

# Precision implementation of early ambulation in elderly patients underwent off-pump coronary artery bypass graft surgery: a randomized controlled clinical trial

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## Research article

**Keywords:** Early ambulation, Physical rehabilitation, Enhanced recovery after surgery, cardiac surgery, elderly patients

**Posted Date:** January 9th, 2020

**DOI:** <https://doi.org/10.21203/rs.2.20274/v1>

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**Version of Record:** A version of this preprint was published on October 14th, 2020. See the published version at <https://doi.org/10.1186/s12877-020-01823-1>.

# Abstract

## Background

Though early ambulation (EA) is associated with improved outcomes for post-operative patients, precision initiative on EA for elderly patients has rarely been reported. The aim of this study is to determine the safety and effectiveness of precision implementation of EA in elderly patients underwent off-pump coronary artery bypass graft (OPCABG) surgery.

## Methods

We conducted a single-center, randomized and controlled clinical trial involving elderly patients ( $\geq 60$  years) in who EA support was implemented after OPCABG surgery. Patients were randomly assigned to precision early ambulation (PEA) group or routine ambulation (Control) group. Innovatively referring age-predicted maximal heart rate (APMHR) and  $VO_{2max}$  was the highlight of PEA. The primary end-point was the postoperative length of stay in hospital (PLOS). The secondary end-point included 90-day mortality, laboratory test, length of stay in ICU, the incidence of multiple organ complications as well as post-traumatic stress disorder (PTSD).

## Results

There were 178 patients were enrolled, with 89 patients assigned to receive PEA and 89 to receive control procedure. By intent-to-treat analysis, during PEA program, participants performed a much longer distance of ambulation on the third day ( $P = 0.000$ ). Mild-to-moderate physical activity in PEA group ameliorates PLOS ( $P = 0.031$ ), Time of first bowel ( $P = 0.000$ ) and partial pressure  $O_2$  ( $P = 0.001$ ). Additionally, patients in PEA group showed significantly lower incidence of PTSD than those in Control group ( $P = 0.000$ ).

## Conclusion

APMHR and  $VO_{2max}$  are valuable for target intensity and exercise formula. PEA after OPCABG surgery is safe and reliable for elderly patients, which not only reduces the hospital stay but also improves patients' postoperative functional status.

## Background

China faces an aging tsunami, and it is estimated that by the end of 2018, the number of adults aged 60 and older had reached 230 million. By 2050, there are expected to be 400 million Chinese citizens aged 65 and older, 150 million of whom will be aged 80 and older[1]. The older an individual patient, the higher a surgeon's threshold is for performing a more extensive or complicated operation[2, 3]. By now, coronary heart disease (CHD) is the leading cause of death, and the mortality of CHD is growing at 9.2% and 7.0% per year for men and women in China, respectively. Off-pump coronary artery bypass grafting (OPCABG) surgery has gradually become an ideal approach for elderly patients[4, 5], yet the present is still grim. Ralf

et al. reported that the incidences of dysfunction, hemorrhage and transfusion for patients over 64 years old after CABG surgery were 18.2%, 11.2%, and 53.3%, respectively[6]. Therefore, Advances in perioperative management for elderly patients underwent OPCABG surgery is still facing huge challenges.

Enhanced recovery after surgery (ERAS) is generated from evidence-based medicine and aimed at achieving an uneventful recovery after surgery[7, 8]. ERAS was proved to improve the outcome of surgery, decrease costs and shorten the length of time to full recovery. Early ambulation (EA) is an important part of ERAS[9]. Burtin et al. reported that early exercise training in critically ill ICU survivors, enhanced not only their recovery of functional exercise capacity and self-perceived functional status, but also their muscle force[10]. However, the status quo is very skinny that patients spent, on average, 83% of their time lying in bed, 13% of the time seated, and 4% of the time walking[11]. Given that an imprudent “changing of the guard” is a justifiable concern with any practice update, there have been concerns that old dogma, different types of surgery and minimal peer-reviewed evidence from multiple subjects, will be maladaptation under the umbrella of “enhanced recovery” without validation in cardiac rehabilitation. Meanwhile, considering the advanced age was often accompanied with stroke, chronic obstructive pulmonary disease, and renal dysfunction, and complications such as fragile, pain and tube contamination were inevitable after OPCABG, EA was quite a difficult task to perform efficiently after cardiac surgery[12, 13]. Yet, the feasibility of start time and the appropriate intensity level of physical rehabilitation for patients with cardiovascular limitations is still unknown. Such knowledge would help clinicians and therapists plan implementation during a rehabilitation program in order to maximize physical recovery and minimize the associated side effects.

To avoid harm from unaccustomed vigorous exercise, the studies of aerobic and resistance exercise were paid more attention to maximal oxygen consumption ( $VO_{2max}$ )[14]. Guaranteeing the safety, the proper exercise intensity would be assessed by accurate prediction of age-predicted maximal heart rates (APMHR) and  $VO_{2max}$ [15]. However, exercise-based cardiac rehabilitation has not been recommended for patients after surgery, the adoption of the guidelines is negatively impacted by insufficient recognition of APMHR. In other words, if APMHR and  $VO_{2max}$  are assessed and better managed, target intensity and exercise formula may be better prescribed.

The aim of this study was to design precision early ambulation (PEA) for patients aged 60 years or older underwent cardiac surgery, focused on APMHR and  $VO_{2max}$  of cardiac rehabilitation, thereby clarified the impact of PEA on the postoperative recovery of elderly patients, which included the postoperative length of stay (PLOS) in hospital, length of stay in ICU (LOSI), the incidence of multiple organ complications as well as the post-traumatic stress disorder (PTSD).

## Materials And Methods

### Trial design and oversight

This single-center, randomized and controlled clinical trial was conducted at Shandong Provincial Hospital between September 2018 and June 2019. This study was approved by the Ethics Committee of the Provincial Hospital affiliated to Shandong University (approval number 2018-239). Besides, this study was registered on the National Clinical Trial Center with the registration number of ChiCTR1800018167. Informed consent was obtained from each patient. All authors affirm that the data and analyses in this trial are accurate and complete, and the trial was conducted in a manner consistent with the study protocol. In this study, quality control and data management were performed by the third party of Shandong Centers for Disease Control and Prevention. The statistical analysis was performed by the School of Public Health of Shandong University.

### **Enrollment procedure and randomization**

All the patients scheduled to undergo OPCABG provided written informed consent. Full inclusion/exclusion criteria are shown in **Additional file 1**. Eligible patients were assigned at random to receive either PEA or routine rehabilitation (Control group) (at a 1:1 ratio) after removal of tracheal intubation. A computer-generated, permuted block sequence stratified according to trial center was used to support study randomization. Patient randomization are detailed in **Figure 1**. All patients in PEA and Control groups were implemented the same EARS procedures expect ambulation, shown in **Additional file 1**.

### **Blinding**

This study was a single-blinded design. Once identified the group of patients, physicians and patients were open-label to treatment assignments. However, data collectors and outcome assessors were kept blinded to study group assignment.

### **Clinical Protocol of PEA**

The PEA protocol was designed by a panel of experts, including a cardiac surgeon, a rehabilitation therapist, two experienced nurses and two respiratory therapists. The PEA protocol was formulated refers to **Table S3**. Here, the exercise physiology concept of maximal oxygen consumption ( $VO_{2max}$ ) and age-predicted maximal heart rate (APMHR) were referred to assess an appropriate intensity.

The flowchart of PEA implementation was shown in **Figure 2**. The protocol of PEA included: 1) On the first day after surgery: patients were assisted to make a transition from a high sitting position to a bedside sitting position, with legs hang down more than 10 min. Orthostatic hypotension (OH) and orthostatic intolerance (OI) should be closely monitored. If patients' clinical indicators were stable, they would be allowed to sit out of bed or stand for 3~5 min. 2) On the second day after surgery: patients were assisted to sit out of bed. Besides, 3~5 min of standing and 20 meters of walk nearby the bed should be conducted with the help of rehabilitation therapist if patients had good conditions. 3) On the third day after surgery: patients were assisted to sit more than 10 min out of bed. Meanwhile, 5 min of standing

and 30 meters of walk should be conducted under the assistance of rehabilitation therapists or family members. The intensity of ambulation should be gradually increased according to the patients' tolerance.

### **Protocol of routine rehabilitation**

The protocol of routine rehabilitation: patients were allowed to do ambulation on the second day after surgery. Ambulation should be determined by patient's self-assessment and the experiences of rehabilitation therapists, as long as there were no sudden events.

### **Ambulation outcomes and adverse events**

The ambulation outcomes of patients in PEA and Control group were respectively collected. The goal of ambulation for the second day after surgery (Goal-2<sup>nd</sup>) was to walk about 30 feet, while for the third day after surgery (Goal-3<sup>rd</sup>) was to walk 60 feet. Adverse events conclude OH and OI. OH was with symptoms of dizziness, nausea, weakness, and palpitation, accompanied by a decrease in systolic blood pressure of more than 30 mmHg. OI is characterized by symptoms of dizziness, nausea, blurred vision, or syncope due to failed orthostatic cardiovascular regulation, a decrease in arterial pressure, and cerebral hypoperfusion during standing.

### **End-points of this study**

The primary end-point was the PLOS. While, the secondary end-points were shown as follows: a) the mortality rate and rehospitalization within 90 days after surgery; b) LOSI; c) the laboratory tests including troponin I (TNI) and Creatine Kinase isoenzyme-MB (CK-MB) (tested at 8:00 pm) as well as arterial blood gas analysis including partial pressure O<sub>2</sub> (PO<sub>2</sub>) and partial pressure CO<sub>2</sub> (PCO<sub>2</sub>) (tested at 8:00 pm); d) multi-organ function assessment or incidence of postoperative complications, such as time of first bowel, time of urinary retention, time of drainage tube retention, pulmonary atelectasis, pulmonary infection, pleural effusion, OH, OI, acute kidney injury and need for renal-replacement therapy; e) patients' mental state assessed on the fifth day after surgery by PTSD Checklist-Civilian screening scale (PCL-C), shown in **Additional file 1**.

### **Statistical analysis**

The sample-size calculation was based on a two-sided alpha error of 0.05 and 90% power. According to previous study, implantation of EA was reported to reduce the PLOS from 8.11 days to 5.33 days[16], we expected 10 days in Control group and 8 days in the PEA group. Accordingly, we calculated that a sample of 80 patients per group was needed. In order to account for 5% participants about protocol deviations and withdrawal of consent, we planned for a total of 178 patients to undergo randomization.

Data are presented as means and standard deviations (mean ± SD) for normally distributed variables and as medians and interquartile ranges (IQR) for nonnormally distributed variables. Qualitative data are expressed as absolute number and frequency (n, %). Continuous variables were compared using Student's t-test or Mann-Whitney test. Qualitative data were compared using Pearson's chi-square test

( $\chi^2$ ). Odds ratios and confidence intervals were estimated from a logistic-regression model with age, BMI and sex included as covariates. PLOS, LOSI, Time of drainage tube retention, Time of first bowel movement, and Time of Urinary catheter retention were analyzed with the use of linear regression with the same covariates. Laboratory tests after surgery were analyzed by repeated measurement (RM-ANOVA) with time as within factor ( $P_w$ ) and PEA or Control group as the grouping factor ( $P_g$ ), with the post-hoc Bonferroni test. Multivariate logistic regression modelling was used to assess associations between baseline factors and early discharge. Definition of early discharge was  $PLOS \leq 7$  day. A two-sided  $P < 0.05$  was considered to be statistically significant. Statistical analyses were performed with SPSS version 25 (SPSS Inc, IBM, Armonk, NY, USA).

## Results

A total of consecutive 239 patients who underwent OPCABG were firstly evaluated for their eligibility. Totally, 21 patients were excluded according to their subjective wishes and 40 patients were excluded after evaluation. The remaining 178 patients were randomly assigned into PEA group and Control group, with 89 patients in each group. The basic clinical features of patients in PEA and Control group were shown in **Table 1**. Patients in the PEA and Control group showed similar clinical characteristics. No significant difference was found in their ages, genders, BMIs, medical histories and Euro SCORE. All survival patients were followed-up for 90 days.

### Ambulation outcomes and adverse events

As shown in **Table 2**, a total of 75 (84.3%) patients in PEA group and 62 (69.7%) patients in Control group achieved the Goal-2<sup>nd</sup>. While, 74 (83.1%) patients in PEA group and 49 (55.1%) patients in Control group completed the Goal-3<sup>rd</sup>. There were 8 (9.0%) patients in PEA group and 15 (16.9%) patients in Control group had OH, 2 (2.2%) patients in Control group but none in PEA group had OI within the first 3 days post-surgery. A total of 4 patients could not get out of bed on the third day after surgery, including 1 in PEA group and 3 in Control group. The distance of ambulation on the third day after surgery was significantly farther in PEA group than in Control group, which were  $76.12 \pm 29.02$  and  $56.80 \pm 24.40$  meters, respectively ( $P=0.000$ ).

### Primary and secondary end-point of this study

PLOS, the primary end-point of this study, was significantly shorter in patients of PEA group ( $9.04 \pm 3.08$  days) than that of Control group ( $10.09 \pm 3.32$  days) ( $P=0.031$ ), shown in **Table 3**. To evaluate the function recovery of major organs, we comparatively analyzed the ICU stay, time of drainage tube retention and time of urinary catheter retention in patients of PEA and Control group, which were  $2.98 \pm 1.40$  vs.  $3.10 \pm 1.50$ ,  $3.82 \pm 0.92$  vs.  $3.89 \pm 0.82$ , and  $3.00 \pm 1.02$  vs.  $3.22 \pm 0.88$ , respectively (all  $P > 0.05$ ). No significant differences were found in incidence of atelectasis (12.4% vs. 19.1%,  $p > 0.05$ ) and pulmonary infection (12.4% vs. 14.6%,  $p > 0.05$ ) between both groups. However, the time of first bowel movement in PEA group was significantly earlier than that in Control group, which were  $3.18 \pm 1.23$  and

3.97±1.26 days, respectively ( $p=0.000$ ). For laboratory test, TNI and CK-MB showed an obvious decreasing trend, no significant difference was found between groups ( $P_g=0.599$ ,  $P_g=0.415$ , respectively). There was better PO<sub>2</sub> in PEA group than Control group ( $P_g=0.001$ ), shown in **Table S3**.

Univariate and multivariate analyses confirmed an association between Early discharge and PEA ( $p=0.021$ ) as shown in **Tables S4 and 4**.

For PTSD score, results showed that patients in PEA group had significantly lower score than patients in Control group, which were 27.72±9.34 and 40.44±12.55, respectively ( $p=0.000$ , shown in **Table S5**).

## Discussion

To our knowledge, this trial is the first to investigate EA in details in elderly patients after cardiac surgery. By innovative reference of APMHR and VO<sub>2max</sub> to EA procedure, we assessed a progressively increasing the intensity of EA as PEA that were suitable for cardiac rehabilitation. We found that significant and favorable associations exist between PEA and clinical outcomes such as PLOS. Multivariate logistic regression analyses confirmed the effect of PEA on early discharge.

The characteristics of our trial were consistent with CHD and predominant in elderly patients. It was commonly noted that aged patients undergoing CABG were subject to a higher risk of perioperative complications and death, also hard to be carried out with PEA. Multivariate logistic regression analysis showed that advanced age was the independent risk factor for the early discharge. Therefore, focus on elderly patients underwent OPCABG has the clinical significance.

The lack of consensus regarding the definition and implement of “early mobilization” has been confused for clinicians. The meaning of “early”, when applied for the beginning of mobilization after surgery, should be varied by many factors according to the surgical procedure and the type of pathology. Among stroke care professionals, 40% of professionals believed that mobilization should begin with 24 hours of stroke onset, while 41% considered it safer and more appropriate to begin the intervention after 24 hours[17]. Marissa et al. implemented a T-ERA<sup>AS</sup> protocol, and set a benchmark distance of 250 feet within the first hour post extubation[18]. However, Jans et al. reported that EA might lead to a high incidence of postoperative OH and OI[19]. Harald et al. reported that bed rest ranging from 2 to 12 days seems to be as safe as longer periods of bed rest[20]. Therefore, there was no consensus on the start time of EA. In our study, the criteria to define early mobilization was different from previous studies, with a light training session, our patients were out of bed within 24-h after extubation. Through monitoring the adverse events and occurrence of OH or OI, our finding appears to support the safety of this time to avoid bed rest for elderly patients after cardiac surgery.

EA should constitute a continuum of care and multiple therapy techniques. The Heart Failure Quality Program defined EA as the patient’s ambulation without assistance[21]. In some superior ICU, novel mobilization techniques such as cycle ergometer, upper body exercises, Kinarm robotic exoskeleton and supported treadmill training were administrated to patients[22, 23]. However, there is no evidence that one

technique is superior to another. Andrew et al. reported that walking provided a well-tolerated and clinically effective alternative to stationary cycling in the early postoperative period after CABG[24]. In our ICU, breath exercises were routinely carried out, and traditional mobilization mainly varied from sitting by the bed, walking without or with assistance at first 3 days after surgery, showing favourable results.

Another important detailed factor regarding PEA is intensity. Moradian et al. has shown that patients received low-frequency monitored exercise programs had higher discharge rates and shorter ICU stay[25]. The expected goal in another study was 100 m of walking with the assistance at second day, and 10-min physiotherapy-supervised walking exercise session at third day after CABG [24]. It surprised us that we thought there are huge risks for elderly patients to achieve these tough goals and the distance of walking in our trial was only performed 76.12 and 56.80 meters at third day after OPCABG surgery. Previous studies have demonstrated that adverse events (such as decreased SPO<sub>2</sub>, tachycardia and frailty) frequently occur in elderly patients. Referencing exercise physiology, we believed APMHR and VO<sub>2max</sub> were novel but valuable to cardiac rehabilitation, primarily with accurate evaluation to physiological responses[26, 27]. Shen et al reported that patients whose heart function decreased more than 50% could not tolerate 70% of APMHR exercises[26]. Thus, we recommended a step-by-step process with low-intensity exercise for those elderly patients after OPCABG surgery. Here, our data showed that under the intensity of 20% VO<sub>2max</sub>, about 85% patients in PEA group achieved ambulation goal on 2nd day and 83% patients completed on 3rd day after surgery, far more than Control group. Moreover, there was a low incidence of OH and OI in PEA group. Thus, we suggested that a principle of progressive intensity of no more than 30% of VO<sub>2max</sub> and 56% of APMHR could accurately reflect elderly patient's tolerance in the early postoperative period and guarantee their safety.

Discharge home has been a surrogate for improved functional status, functional independence, and mental capacity. There is growing evidence that early mobilization in ICU could reduce the length of hospital and ICU stays[28]. Klein reported that early mobility protocol increased highest neurologic ICU mobility and discharge home and decreased length of stay from 15.2d to 10.2d[29]. Schaller et al. reported that the length of ICU/hospital stay was 7/15 days in the intervention group and 10/21.5 days in the control group, respectively[30]. However, in contrast with these results, some other trials did not identify this effect of early mobilization. Katherine noted that there was insufficient evidence on the effect of early mobilization of critically ill people in the ICU on physical function or performance, adverse events, muscle strength and health-related quality of life at this time[31]. Our result was inconsistent with the previous findings. Our data indicated that PEA was able to exhibit its effect in shortening the length of PLOS stay, but failed of reducing the length of ICU stay. It was supposed that a less proportion of severe ill patients and the long duration of mechanical ventilation were out of our enrolment. Therefore, the length of ICU stay in both group was short.

EA is also an effective candidate intervention for preventing the occurrence of multiple organ complications post-surgery. Li et al reported that ERAS effectively brought forward the time of first bowel movement about 1.0 day[32]. Our data also confirmed that PEA promoted gastrointestinal function recovery, with an average reduction of first bowel movement for 0.7 day. In our trial, the occurrence rate of

pulmonary atelectasis and pulmonary infection was reduced by 7% and 2% in PEA group, respectively, different from the study of Moradian et al, which showed EA reduced about 34% of pleural effusion and 29% of atelectasis occurrence[25]. Also, we found that arterial oxygen level was significantly improved in PEA group, suggesting that PEA could contribute to lung recovery, and postoperative moderate exercise could improve the circulatory function and muscle tone.

Growing evidence highlights the influence of psychological determinants in CHD. Indeed, positive affectivity was shown to be associated with better cardiac rehabilitation adherence and play a role as an independent factor influencing cardiac outcomes. Approximately 20%-51% of patients with CHD have been afflicted by clinical psychological symptoms[33]. PTSD is an abnormal psychological reaction characterized by a series of anxious manifestations such as recurrence, avoidance, and high alertness. Gao et al. have proposed that 25.8% of patients with myocardial infarction had PTSD[34]. Deng et al have reported that the incidence of post-operative PTSD in 134 adults with congenital heart disease was 21% [35]. Our trial confirmed strong negative linking of PTSD with PEA, which indicated that positive psychological functioning, like positive affect and optimism, stimulates goal-striving activities, to adopt protective health behavior and to adhere to therapies.

Our study has some limitations. First, a less proportion of severe ill patients (such as advanced age > 80 years) were enrolled, and the patients with long duration of mechanical ventilation were also excluded. Secondly, a randomized Controlled trial would have provided a higher level of evidence; however, it would have been impossible to blind participants and healthcare providers from the intervention and we could not avoid the subjective operation by rehabilitation therapists and nurses during the EA implementation in this trail. Thirdly, the clinical efficacy analysis was also influenced by many factors, such as pain control, oxygen inhalation mode, etc., which was not further analyzed in this study.

## Conclusion

In summary, our data confirmed PEA could shorten the PLOS, promote the digestive system restoration, improve perioperative oxygenation state, and accelerate psychological rehabilitation for elderly patients after OPCABG surgery. Our trial also revealed that APMHR and  $VO_{2max}$  would be important symbols in the implementation of PEA. Further work should be conducted to improve the formulation and implementation of EA, such as by focusing on cross-disciplinary integration, systematic training and individualized treatment.

## Abbreviations

EA: Early ambulation; OPCABG: Off-pump coronary artery bypass graft; PEA: Precision early ambulation; APMHR: Age-predicted maximal heart rate; PLOS: Postoperative length of stay; PTSD: Post-traumatic stress disorder;  $PO_2$ : Pressure  $O_2$ ;  $PCO_2$ : Partial pressure  $CO_2$ ; OH: Orthostatic hypotension; OI: Orthostatic intolerance; CABG: Coronary artery bypass grafting; ICU: Intensive care unit; ERAS: Enhanced recovery after surgery; LOSI: Length of stay in ICU; TNI: Troponin I; CK-MB: Creatine Kinase isoenzyme-MB.

# Declarations

## Funding

This work was supported by Clinical Science and Technology Innovation Program of Jinan City (201805040), Medicine and Health Science Technology Development of Shandong Province (2017WS191), Cardiovascular Multidisciplinary Integrated Research Fund (CIMF-Z-2016-23-1823) and the Natural Science Foundation of Shandong Province (ZR201702210404).

## Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

Qi Tan, Zhaomei Cui came up with the study concept. All authors developed the study design and protocol. Yiou Fan, Xin Zhuang, Jing Liu and Jie Zhang collected the study data. Na Li was involved in the analysis and interpretation of data. All co-authors provided input and critical review of the manuscript leading to the final version. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Provincial Hospital affiliated to Shandong University (approval number 2018-239) and registered at [chictr.org.cn](http://chictr.org.cn) (ChiCTR1800018167).

## Consent for publication

Not applicable

## Competing interests

The authors declare that they have no competing interests.

## Acknowledgements

The authors would like to thank all of the clinicians and staff in the ICU for their assistance in implementing the early ambulation in this trial.

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## Supplementary Information

**Additional file 1.** Supplemental description of methods and results, including Study eligibility criteria, Rehabilitation measure, PTSD Checklist-Civilian screening scale (PCL-C), and Table S1-S5.

## Tables

**Table 1.** Baseline of patients in PEA and Control group.

	PEA Group (n=89)	Control Group (n=89)	P value
Age (years-old)	65.1±4.6	66.2±4.5	0.118
Female patients (%)	24 (27.0)	27 (30.3)	0.740
BMI (kg/m <sup>2</sup> )	25.8±3.2	25.8±2.6	0.908
Medical history			
Hypertension (%)	19 (21.3)	30 (33.7)	0.185
Diabetes (%)	13(14.6)	21 (23.6)	0.181
Renal insufficiency (%)	2 (2.2)	5(5.6)	0.444
Cerebral infarction (%)	10 (11.2)	6 (6.7)	0.443
Smoking (%)	29 (32.6)	27 (30.3)	0.875
Preoperative ejection fraction (%)	59.2±3.3	58.8±3.7	0.536
Number of heart bypass	4.10±0.45	4.11±0.44	0.465
Euro Score	7.61±2.14	7.79±2.34	0.453

Note: Data were presented as mean ± standard deviation (SD) for continuous variables, and number of subjects (n) and percentage (%), respectively, for categorical variables. BMI: body mass index.

**Table 2.** Ambulation outcomes in patients of the PEA and Control group.

	PEA group (n=89)	Control group (n=89)	P-value
Goal-2nd	75 (84.3%)	62 (69.7%)	0.021
Goal-3rd	74 (83.1%)	49 (55.1%)	0.000
No ambulation on the 3 <sup>rd</sup> post-surgery	1 (1.1%)	3 (3.4%)	0.621
The distance of ambulation on the 3 <sup>rd</sup> post-surgery	76.12±29.02	56.80±24.40	0.000
Orthostatic hypotension	8 (9.0%)	15 (16.9%)	0.179
Orthostatic intolerance	0 (0%)	2 (2.2%)	0.497

Note: Data were presented as mean ± standard deviation (SD) for continuous variables, and number of subjects (n) and percentage (%), respectively, for categorical variables.

**Table 3.** Comparative analysis of the primary and secondary endpoints of this study in patients of the PEA and Control group.

	PEA Group (n=89)	Control Group (n=89)	OR (95%CI)	P-value
<b>Primary end-point</b>				
PLOS (days)	9.04±3.08	10.09±3.32	-	0.031
<b>Secondary end-point</b>				
Incidence of mortality within 90 days after surgery (%)	1 (1.1)	1 (1.1)	1.5(0.06,34.9)	1.000
LOSI (days)	2.98±1.40	3.10±1.50	-	0.570
Time of drainage tube retention (days)	3.82±0.92	3.89±0.82	-	0.648
Time of first bowel movement (days)	3.18±1.23	3.97±1.26	-	0.000
Time of Urinary catheter retention (days)	3.00±1.02	3.22±0.88	-	0.129
Incidence of acute kidney injury (%)	6 (6.7)	6 (6.7)	1.0(0.3,3.4)	1.000
Number of patients with renal-replacement therapy	0	1 (1.1)	-	0.323
Incidence of pulmonary atelectasis (%)	11 (12.4)	17 (19.1)	1.8(0.8,4.1)	0.174
Incidence of pulmonary infection (%)	11 (12.4)	13 (14.6)	1.3(0.5,3.0)	0.613

Note: Data were presented as mean ± standard deviation (SD) for continuous variables, and number of subjects (n) and percentage (%), respectively, for categorical variables.

PLOS: postoperative length of stay in hospital;

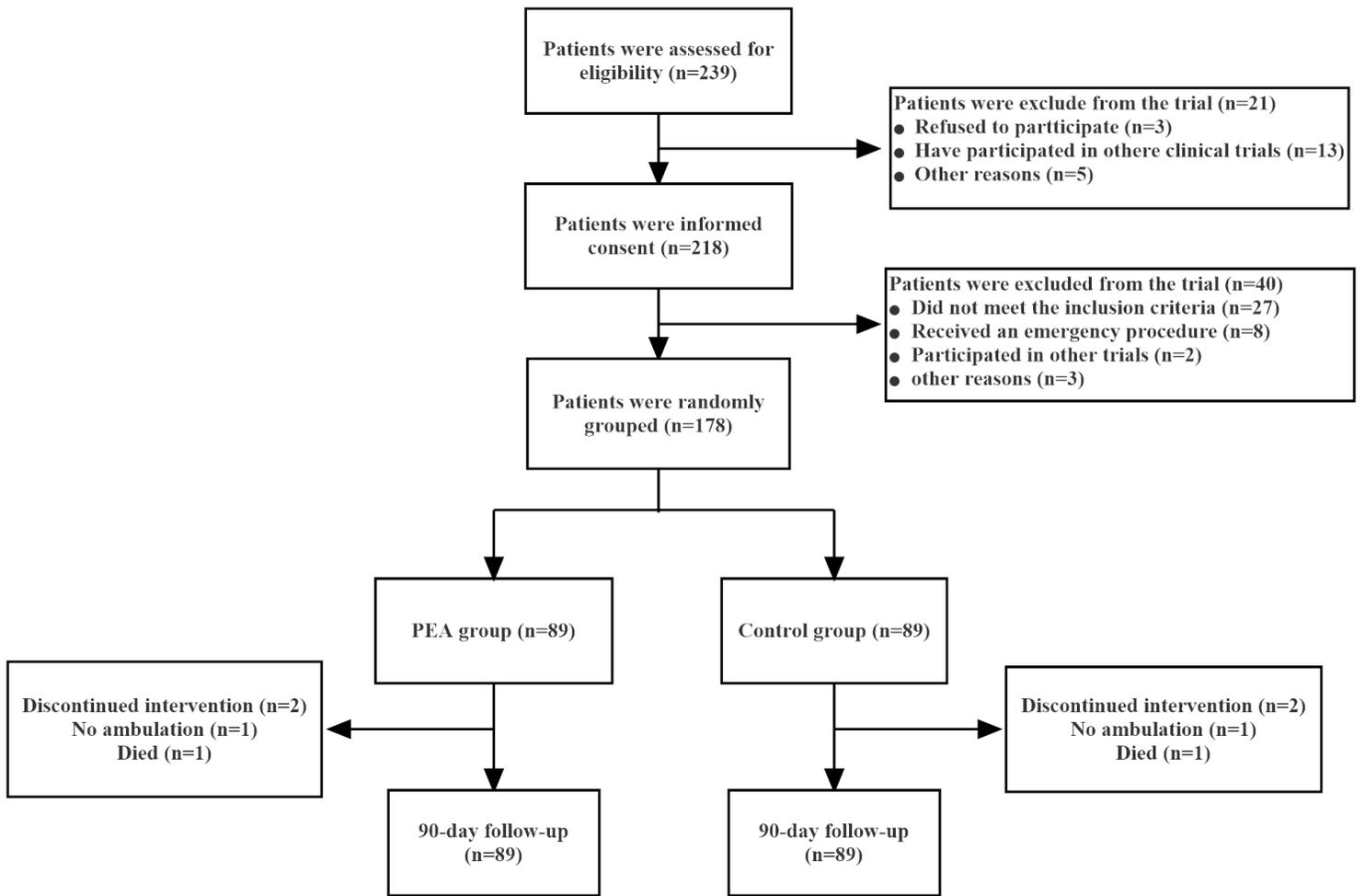
LOSI: length of stay in ICU.

**Table 4** Baseline factors predictive of Early discharge based upon a multivariate logistic regression analysis

Variable	OR	95%CI	Pvalue
Randomization to PEA	2.21	1.13-4.32	0.021
Age	0.904	0.836-0.977	0.010
Euro score	0.750	0.608-0.923	0.007
Cerebral infarction	5.315	1.092-25.875	0.039

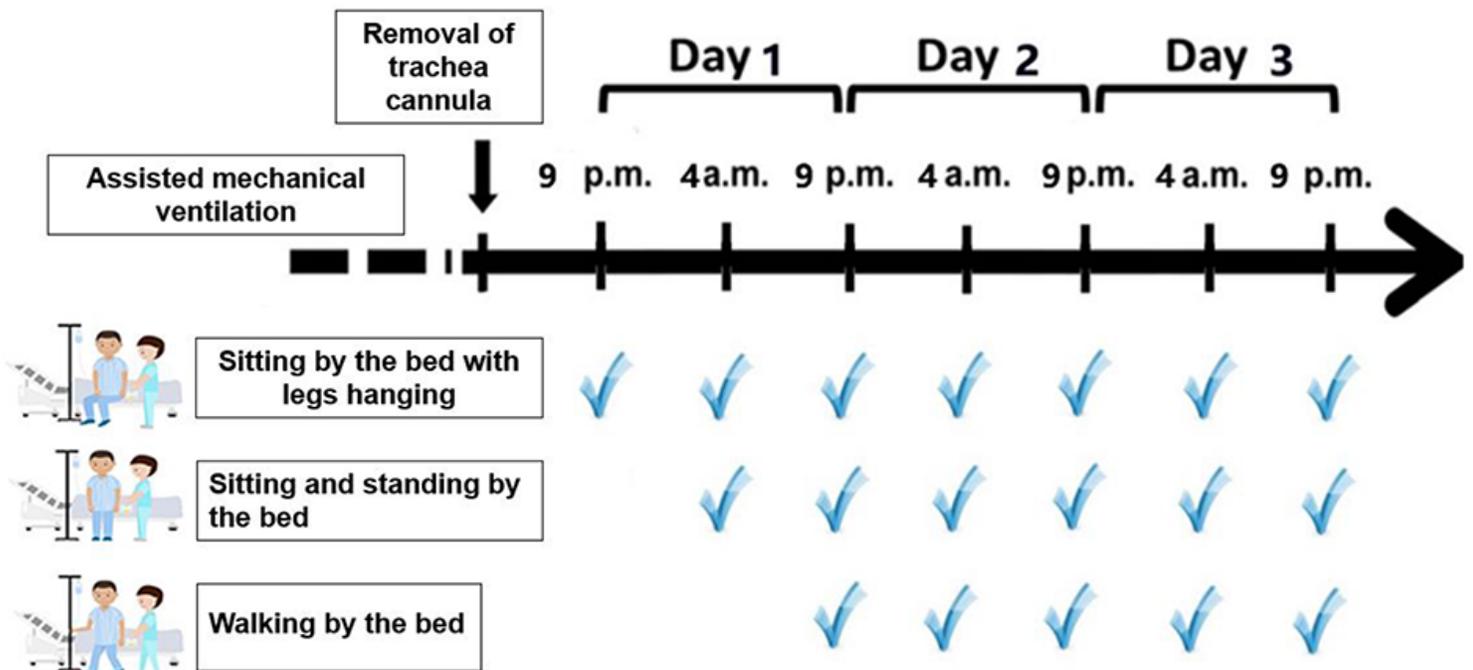
OR: odds ratio; CI: confidence interval.

## Figures



**Figure 1**

Flowchart of patients' enrollment. The detailed procedure of this study was shown in this flowchart, from patients' recruitment, random allocation to follow-up.



## Figure 2

Protocol of early ambulation (EA). The precision implementation of EA within three days after surgery was shown.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [supplymentary.docx](#)