (n = 21), following recruitment, each individual optimal PEEP was detected and the V_t adjusted to 6 mL/kg (PCV) with an *I:E* ratio of 1:2 and an end-tidal CO_2 of 35–45 mmHg.

Recruitment was performed directly after intubation (first recruitment). It was repeated after the application of surgical retractors (second recruitment). ARM was initiated with PCV with a maximum 15 cmH_2O driving pressure and a step-by-step PEEP increase of 5 cmH_2O every 3–4 respiratory cycles. The dynamic compliance (C_{dyn}) was measured until the best compliance. This was followed by a progressive reduction of PEEP, again step by step, with decrement of 5 cmH_2O until 15 cmH_2O PEEP. Decremental reduction of 2 cmH_2O followed this until reaching the PEEP level at which the C_{dyn} decreased abruptly. Adding 2 cmH_2O above this PEEP, it became the optimal PEEP defined by the authors. Optimal PEEP is the individual level of PEEP that correlates with the point at which alveolar de-recruitment does not occur. The recruitment cycle was repeated with the detected optimal PEEP and a driving pressure to achieve a tidal volume of 6 mL/kg.[8,9] The software program used was Cycling Procedure from General Electric (AVANCE CS, Madison, USA). If the driving pressure obtained did not result in a minimum V_t of 6 mL/kg at any time, the ARM needed repetition, and the driving pressure needed elevation to achieve the required V_t. Hypotension (invasive arterial [IBP] <60 mm Hg) during recruitment was treated initially with fluids if hypovolemic, as indicated by CVP, or otherwise by ephedrine boluses (5 mg). Recruitment was aborted any time if hemodynamic instability persisted despite the above measures.

Every patient was preoxygenated for 3–5 min with O_2/air mixture (FiO_2 0.8). GA was induced intravenously with fentanyl (1–2 µg/kg), propofol (1.5–2.5 mg/kg), and rocuronium (0.6–0.9 mg/kg) followed by endotracheal intubation. Maintenance was done with sevoflurane in 40% oxygen and air with intravenous fentanyl (1 µg/kg/h). Anesthesia depth was monitored for each patient during surgery. Rocuronium boluses (0.1–0.2 mg/kg) were administered using train of four (TOF) monitoring.

In both the groups, Ringer's acetate was infused at 10 mL/kg/h during surgery to cover basal fluid requirements and maintain CVP within normal ranges (excluding resection phase). Fluid restriction was practiced during resection to lower the (Keeping CVP <5 cmH_2O) without drug interference. Hemoglobin level >10 g/dL was maintained with packed red blood cells. Following resection, additional boluses of 3 mL/kg hydroxy-ethyl-starch 130/0.4 were infused if CVP was <5 cmH_2O.

The patients were **e**xtubated following the reversal of muscle relaxants with sugammadex (at TOF ratio 0.9–1) and transferred to the ICU Ventilation support was provided only if required; otherwise, oxygen was supplemented by mask if oxygen saturation was <94% postoperatively.[10] Combined transversus abdominus and rectus sheath regional blocks (0.25% bupivacaine, max 1 mg/kg) was performed for each patient following surgery. Intravenous fentanyl patient-controlled analgesia was also made available for every patient during the postoperative period.[11]

For electrical cardiometry (EC), four electrodes (ICON monitor; Osypka, La Jolla, CA, USA) were applied following skin sterilization with an alcohol swab. The first electrode was applied 5 cm above the left base of the neck; the second on the left base of the neck; the third on the lower left thorax at the level of xiphoid; and the fourth on the lower left thorax. Patient data was provided and the correct signal quality was verified by the ECG impedance waveform. EC data included SVV, SVR, and CO.[12]

SVV was used in this trial to monitor patients' response to fluid infused, but not to guide fluid intake; for which CVP was used. The interrelationship between SVV and CVP readings was investigated and the effect of high recruitment PEEP on both was studied.

Type of liver resection, catecholamine support, operative time (h) intraoperative fluid volume (mL) and blood transfusion (U) were recorded. Blood loss was calculated (ml) by weighing the surgical gauze and adding the blood volume in the suction device after subtracting the saline used for washing.

Postoperative complications including oxygen desaturation (<94%), chest infection, wound infection, and liver dysfunction were noted. Remnant liver function was measured by peak postoperative alanine transaminase (ALT) and aspartate aminotransferase (AST, U/L) blood levels. ICU stay and the 3-month mortality were also noted.

Statistics: A sample size of 21 patients per group was required to detect a standardized effect size of 0.80 (minimum difference in mean PaO_2 divided by pooled variance) in the primary outcome as statistically significant with 80% power and at a significance level of 95% (alpha error probability = 0.05). Sample size per group does not need to be increased to control attrition bias. The sample size was calculated using G-Power version 3.1.9.2.[13,14] Allocation sequence was generated using sealed opaque envelopes. Masking/blinding was employed for the participants. Outcome assessors were blinded to the group allocation. Kolmogorov–Smirnov test of normality revealed significance in the distribution of most of the variables, so nonparametric statistics were adopted. Data were described as the median and interquartile range (IQ). Comparisons were carried out between the two studied, independent, not-normally distributed subgroups using the Mann–Whitney *U* test. Comparisons were carried out among related samples using Friedman test. Pairwise comparison when Friedman test was significant was carried out using Dunn–Šidák method. An alpha level was set to 5% with a significance level of 95%, and a beta error accepted up to 20% with a power of study of 80% when calculating the sample size.

Results

46 patients were enrolled in the trial; only 42 were randomized into two groups, as presented in the CONSORT flow chart [Figure 1]. Data was presented as median (IQ). Table 1 demonstrates the demographics for Group ARM vs C group. Demographics were comparable for age, sex and weight. BMI for ARM group was 25.95 (24.22–27.68) vs. in C group 26.12 (24.24–27.78) kg/m^2, $P = 0.67$. Table 1 also presents the preoperative MELD score and operative time for both groups.

The types of hepatic resection are presented are in Table 2. More crystalloids were infused in the ARM group (3500 (3000–3880) vs 3000 (2580–3100) in C, $P = 0.002$) which may be due to the longer surgery time in the ARM group. However, the total urine output was not different ($P = 0.53$). Hydroxyethyl starch (500 mL) was infused to 13 out of 21 patients in the ARM group vs 10 out of 21 in the control group ($P = 0.94$). The surgical blood loss in the ARM group was higher than that in C group, but failed to reach significance (1700 (1150–2000) vs 1110 (900–2400) mL, $P = 0.57$). The percentage of patients needing blood transfusion was 23.81% with ARM vs 14.29% for C groups ($P = 0.694$).

PEEP increased significantly with the recruitment maneuver, and the ventilator driving pressures were reduced when more of the collapsed alveoli were recruited. Higher tidal volumes were delivered to the ARM group at the same comparable peak airway pressures compared to controls [Table 3]. Alveolar recruitment improved lung compliance at all phases compared to controls [Figure 2], and increased PaO_2 and *P*/*F* ratio [Figures 3 and 4]. This increase in PaO_2 continued until the end of surgery.

Heart rate and invasive blood pressure (IBP) were stable in both groups and comparable ($P > 0.05$) with and without recruitment. Catecholamine support was not required at any stage. Most of the surgeries were done on the left lobe or to non-anatomical segments [Table 1]. CO and SVR were not affected by ARM [Table 4]. CVP readings were affected by the high PEEP of recruitment, but the SVV was not [Table 4]. CVP and SVV changes with time are presented in Table 4. No significant correlation existed between CVP and SVV ($n = 254$, Kendall's tau $t = 0.001$, $P = 0.981$)

Arterial oxygenation and *P*/*F* ratio three hours following PACU discharge were higher in the recruited patients. ($P = 0.000$) [Figures 2 and 3]. In ARM group, 4.7% vs 38.1% in the group C ($P = 0.02$) patients had desaturation (SaO_2 <94%) in the postoperative period and required supportive oxygen (FiO_2 0.35). In total, 4.7% of the patients ($n = 1$) in the ARM group developed clinical symptoms of chest infection compared to 19.05% in the group C ($n = 4$). No patient suffered from wound infection in the ARM group versus two in the group C ($P > 0.05$).

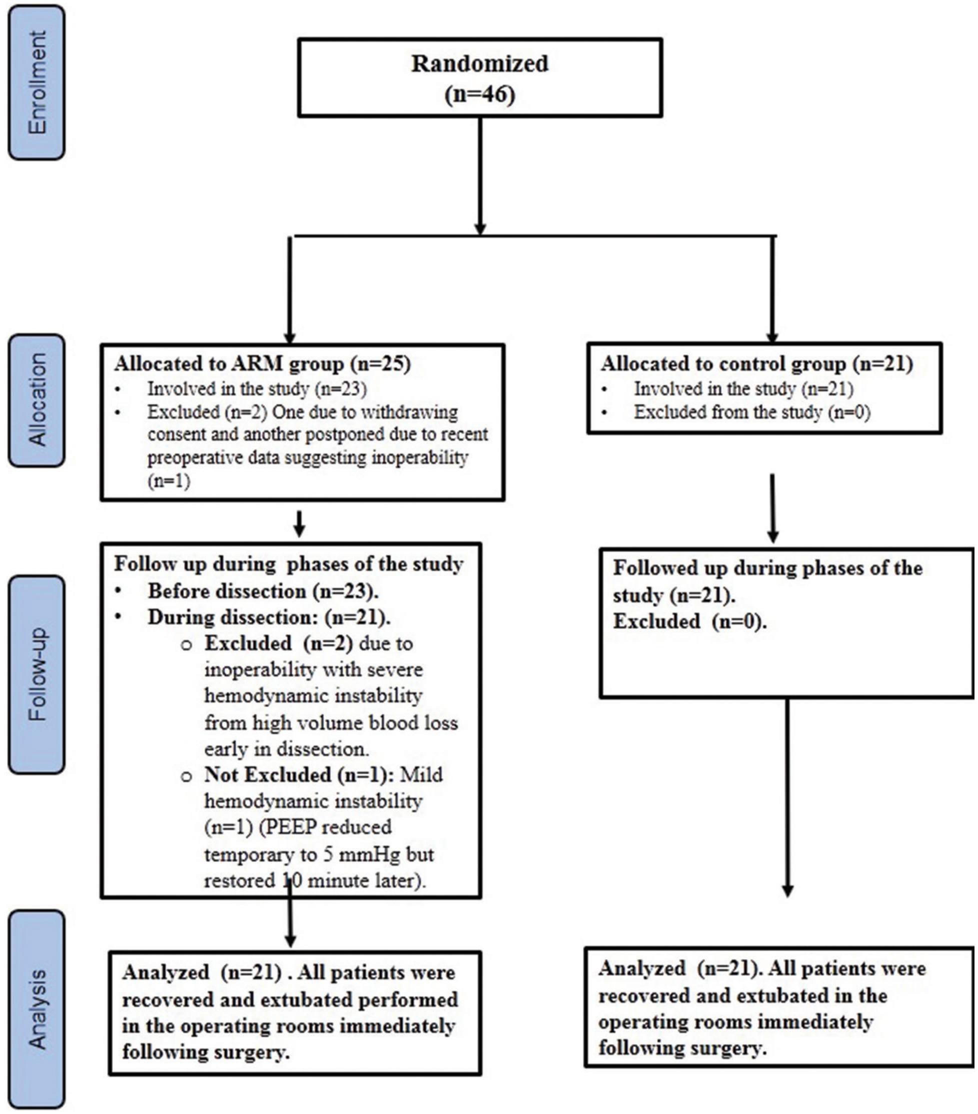

Figure 1: CONSORT flow chart showing patients' allocation at different stages of the study

The 3-month mortality was comparable (two in ARM vs one in C). The postoperative liver function enzymes (AST/ALT) were not different but increased in both groups due to liver resection and the induced injury to remnant cirrhotic liver tissues. Postoperative ALT was 129.50 (89.50–175.0) U/L in ARM group versus 169.00 (97.00–218.00) U/L in C group (P = 0.54). AST was 225.00) 105.00–365.00) U/L in ARM group versus 139.00) 105.00–251.00) U/L in C group (P = 0.419). No significant difference was noted in ICU or hospital stay with ARM group compared to C group (1.00 (1.00–2.00) vs 1.00 (1.00–2.00) day, P = 0.68; and 4.00 (3.00–5.00) vs 5.00 (4.00–8.00) day, P = 0.07, respectively).

Discussion

This trial demonstrated the beneficial role of lung recruitment in improving the lungs' dynamic compliance and the arterial oxygen tension during liver surgery. This was reflected in the reduced episodes of postoperative oxygen desaturation due to recruiting a significant portion of peripherally collapsed alveoli. Another finding was that the stepwise approach during the recruitment maneuver identified optimal PEEP for each individual, which contributed to stabilizing the systemic hemodynamics throughout the surgery. In a trial by Hemmes *et al.*,[15] the blind application of a high and fixed level of PEEP during abdominal surgery to every patient without considering the individual variations led to intraoperative hypotension and increased consumption of vasoactive drugs. Ferrando *et al.*,[16] in 2017, noted that the hemodynamic stability during recruitment requires respect to the individual variations in PEEP requirements. They also noted a reduced required ventilator driving pressure with lung compliance improvements. This was similar to the current trial findings. Several researchers, such as Severgnini

Table 1: Demographic data [age, sex and weight], Model of End stage disease score (MELD) and operation duration for alveloar recruitment maneuver (ARM) and control (C) groups

	ARM (n=21)	C (n=21)	P
Age [year]			
n	21	21	Z[MW]=1.829
Median [IQR]	55.00 [47.00-60.00]	58.00 [55.00-63.00]	P=0.067 NS
KS test of normality	D=0.127, P=0.200 NS	D=0.145, P=0.200 NS	
Sex			
Male [n=32] [76.19%]			
n	17	15	X^2[df=1]=0.525
Female [n=10] [23.81%]			P=0.469 NS
n	4	6	
Weight [Kg]			
n	21	21	$Z_{[MW]}$=0.733
Median [IQR]	78.00 [70.00-80.00]	78.00 [73.00-85.00]	P=0.463 NS
KS test of normality	D=0.154, P=0.200 NS	D=0.176, P=0.087 NS	
MELD			
n	21	21	$Z_{[MW]}$=1.572
Median [IQR]	9.00 [6.00-10.00]	9.00 [9.00-11.00]	P=0.116 NS
KS test of normality	D=0.183, P=0.064 NS	D=0.150, P=0.200 NS	
Operative Time [hour]			
n	21	21	$Z_{[MW]}$=3.572
Median [IQR]	4.00 [4.00-5.00]	3.50 [3.50-4.00]	P=0.000
KS test of normality	D=0.299, P=0.000*	D=0.237, P=0.003*	

The values are expressed as median [Interquartile range]. n: Number of patients, ARM: alveolar recruitment manoeuvre, and C: control group. n : Number of patients, KS: Kolmogorov-Smirnov. χ^2: Chi-squared of Friedman test; df: degree of freedom; P<0.05 indicates significance; NS: non-significant. MW: Mann–Whitney U test for comparison at each time measurement

Table 2: Type of liver resection for alveolar recruitment maneuver (ARM) and control (C) groups

Type of resection	ARM (n=21)	C (n=21)	P
Right formal	4 (19.05%)	1 (4.76%)	0.1528
Left formal	2 (9.52%)	1 (4.76%)	0.5492
Non-anatomical (>3 segments)	9 (42.85%)	14 (66.67%)	0.1211
Left lateral (<3 segments)	5 (23.81%)	5 (23.81%)	NA
Caudate lobe resection	1 (4.76%)	0 (0.00%)	0.3114

P-value of Z test for comparison of two proportions. NA: Non-applicable statistics (due to exact match). Values are expressed as numbers (percentage). ARM: Alveolar recruitment maneuver; C: control group

et al.[17] and Whalen *et al.*,[18] reported their experience with lung recruitment during open and laparoscopic surgeries with the least hemodynamic effects.

One of the observations in the current trial was the effect of high PEEP values on CVP readings, in contrast to SVV, which was not affected. This could question the CVP efficiency as a reference for volume monitoring when recruitment is applied. A negligible correlation existed between SVV and CVP in the current trial, similar to that reported by Lee *et al.*[19] in 2017 during live liver donor resection. Studies among larger hepatic populations still needed to validate SVV as a sole monitor.

Recruitment led to an increase in blood oxygen tension, as expected and reported by Whalen *et al.*,[18] but it was noticed that the PaO_2 increase could exceed 150 mmHg and occasionally 200 mmHg despite fixing FiO_2 to 0.4. Few data are available to our knowledge about the effect of high blood oxygen tension on remnant liver tissues, and whether it is of benefit or not. Watson *et al.*,[20] in 2017, discovered that avoiding hyperoxia during transplantation may prevent postreperfusion syndrome and vasoplegia. However, Corradini *et al.*[21] noticed that the donor hyperoxia of 152 (136–168) prior to liver harvesting could improve graft function and survival.

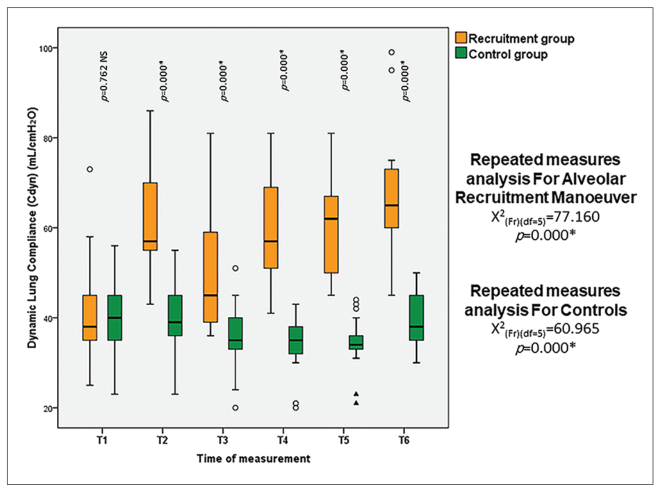

Figure 2: The box and whisker graph of dynamic lung compliance (C_{dyn}) (ml/cmH_2O). The thick line in the middle of the box represents the median, the box represents interquartile range (25th–75th percentiles), and whiskers represent minimum and maximum after excluding outliers (black-filled circles) and extremes (black triangle). Post-anesthesia induction (T1)–Post first recruitment (20 min after, T2)–postsurgical retraction (T3)–second recruitment (20 min after, (T4)–during dissection (T5), and end of surgery before muscle relaxant reversal (T6)

Table 3: Positive end-expiratory pressure (PEEP), ventilator driving pressure (cmH_2O), tidal volume (mL), and peak airway pressure (cmH_2O) for alveolar recruitment maneuver (ARM) and control (C) groups

	Post first recruitment T2	Post-retractor T3	Post second recruitment T4	During dissection T5	End of surgery T6	Friedman test Chi-square *P*
PEEP (cmH_2O)						
ARM (n=21)	9 [7-9.]	9 [7-9]	9 [7-9]	9 [7-9]	9 [7-9]	$\chi^2_{[df=5]}$=100.455 P<0.001*
C (n=21)	All reading=5	All reading=5	All reading=5	All reading=5	All reading=5	NA
P	P<0.001*	P<0.001*	P<0.001*	P<0.001*	P<0.001*	
Driving pressure (cmH_2O)						
ARM (n=21)	8.00 [8.00-9.00]	8.00 [8.00-9.00]	8.00 [8.00-8.00]	9.00 [8.00-10.00]	8.00 [8.00-8.00]	$\chi^2_{(df=4)}$=39.135 P=0.000*
C (n=21)	10.00 [9.0-10.00]	10.00 [9.00-10.00]	10.00 [9.00-10.00]	12.00 [9.00-13.00]	10.00 [9.00-10.00]	$\chi^2_{(df=4)}$=26.154 P=0.000*
P	P<0.001*	P<0.001*	P<0.001*	P=0.010*	P<0.001*	
Tidal Volume (ml/kg)						
ARM (n=21)	460.00 [430.00-497.00]	460.00 [446.00-480.00]	468.00 [449.00-480.00]	456.00 [445.00-518.00]	469.00 [449.00-495.00]	$\chi^2_{(df=4)}$=4.875 P=0.431 NS
C (n=21)	430.00 [423.00-450.00]	436.00 [412.00-456.00]	430.00 [421.00-452.00]	430.00 [422.00-455.00	431.00 [415.00-460.00]	$\chi^2_{(df=4)}$=1.884 P=0.865 NS
P	P=0.008*	P=0.033*	P=0.001*	P=0.009*	P=0.003*	
Peak airway pressure (cmH_2O)						
ARM (n=21)	18.00 [15.00-20.00]	18.00 [16.00-19.00]	18.00 [15.00-20.00]	18.00 [11.00-20.00]	18.00 [15.00-20.00]	$\chi^2_{(df=4)}$=2.337 P=0.6 NS
C (n=21)	18.00 [16.00-20.00]	17.00 [16.00-19.00]	17.00 [14.00-19.00]	17.00 [15.00-19.00]	17.00 [15.00-19.00]	$\chi^2_{(df=4)}$=6.048 P=0.1 NS
P	P=0.742 NS	P=0.601 NS	P=0.282 NS	P=0.771 NS	P=0.909 NS	

Measurement during pressure control ventilation post first recruitment. The values are expressed as median [Interquartile range]. n: Number of patients, ARM: alveolar recruitment manoeuvre, and C: control group. χ^2: Chi-squared of Friedman test; df: degree of freedom; P<0.05 indicates significance; NS: nonsignificant; and NA: nonapplicable statistics. MW: Mann–Whitney U test for comparison at each time measurement

Table 4: Mean invasive blood pressure (IBP), cardiac output (CO), central venous pressure (CVP), and stroke volume variation for alveolar recruitment maneuver (ARM) and control (C) groups

	Postinduction T1	Post first recruitment T2	Post retractor T3	Second recruitment T4	Dissection T5	End of surgery T6	Friedman test
IBP (mmHg)							
ARM (n=21)	72.0 [68.0-83.0]	83.0 [71.0-102.0]	82.0 [75.0-87.0]	80.0 [70.0-87.0]	73.0 [63.0-83.0]	80.0 [73.0-87.0]	$\chi^2_{(df=5)}$=7.292 P=0.200 NS
C (n=21)	85.0 [70.0-90.0]	85.0 [72.0-89.0]	88.0 [74.0-93.0]	85.0 [80.0-90.0]	82.0 [78.0-90.0]	83.0 [76.0-88.0]	$\chi^2_{(df=5)}$=4.379 P=0.496 NS
P	P=0.087 NS	P=0.687 NS	P=0.420 NS	P=0.147 NS	P=0.003 NS	P=0.194 NS	
CO (L/min)							
ARM (n=21)	6.10 [5.40-6.80]	6.0 [5.5-7.5]	6.0 [5.5-7.7]	6.1 [5.5-7.3]	6.5 [6.0-7.3]	6.5 [5.5-7.2]	$\chi^2_{(df=5)}$=6.034 P=0.303 NS
C (n=21)	6.40 [5.5-7.0]	6.3 [5.5-7.0]	6.8 [5.5-7.4]	6.8 [5.6-7.5]	6.2 [5.5-7.2]	6.0 [5.6-7.0]	$\chi^2_{(df=5)}$=8.223 P=0.144 NS
P	P=0.364 NS	P=0.569 NS	P=0.743 NS	P=0.743 NS	P=0.262 NS	P=0.840 NS	
CVP (cmH2O)							
ARM (n=21)	9.0 [7.0-10.0]	15.0 [12.0-16.0]	15.0 [14.0-17.0]	16.0 [12.0-17.0]	13.0 [12.0-16.0]	15.0 [12.0-16.0]	$\chi^2_{(df=5)}$=53.247 P=0.000*
C (n=21)	11.0 [10.0-12.0]	11.0 [10.0-13.0]	11.0 [10.0-12.0]	11.0 [10.0-12.0]	11.0 [10.0-12.0]	11.0 [10.0-12.0]	$\chi^2_{(df=5)}$=2.817 P=0.728 NS
P	P=0.001*	P=0.004*	P=0.000*	P=0.000*	P=0.001*	P=0.003*	
SVV (%)							
ARM (n=21)	12.0 [9.0-14.0]	11.0 [9.0-14.0]	12.0 [10.0-16.0]	11.0 [10.0-13.0]	11.0 [10.0-13.0]	10.0 [9.0-13.0]	$\chi^2_{(df=5)}$=7.541 P=0.183 NS
C (n=21)	14.0 [11.0-7.0]	13.0 [11.0-13.0]	11.0 [10.0-13.0]	11.0 [10.0-12.0]	11.0 [10.0-12.0]	11.0 [10.0-12.0]	$\chi^2_{(df=5)}$=16.596 P=0.005*
P	P=0.154 NS	P=0.613 NS	P=0.349 NS	P=0.929 NS	P=0.186 NS	P=0.423 NS	

The values are expressed as median [Interquartile range], n: Number of patients], ARM: alveolar recruitment manoeuvre, and C: control group. χ^2: Chi-squared of Friedman test; df: degree of freedom; P<0.05 indicates significance; NS: nonsignificant; and NA: nonapplicable statistics MW: Mann–Whitney U test for comparison at each time measurement

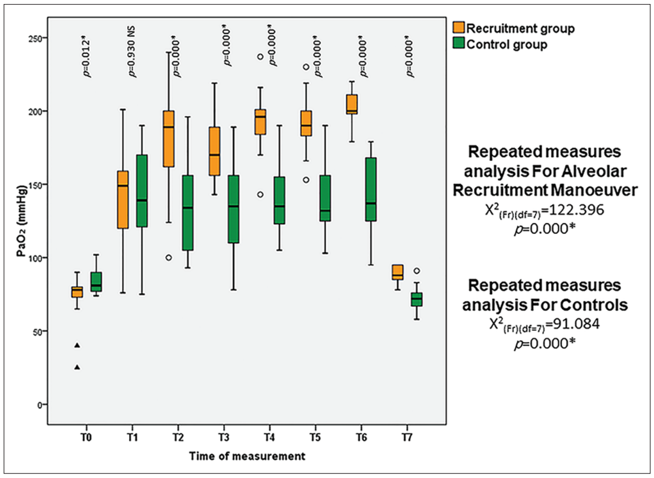

Figure 3: The box and whisker graph of partial pressure of oxygen in arterial blood (PaO_2, mmHg) and the thick line in the middle box represents the median. The box represents interquartile range (25th–75th percentiles) and whiskers represent minimum and maximum after excluding outliers (black-filled circles) and extremes (black triangle). Baseline preoperative (T0)—post anesthesia induction (T1)–post first recruitment (20 min after, T2)—postsurgical retraction (T3)—second recruitment (20 min after, T4)—during dissection (T5), end of surgery before muscle relaxant reversal (T6), and three hours postoperative (T7)

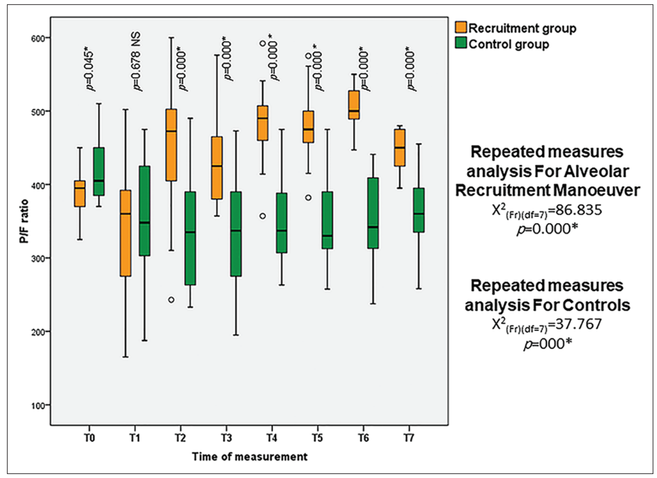

Figure 4: The box and whisker graph of partial pressure of oxygen in arterial blood (PaO_2)/fraction inspired oxygen (FiO_2) named *P/F* ratio. The thick line in the middle of the box represents the median, the box represents interquartile range (25th–75th percentiles), and whiskers represent minimum and maximum after excluding outliers (black-filled circles) and extremes (black triangle). Baseline preoperative (T0)—post anesthesia induction (T1)—post-first recruitment (20 min after, T2)—postsurgical retraction (T3)—second recruitment (20 min after, T4)—during dissection (T5), end of surgery before muscle relaxant reversal (T6), and three hours postoperative (T7)

The increase in blood loss in the ARM group compared to the C group failed to reach statistical significance; this could be due to the longer operative time in the ARM group. However, blood loss in the current trial was high in both groups compared to other published trials performed among healthy liver patients. This could be due to the surgical difficulty encountered when dissecting cirrhotic tissues and the effect of the hepatic congestion from the high CVP during lung recruitment. Most of the related published data were among healthy livers.[22,23] However, few trials presented their findings among cirrhotic livers. The study by McNally *et al.*[22] included patients with healthy livers suffering from colorectal liver metastases and undergoing liver resection. They reported a median blood loss of 782 mL, significantly lower than in the current trial. They confirmed a relationship between high CVP and blood loss. Cheng *et al.*[23] demonstrated that other multiple factors were also behind blood loss and not only the increase in CVP, including gender and surgery time. Dissecting cirrhotic liver tissues is another factor reported by McCormack *et al.* and Hackl *et al.*[24,25] Minimizing blood loss is important; however, it needs cooperation between the surgical and anesthesia teams. Unfortunately, increasing the PEEP during ARMs could elevate the CVP and induce hepatic venous congestion during liver surgery, which could lead to more blood loss, as presented by Li *et al.*[26] However, Neuschwander *et al.*, in a randomized control trial named IMPROVE disagree with the above beliefs. They stated that mechanical ventilation with PEEP during liver surgery and with lung-protective strategy was not associated with an increase in blood loss.[27] Halawa *et al.*[28] also reported that a transfusion-free surgical transplant was possible in a considerable number of liver transplant recipients undergoing lung recruitment with high PEEP values. No increase in blood loss was reported during the dissection phase of the transplant procedure. They also reported that during the periods of hypotension and reperfusion, it is possible to abort the recruitment maneuver temporarily when fluid replacement and catecholamine boluses fail to normalize the hemodynamics.

Park *et al.*[29] in 2016, Ferrando *et al.*[16] in 2017 and Cui *et al.*[8] in 2019 reported the ability of lung recruitment maneuvers with protective ventilation strategy to reduce PPCs. On the contrary, an international multicenter trial in 2014 (PROVHILO) found no difference in PPC.[30] This was supported later by another trial published in 2016, which found no significant difference in PPC.[30] Our current trial was one of the few to address this issue among hepatic patients with cirrhosis and found no statistically significant reduction in PPC with recruitment, despite the reduction in complications. The limited number of patients in the trial is considered a limitation due to including only cirrhotic hepatic patients undergoing liver resection.

In conclusion, alveolar recruitment improved lung compliance blood oxygenation, and reduced the ventilator driving pressure. ARM was tolerated from a hemodynamic perspective by most hepatic patients, as monitored by the EC and the invasive blood pressures. No significant effect on PPC was observed but instead, a reduction in desaturation episodes during recovery was observed.

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Conflicts of interest

There are no conflicts of interest.

References

1. AbdelWahab M, ElHusseiny T, ElHanafy E, El Shobary M, Hamdy E. Prognostic factors affecting survival and recurrence after hepatic resection for hepatocellular carcinoma in cirrhotic liver. Langenbecks Arch Surg 2010;395:625-32.
2. Paugam-Burtz C, Wendon J, Belghiti J, Mantz J. Case scenario: Postoperative liver failure after liver resection in a cirrhotic patient. Anesthesiology 2012;116:705-11.
3. Møller S, Hillingsø J, Christensen E, Henriksen JH. Arterial hypoxaemia in cirrhosis: Fact or fiction? Gut 1998;42:868-74.
4. Choudhuri AH, Chandra S, Aggarwal G, Uppal R. Predictors of postoperative pulmonary complications after liver resection: Results from a tertiary care intensive care unit. Indian J Crit Care Med 2014;18:358-62.
5. Lepere V, Vanier A, Loncar Y, Lemoine L, Vaillant JC, Monsel A, *et al.* Risk factors for pulmonary complications after hepatic resection: Role of intraoperative. J Crit Care Med 2014;18:358–62.
6. Gattinoni L, Collino F, Maiolo G, Rapetti F, Romitti F, Tonetti T, *et al*. Positive end-expiratory pressure: How to set it at the individual level. Ann Transl Med 2017;5:288.
7. Kredel M, Muellenbach RM, Brock RW, Wilckens HH, Brederlau J, Roewer N, *et al.* Liver dysfunction after lung recruitment manoeuvres during pressure-controlled ventilation in experimental acute respiratory distress. Critical Care 2007;11:R13. doi: 10.1186/cc5674.
8. Cui Y, Cao R, Li G, Gong T, Ou Y, Huang J. The effect of lung recruitment maneuvers on postoperative pulmonary complications for patients undergoing general anesthesia: A meta-analysis. PLoS One 2019;14:e0217405.
9. Squadrone V, Coha M, Cerutti E, Schellino MM, Biolino P, Occella P. Continuous positive airway pressure for treatment of postoperative hypoxemia: A randomized controlled trial. JAMA 2005;293:589-95.
10. Siddiqui N, Arzola C, Teresi J, Fox G, Guerina L, Friedman Z. Predictors of desaturation in the postoperative anesthesia care unit: An observational study. J Clin Anesth 2013;25:612-7.
11. Yassen K, Lotfy M, Miligi A, Sallam A, Hegazi EAR, Afifi M. Patient-controlled analgesia with and without transverse abdominis plane and rectus sheath space block in cirrhotic patients undergoing liver resection. J Anaesthesiol Clin Pharmacol 2019;35:58–64.
12. Rajput RS, Das S, Chauhan S, Bisoi AK, Vasdev S. Comparison of cardiac output measurement by noninvasive method with electrical cardiometry and invasive method with thermodilution technique in patients undergoing coronary artery bypass grafting. World J Cardiovasc Surg 2014;4:123-30.
13. Abou-Khaber H, El-Mehalawy A, Nasreldin M, El-Far W. Stepwise PEEP elevation with determination of the alveolar collapsing pressure versus sustained lung inflation as a recruitment maneuver in patients with ARDS. J Am Sci 2011;7:742-9.
14. Killeen PR. An alternative to null-hypothesis significance tests. Psychol Sci 2005;16:345-53.
15. Hemmes SN, Gama de Abreu M, Pelosi P, Schultz MJ. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): A multicenter randomised controlled trial. Lancet 2014;384:495-503.
16. Ferrando C, Suarez-Sipmann F, Tusman G, León I, Romero E, Gracia E, *et al.* Open lung approach versus standard protective strategies: Effects on driving pressure and ventilatory efficiency during anesthesia-A pilot, randomized controlled trial. PLoS One 2017;12:e0177399.
17. Severgnini P, Selmo G, Lanza C, Chiesa A, Frigerio A, Bacuzzi A, *et al.* Protective mechanical ventilation during general anesthesia for open abdominal surgery improves postoperative pulmonary function. Anesthesiology 2013;118:1307-21.
18. Whalen FX, Gajic O, Thompson GB, Kendrick ML, Que FL, Williams BA, *et al*. The effects of the alveolar recruitment maneuver and positive end-expiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. Anesth Analg 2006;102:298-305.
19. Lee J, Kim WH, Ryu HG, Lee HC, Chung EJ, Yang SM, *et al*. Stroke volume variation–guided versus central venous pressure–guided low central venous pressure with milrinone during living donor hepatectomy: A randomized double-blinded clinical trial. Anesth Analg 2017;125:423-30.
20. Watson CJE, Kosmoliaptsis V, Randle LV, Gimson AE, Brais R, Klinck JR, *et al.* Normothermic perfusion in the assessment and preservation of declined livers before transplantation: Hyperoxia and vasoplegia-important lessons from the first 12 cases. Transplantation 2017;101:1084-98.
21. Corradini SG, Elisei W, De Marco R, Siciliano M, Iappelli M, Pugliese F, *et al.* Preharvest donor hyperoxia predicts good early graft function and longer graft survival after liver transplantation. Liver Transpl 2005;11:140–51.
22. McNally SJ, Revie EJ, Massie LJ, McKeown DW, Parks RW, Garden OJ, *et al.* Factors in perioperative care that determine blood loss in liver surgery. HPB 2012;14:236-41.
23. Cheng ES, Hallet J, Hanna SS, Law CH, Coburn NG, Tarshis J, *et al*. Is central venous pressure still relevant in the contemporary era of liver resection? J Surg Res 2016;200:139–46.
24. McCormack L, Capitanich P, Quiñonez, E. Liver surgery in the presence of cirrhosis or steatosis: Is morbidity increased? Patient Saf Surg 2008;2:8.
25. Hackl C, Schlitt HJ, Renner P, Lang SA. Liver surgery in cirrhosis and portal hypertension. World J Gastroenterol 2016;22:2725–35.
26. Li Z, Sun YM, Wu FX, Yang LQ, Lu ZJ, Yu WF. Controlled low central venous pressure reduces blood loss and transfusion requirements in hepatectomy. World J Gastroenterol 2014;20:303-9.
27. Neuschwander A, Futier E, Jaber S, Pereira B, Eurin M, Marret E, *et al*. The effects of intraoperative lung protective ventilation with positive end-expiratory pressure on blood loss during hepatic resection surgery: A secondary analysis of data from a published randomised control trial (IMPROVE). Eur J Anaesthesiol 2016;33:292–8.
28. Halawa NM, Elshafie MA, Fernandez JG, Metwally AA, Yassen KA. Respiratory and hemodynamic effects of prophylactic alveolar recruitment during liver transplant: A randomized controlled trial. Exp Clin Transplant 2021;19:462-72.
29. Park SH. Perioperative lung-protective ventilation strategy reduces postoperative pulmonary complications in patients undergoing thoracic and major abdominal surgery. Korean J Anesthesiol 2016;69:3-7.
30. The PROVE Network Investigators for the Clinical Trial Network of the European Society of Anaesthiology. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial) multicenter randomized controlled trial. Lancet 2014;384:495-503.