PLOS ONE

RESEARCH ARTICLE

Effects of low versus high inspired oxygen fraction on myocardial injury after transcatheter aortic valve implantation: A randomized clinical trial

Youn Joung Cho[1], Cheun Hyeon[1], Karam Nam[1], Seohee Lee[1], Jae-Woo Ju[1], Jeehoon Kang[2], Jung-Kyu Han[2], Hyo-Soo Kim[2], Yunseok Jeon[1]*

1 Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea, **2** Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

* jeonyunseok@gmail.com

OPEN ACCESS

Citation: Cho YJ, Hyeon C, Nam K, Lee S, Ju J-W, Kang J, et al. (2023) Effects of low versus high inspired oxygen fraction on myocardial injury after transcatheter aortic valve implantation: A randomized clinical trial. PLoS ONE 18(8): e0281232. https://doi.org/10.1371/journal.pone.0281232

Editor: Mohamed R. El-Tahan, Imam Abdulrahman Bin Faisal University College of Medicine, SAUDI ARABIA

Received: January 17, 2023

Accepted: July 18, 2023

Published: August 2, 2023

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Funding: The authors received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

Abstract

Background

Oxygen therapy is used in various clinical situation, but its clinical outcomes are inconsistent. The relationship between the fraction of inspired oxygen (F_IO_2) during transcatheter aortic valve implantation (TAVI) and clinical outcomes has not been well studied. We investigated the association of F_IO_2 (low vs. high) and myocardial injury in patients undergoing TAVI.

Methods

Adults undergoing transfemoral TAVI under general anesthesia were randomly assigned to receive F_IO_2 0.3 or 0.8 during procedure. The primary outcome was the area under the curve (AUC) for high-sensitivity cardiac troponin I (hs-cTnI) during the first 72 h following TAVI. Secondary outcomes included the AUC for postprocedural creatine kinase-myocardial band (CK-MB), acute kidney injury and recovery, conduction abnormalities, pacemaker implantation, stroke, myocardial infarction, and in-hospital mortality.

Results

Between October 2017 and April 2022, 72 patients were randomized and 62 were included in the final analysis (n = 31 per group). The median (IQR) AUC for hs-cTnI in the first 72 h was 42.66 (24.82–65.44) and 71.96 (35.38–116.34) h·ng/mL in the F_IO_2 0.3 and 0.8 groups, respectively (p = 0.066). The AUC for CK-MB in the first 72 h was 257.6 (155.6–322.0) and 342.2 (195.4–485.2) h·ng/mL in the F_IO_2 0.3 and 0.8 groups, respectively (p = 0.132). Acute kidney recovery, defined as an increase in the estimated glomerular filtration rate $\geq$ 25% of baseline in 48 h, was more common in the F_IO_2 0.3 group (65% vs. 39%, p = 0.042). Other clinical outcomes were comparable between the groups.

Conclusions

The F_IO_2 level did not have a significant effect on periprocedural myocardial injury following TAVI. However, considering the marginal results, a benefit of low F_IO_2 during TAVI could not be ruled out.

Introduction

Although a fraction of inspired oxygen (F_IO_2) higher than that of ambient air is generally used during general anesthesia, there is continuing debate about the optimal F_IO_2. High oxygen tension is beneficial for reducing surgical site infection and in 2016 World Health Organization recommended that adults receive F_IO_2 0.8 during mechanical ventilation under general anesthesia [1]. However, a more recent systematic review found no difference in the surgical site infection rate according to the intraoperative F_IO_2 amount, and suggested a negative effect of high F_IO_2 on long-term outcomes [2]. Other investigators did not find any difference in the degree of myocardial injury between perioperative F_IO_2 0.3 and 0.8, and suggested that F_IO_2 0.8 is safe for major non-cardiac surgery [3].

High oxygen tension may cause oxidative stress, coronary vasoconstriction, and altered microvascular perfusion, resulting in adverse systemic effects including myocardial injury [4]. In a meta-analysis of acute myocardial infarction (MI), there was no evidence to support the routine use of oxygen treatment and the authors could not rule out a harmful effect of unnecessary oxygen therapy [5]. Constant and brief intermittent hyperoxia both induced inflammatory responses and cytotoxicity in cardiomyocytes from adult humans [6]. Although myocardial injury is common following transcatheter aortic valve implantation (TAVI) [7], even minor elevation of troponin I [8] in low-risk patients [9] was associated with poor postoperative outcomes after noncardiac surgery [10]. Moreover, abnormally increased cardiac biomarkers were associated with poor outcomes including periprocedural kidney injury and 30-day and 1-year mortality following TAVI [11].

The relationship between the F_IO_2 level and myocardial injury has not been well studied in patients undergoing TAVI. In this study, we investigated the effects of low (0.3) and high (0.8) F_IO_2, using the most widely studied fractions to compare different clinical impact of low vs. high oxygen contents [2], during transfemoral TAVI under general anesthesia on post-procedural myocardial injury, as indexed by serum cardiac troponin in the early post-TAVI period.

Methods

Ethics approval

This randomized controlled trial was approved by the Institutional Review Board of Seoul National University Hospital (#1707-109-871, on September 11, 2017) and registered at clinicaltrials.gov (NCT03291210, on September 25, 2017) before patient enrollment. The study was conducted according to the Good Clinical Practice guidelines and Declaration of Helsinki. Written informed consent was obtained from all participants, who could withdraw at any time.

Study population and randomization

Adults (aged 20–99 years) with aortic stenosis (AS), undergoing elective TAVI under general anesthesia via the transfemoral approach in a single tertiary academic center (Seoul National

University Hospital, South Korea), were eligible for the study. Eligibility for TAVI was determined based on the consensus of an institutional multidisciplinary heart team, including clinical cardiologists, cardiac interventionists, cardiac surgeons, imaging specialists, and anesthesiologists, and followed the current practice guidelines [12,13]. The predicted operative mortality risk was calculated using the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score, European System for Cardiac Operative Risk Evaluation (EuroSCORE) II, and logistic EuroSCORE. The heart team determined the anesthetic method (general anesthesia or conscious sedation) based on the patients' comorbidities, preference, and ability to maintain a supine position without profound dyspnea or restlessness during the procedure. The exclusion criteria were a non-transfemoral approach, pre-procedural arterial partial pressure of oxygen (PaO_2) <65 mmHg or receiving oxygen treatment, severe pre-procedural renal dysfunction (defined as an estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m^2), chronic pulmonary obstructive disease or symptomatic asthma, tuberculosis-destroyed lung, history of lung cancer, acute coronary syndrome within the past 6 months, documented pre-procedural cardiac troponin I (cTnI) or creatine kinase-myocardial band (CK-MB) elevation, stroke or transient ischemic attack within 6 months, pregnancy, and refusal to participate.

After enrollment and the informed consent process, the patients were randomized to receive F_IO_2 0.3 or 0.8 during TAVI (1:1 allocation ratio) (Fig 1). Block randomization (blocks of four or six) was conducted using a computer-generated program (Random Allocation Software, ver. 2.0; software.informer.com) by an independent research nurse (Y.L) on the morning of the intervention. The group assignments according to the randomization list were concealed in an opaque envelop by an independent nurse, and the concealed envelop was opened by an anesthesiology in charge just before anesthesia induction while patients, interventionists, and data analyzers were blinded to the group allocations. Involved patients and interventionists could not see the F_IO_2 settings as they were blinded with a screen. However, anesthesiologists in charge of intraprocedural patient management could not be blinded as they monitored and controlled F_IO_2 during the procedure. Group allocation concealment was kept until data analyses.

Study protocol

The routine monitoring techniques of our institution for patients under general anesthesia were applied, except F_IO_2 management. Without premedication, 12-lead electrocardiogram, pulse oxygen saturation (SpO_2), invasive and noninvasive arterial blood pressure, cerebral oxygen saturation ($ScrbO_2$), and bispectral index monitoring were performed. Left and right $ScrbO_2$ were measured using near-infrared spectroscopy (Somanetics INVOS oximeter; Covidien, Mansfield, MA, USA). Transesophageal or transthoracic echocardiography was performed to evaluate the valve position and presence of paravalvular regurgitation, as required by the interventionists.

Before inducing anesthesia, all participants were preoxygenated for 3 min using an anesthesia machine (Primus; Drägerwerk, Lubeck, Germany) with F_IO_2 0.3 or 0.8 according to the group allocation. After stabilization, general anesthesia was induced and maintained by a target-controlled infusion of propofol (effect-site concentration [Ce], 2.5–4.0 μg/mL) and remifentanil (Ce, 1.0–4.0 ng/mL) using a commercial infusion pump (Orchestra, Fresenius Vial, Brézins, France). Neuromuscular blockade was established by administering rocuronium (0.6 mg/kg). Then the trachea was intubated and the lungs were ventilated in volume-controlled mode with a tidal volume of 0.6–0.8 mL/kg and ventilatory rate of 9–12 /min to maintain end-tidal CO_2 35–45 mmHg. The alveolar recruitment maneuver was performed at 25 cmH_2O for 10 s after tracheal intubation, and a positive end-expiratory pressure of 5 cmH_2O was applied

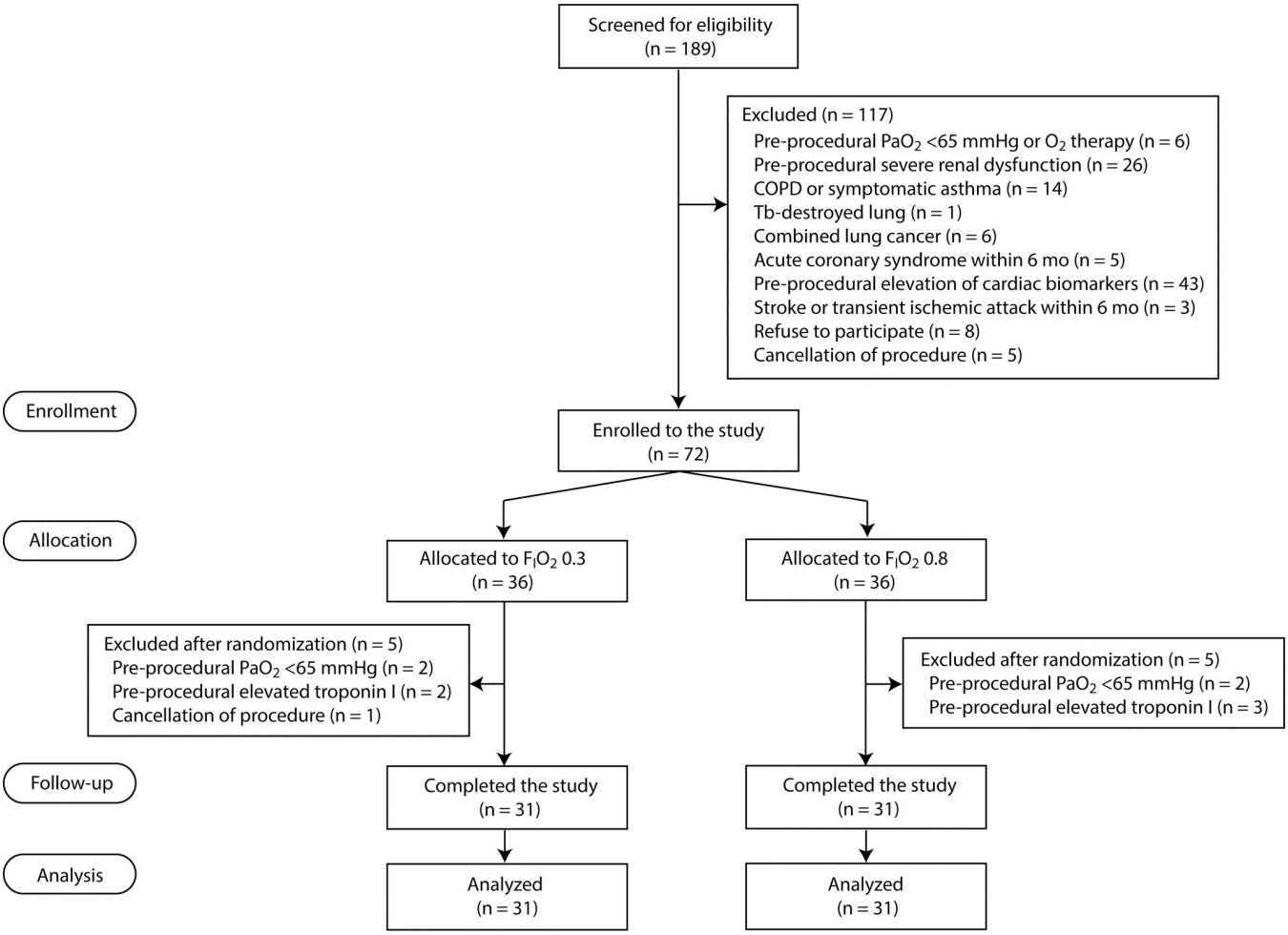

Fig 1. CONSORT diagram. CK-MB, creatine kinase-myocardial band; COPD, chronic obstructive pulmonary disease; F_IO_2, fraction of inspired oxygen; PaO_2, arterial partial pressure of oxygen.

https://doi.org/10.1371/journal.pone.0281232.g001

in all patients. According to the group assignment, F_IO_2 was maintained at 0.3 or 0.8 until the end of the TAVI procedure, unless the SpO_2 was <93%. If desaturation occurred, F_IO_2 was increased by 0.05–0.1, and an additional alveolar recruitment maneuver was performed as needed to maintain SpO_2 ≥93% by the attending anesthesiologists. Treatment of desaturation was triggered by low SpO_2 rather than PaO_2 from ABGA, as SpO_2 deterioration could be recognized promptly, and immediate intervention could be delivered. On completing the procedure, 100% O_2 was provided to all patients during anesthesia emergence. Patients were extubated in the intervention room, monitored in the cardiovascular care unit for 1–2 days, and then transferred to a general ward. Patients were discharged 5–7 days post-TAVI if they had no procedure-related complications.

The TAVI was conducted in accordance with the standard procedures in our institution. Using a transfemoral approach, a balloon-expandable Sapien III valve (Edwards Lifesciences, Irvine, CA, USA), self-expandable Evolut Pro or R valve (Medtronic, Minneapolis, MN, USA), or Lotus valve (Boston Scientific, Natick, MA, USA) was implanted at the diseased aortic valve. The valve was chosen by the heart team based on the size and structure of the native valve and sinus, heights of the coronary artery openings, and considerations regarding future coronary access, the risk of conduction disturbances, and annular calcification. The iliofemoral arteries

were accessed under fluoroscopic guidance and closed percutaneously using Perclose ProGlide vascular suture-mediated closure devices (Abbott Vascular Devices, Redwood City, CA, USA). Before the procedure, the patients were given loading doses of dual antiplatelet agents: acetylsalicylic acid and clopidogrel (both 300 mg). During the procedure, the patients were heparinized with unfractionated heparin to achieve an activated clotting time >250 s. At completion of the valve implantation, the effects of heparin were reversed by protamine infusion.

During the procedure, arterial blood gas analysis (ABGA) was performed at four time points: baseline (before anesthesia induction, T1), after inducing general anesthesia (T2), after valve implantation (T3), and at the end of the procedure (T4). ABGA was performed using a GEM® Premier 3000 device (Model 5700; Instrumentation Laboratory, Lexington, MA, USA). Oxygenation variables, including PaO_2, arterial oxygen saturation (SaO_2), SpO_2, and $ScrbO_2$, were recorded at the same time with ABGA measurements. During the procedure, transfusion was triggered to maintain hematocrit 21–24% or by clinical judgement of anesthesiologists in charge based on ongoing blood loss and patients' comorbidity. Trigger to treat hypotension was systolic blood pressure <90 mmHg or ≥20% drop from baseline.

Two serum cardiac biomarkers of myocardial injury, high-sensitivity cTnI (hs-cTnI) and CK-MB, were measured at baseline (before the procedure) and 1, 4, 8, 24, 48, and 72 h after TAVI. hs-cTnI was measured using an Abbott Architect Plus Analyzer (i2000SR; Flex, San Jose, CA, USA), which has a limit of detection of 0.0011 μg/L and limit of blank of 0.0007–0.0013 μg/L. An hs-cTnI concentration ≥99^{th} percentile in the normal population (0.028 μg/L) was deemed abnormal. Serum creatinine concentrations were calibrated using isotope dilution mass spectrometry (IDMS). To evaluate the baseline kidney function, we calculated eGFR using the modified diet in renal disease (MDRD) Eq [14] as a surrogate of GFR, which was routinely adopted in our institution during the study period. Although Chronic Kidney Disease Epidemiology (CKD-EPI) creatinine equation had better performance compared with MDRD equation for high levels of GFR, equal accuracy has been observed when GFR is <60 mL/min/1.73 m^2 [15].

$$\text{IDMS MDRD eGFR} = 175 \times (\text{serum creatinine})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ for women})$$

Postprocedural acute kidney injury (AKI) was determined based on the serum creatinine level and urine output according to the Kidney Disease: Improving Global Outcomes Clinical Practice Guidelines criteria for AKI [16]. AKI was defined as an increase in serum creatinine ≥1.5 times the baseline level or by ≥0.3 mg/dL (≥26.5 μmol/L) [$AKI_{creatinine}$], or a urine output <0.5 mL/kg/h for ≥6 h within 7 days [$AKI_{urine\ output}$]. AKI occurring >7 days after the procedure was excluded because it might have been unrelated to the procedure. Acute kidney recovery (AKR) was defined as an increase in eGFR of ≥25% relative to baseline at 48 h post-TAVI [17]. Post-TAVI AKR has been acknowledged as a potential benefit following improvement of cardiac output with relief of aortic stenosis, and was observed in up to 1/3 of patients undergoing TAVI, occurring more frequently than AKI [18] and associated with improved survival than those who developed AKI [19].

The postprocedural development of new conduction abnormalities and incidence of permanent pacemaker insertion was assessed. Stroke was defined as an acute episode of a focal or global neurological deficit as a result of hemorrhage or infarction, based on the Valve Academic Research Consortium-2 (VARC-2) definition [20]. Periprocedural MI was defined based on a combination of new ischemic symptoms or signs and elevated cardiac biomarkers within 72 h following TAVI, according to the VARC-2 definition [20].

Postprocedural pulmonary complications, including reintubation, prolonged mechanical ventilation, and pneumonia, occurred within 7 days following the procedure or until discharge

were assessed. Prolonged mechanical ventilation was defined as requirement of mechanical ventilation for more than 12 h after procedure. Pneumonia was defined using the Centers for Disease Control and Prevention (CDC) criteria [21]. The CDC definition includes progressive infilrates, consolidation, or cavitation on chest radiography; either fever (>38˚C), leukopenia or luekoytosis, or altered mental status; and sputum changes suggesting infection, worsening cough or dyspnea, rales or bronchial breath sounds, or worsening gas exchange (hypoxemia, increased oxygen requirements, or increased ventilator demand) [21].

Study endpoints and sample size calculation

The primary study outcome was periprocedural myocardial injury, as reflected by the geometric area under the curve (AUC) for periprocedural serum hs-cTnI in the first 72 h post-TAVI, calculated according to the trapezoidal rule. Secondary outcomes were the AUC for serum CK-MB in the first 72 h post-TAVI, and the peak serum hs-cTnI and CK-MB levels in the same period. Post-procedural clinical outcomes were also evaluated, including AKI, AKR, new conduction abnormalities, permanent pacemaker insertion, stroke, MI, pulmonary complications, in-hospital cardiovascular mortality, and hospital length of stay.

To calculate the sample size, we conducted a pilot study of 10 patients undergoing transfemoral TAVI under general anesthesia. The AUC for serum hs-cTnI in the first 72 h after TAVI was 40.24 ± 28.16 ng/mL. To detect a 50% difference in hs-cTnI levels between the two treatment groups in the first 72 h, which was chosen to be clinically relevant by the study investigators, 32 patients were required for each group at 80% power and an alpha error of 5% when compared using an independent *t*-test using G*Power software package (ver. 3.1.9.2; Franz Faul, Universitat Kiel, Germany). Considering a 10% dropout rate, we recruited 36 patients to each group (a total of 72 patients).

Statistical analysis

Data are presented as the mean ± SD, median (interquartile range, IQR), or number (%) according to the data distribution. The primary endpoint, the AUC for serum hs-cTnI in the first 72 h post-TAVI, was analyzed using the independent *t*-test assuming the equal variance. For primary and secondary endpoints, sensitivity analysis was performed by using bootstrap inference for multiple imputation in the intention-to-treat dataset (n = 72). The bootstrap for multiple imputation was carried out with 2,000 bootstrap replicates and 10 multiple imputations by using functions bootMice and bootImputeAnalyse in the R package bootImpute. Missing values were replaced by using multivariate imputation by chained equations and an imputation model for each endpoint included the F_IO_2 group and baseline variables that achieved statistical significance at p value 0.2 via stepwise variable selection procedure in a linear regression model for each endpoint because of many variables (43 variables) compared to the number of observations.

Other continuous variables were analyzed using the independent *t*-test or Mann–Whitney *U* test according to the data distribution. Categorical variables were analyzed using Pearson's chi square test or Fisher's exact test. For repeated measures data, the groups were compared using a linear mixed-effects model, which included independent fixed effects for group, measurement time, and their interaction, and a random effect for subject (a random intercept), with a compound symmetry covariance structure. When the interaction between group and time was significant, mean difference between the groups at each measurement time (after induction, at valve implant, and at the end of procedure) was estimated by using linear contrast in the linear mixed-effects model and the p value from the linear contrast test was multiplied by 3 for Bonferroni correction for multiple comparisons. The analysis was done in an

intention-to-treat manner. All analyses were performed using IBM SPSS Statistics (ver. 21.0; IBM Corp., Armonk, NY, USA) or R software (ver. 3.5.1; R Development Core Team, Vienna, Austria). A p value <0.05 was considered statistically significant.

Results

Patients were screened for eligibility between October 18, 2017 and April 6, 2022. Of 189 patients, 117 were excluded based on the exclusion criteria (Fig 1). After 72 patients were randomized to the F_IO_2 0.3 or 0.8 groups (n = 36 each) and received their assigned F_IO_2 without deviation from random allocation, 10 patients were excluded due to pre-procedural PaO_2 <65 mmHg (n = 4), elevated pre-procedural cTnI (n = 5), or procedure cancellation (n = 1). We noted violations of the exclusion criteria (pre-procedural PaO_2 <65 mmHg or elevated cardiac biomarkers) in nine patients and excluded them from the analysis. Thus, a total of 62 patients (31 per group) were included in the final analysis. We performed additional sub-analysis including five patients (n = 2 in the F_IO_2 0.3 group and n = 3 in the F_IO_2 0.8 group) who had elevated cardiac biomarkers after randomization.

Tables 1 and 2 present the baseline characteristics of the included patients and procedural variables. Baseline characteristics were well balanced between the groups. The median (IQR) age of the included patients was 79 (77–83) years. The median (IQR) procedural duration was 80 (70–95) min.

During the procedure, PaO_2, SaO_2, and SpO_2 were higher in the F_IO_2 0.8 than F_IO_2 0.3 group (Fig 2). Two patients in the F_IO_2 0.3 group required adjustment of F_IO_2 to 0.4 during the procedure because transient SpO_2 <93% was observed. The mean left and right cerebral oximetry values were higher in the F_IO_2 0.8 than F_IO_2 0.3 group (Fig 2). For serial measurements, interactions between measurement time and group were significant for PaO_2, SaO_2, and the mean $ScrbO_2$ ($p<0.001$, <0.001, and 0.032, respectively), but not for SpO_2 (p = 0.330). Hemodynamics and hematocrit were comparable and well maintained in the two groups (S1 Fig).

The primary outcome, the AUC for serum hs-cTnI in the first 72 h post-TAVI, was higher in the F_IO_2 0.8 than F_IO_2 0.3 group (71.96 [35.38–116.34] vs. 42.66 [24.82–65.44] h·ng/mL), but the difference was not statistically significant (p = 0.114) (Table 3). The secondary outcome (AUC for CK-MB in the first 72 h post-TAVI) was also higher in the F_IO_2 0.8 group, but not significantly (342.2 [195.4–485.2] vs. 257.6 [155.6–322.0] h·ng/mL; p = 0.093). The peak hs-cTnI (1.79 [1.09–3.77] vs. 1.30 [1.00–1.58] ng/mL, p = 0.185) and CK-MB levels (10.9 [5.7–15.6] vs. 7.5 [6.0–11.9] ng/mL, p = 0.105) during the first 72 h post-TAVI were comparable in the F_IO_2 0.8 vs. 0.3 groups, respectively. For periprocedural serial measurements, the group differences in hs-cTnI and CK-MB did not reach statistical significance (p = 0.125 and 0.084, respectively; mixed model) (Table 4). The interaction between measurement time and group was not significant (p = 0.200 and 0.096 for hs-cTnI and CK-MB, respectively). When including the five patients who completed the study protocol and were excluded from the final analysis due to elevated baseline hs-cTnI after randomization, there were no significant differences in the AUCs for hs-cTnI and CK-MB in the first 72 h post-TAVI between the groups (S2 Fig).

The postprocedural incidence of AKI did not differ between F_IO_2 0.3 and 0.8 groups (36% vs. 42%; p = 0.602) (Table 5). However, AKR was more frequent in the F_IO_2 0.3 than F_IO_2 0.8 group (65% vs. 39%; p = 0.042). Other postprocedural clinical outcomes, such as pulmonary complications, cardiovascular mortality or hospital length of stay, were comparable between the two groups (Table 5).

Two patients experienced complications during the procedure. One patient in the F_IO_2 0.3 group developed vascular tear from the right external iliac extending to the common femoral artery and received immediate surgical primary repair of the injured vessels. In one patient in

Table 1. Baseline characteristics in patients undergoing transfemoral transcatheter aortic valve implantation.

	F_IO_2 0.3 (n = 31)	F_IO_2 0.8 (n = 31)
Demographics		
Age, yr	79 (76–82 [range 64–90])	79 (77–84 [range 58–94])
Male	12 (39%)	12 (39%)
Height, cm	156 ± 10.0	157 ± 10
Weight, kg	59.1 ± 10.7	60.0 ± 11.0
Body mass index, kg/m^2	24.29 ± 3.72	24.42 ± 3.69
Body surface area, m^2	1.58 ± 0.17	1.59 ± 0.18
Current smoker	1 (3%)	0 (0%)
NYHA functional class		
I	8 (26%)	6 (19%)
II	14 (45%)	18 (58%)
III/IV	9 (29%)	7 (23%)
Predicted risk calculation		
STS PROM, %	2.759 (1.936–3.724)	3.162 (2.370–4.060)
EuroSCORE II, %	2.72 (1.64–3.95)	3.54 (1.35–7.01)
Logistic EuroSCORE, %	4.52 (1.56–7.46)	4.83 (1.95–7.01)
Echocardiographic and CT data		
LV EF, %	63 (59–67)	66 (61–68)
AV area, cm^2	0.7 (0.6–0.8)	0.7 (0.6–0.9)
AV peak velocity, m/s	4.6 ± 0.4	4.6 ± 0.6
AV mean pressure gradient, mmHg	49 (44–60)	50 (43–66)
AV perimeter, mm	73.0 ± 6.4	72.0 ± 5.6
LVIDd, mm	46 (42–50)	46 (41–49)
LVIDs, mm	28 (25–32)	27 (24–31)
Stroke volume, mL	77 ± 22	81 ± 17
Height of LMCA os from annulus, mm	12.7 ± 2.4	12.2 ± 2.2
Height of RCA os from annulus, mm	14.7 ± 2.3	14.2 ± 2.5
Baseline laboratory findings		
Hematocrit, %	36.0 ± 4.3	34.8 ± 4.6
eGFR, ml/min/1.73 m^2	67.5 ± 16.9	66.5 ± 16.0
Creatinine, mg/dL	0.88 (0.81–1.05)	0.91 (0.76–1.13)
Albumin, g/dL	4.0 (3.9–4.3)	4.0 (3.7–4.3)
hs-cTnI, ng/mL	0.00 (0.00–0.00)	0.00 (0.00–0.00)
CK-MB, ng/mL	1.1 (1.1–1.4)	1.0 (0.8–1.2)
hs-CRP, mg/dL	0.07 (0.04–0.33)	0.07 (0.04–0.14)
Comorbidities		
Hypertension	26 (84%)	22 (71%)
Diabetes	7 (23%)	11 (36%)
Dyslipidemia	17 (55%)	21 (68%)
Coronary artery disease	6 (19%)	7 (23%)
Angina/previous MI	7 (23%)	6 (19%)
Medications		
Aspirin	13 (42%)	13 (42%)
Anti-platelet agents	12 (39%)	16 (52%)
Non-vitamin K anticoagulants	3 (10%)	3 (10%)
Beta-blockers	19 (61%)	16 (52%)

(*Continued*)

Table 1. (Continued)

	F_IO_2 0.3 (n = 31)	F_IO_2 0.8 (n = 31)
ARB/ACEi	20 (65%)	18 (58%)
Calcium channel blockers	11 (36%)	15 (48%)
Oral hypoglycemic agents	8 (26%)	9 (29%)
Diuretics	17 (55%)	14 (45%)
Nitrates	6 (19%)	4 (13%)
Statin	19 (61%)	22 (71%)

Values are median (interquartile range), n (%), or mean ± SD.

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; AV, aortic valve; CK-MB, creatine kinase-myocardial band; COPD, chronic obstructive pulmonary disease; CT, computed tomography; EF, ejection fraction; eGFR, estimated glomerular filtration rate; EuroSCORE, European System for Cardiac Operative Risk Evaluation; F_IO_2, fraction of inspired oxygen; hs-CRP, high-sensitivity C-reactive protein; hs-cTnI, high-sensitivity cardiac troponin I; LMCA, left main coronary artery; LV, left ventricular; LVIDd, left ventricular internal diameter end diastole; LVIDs, left ventricular internal diameter end systole; MI, myocardial infarction; NYHA, New York Heart Association; RCA, right coronary artery; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TIA, transient ischemic attack.

https://doi.org/10.1371/journal.pone.0281232.t001

the F_IO_2 0.8 group, intramural hematoma of the ascending aorta was found on the computed tomography scan following the procedure, which resolved without further intervention.

Discussion

Compared to the F_IO_2 0.3 group, the F_IO_2 0.8 group showed a greater postprocedural elevation of cardiac biomarkers, albeit without statistical significance. Postprocedural AKR was more

Table 2. Valve characteristics and procedural variables in patients undergoing transfemoral transcatheter aortic valve implantation.

	F_IO_2 0.3 (n = 31)	F_IO_2 0.8 (n = 31)
Prosthetic valve type		
Sapien III	13 (42%)	14 (45%)
Evolut Pro or R	15 (48%)	12 (39%)
Lotus valve	3 (10%)	5 (16%)
Prosthetic valve size, mm		
23	6 (19%)	9 (29%)
25	1 (3%)	2 (7%)
26	18 (58%)	14 (45%)
29	6 (19%)	6 (19%)
Paravalvular regurgitation		
No	12 (39%)	13 (42%)
Trivial	9 (29%)	15 (48%)
Mild	9 (29%)	2 (7%)
Moderate	1 (3%)	1 (3%)
Procedure duration, min	80 (70–95)	80 (70–95)
Anesthesia duration, min	140 (120–155)	135 (120–160)
Amount of contrast media, mL	250 (200–288)	250 (210–326)
Transfusion of pRBC, unit	0 (0–1)	0 (0–1)

Values are n (%) or median (interquartile range).

F_IO_2, fraction of inspired oxygen; pRBC, packed red blood cell.

https://doi.org/10.1371/journal.pone.0281232.t002

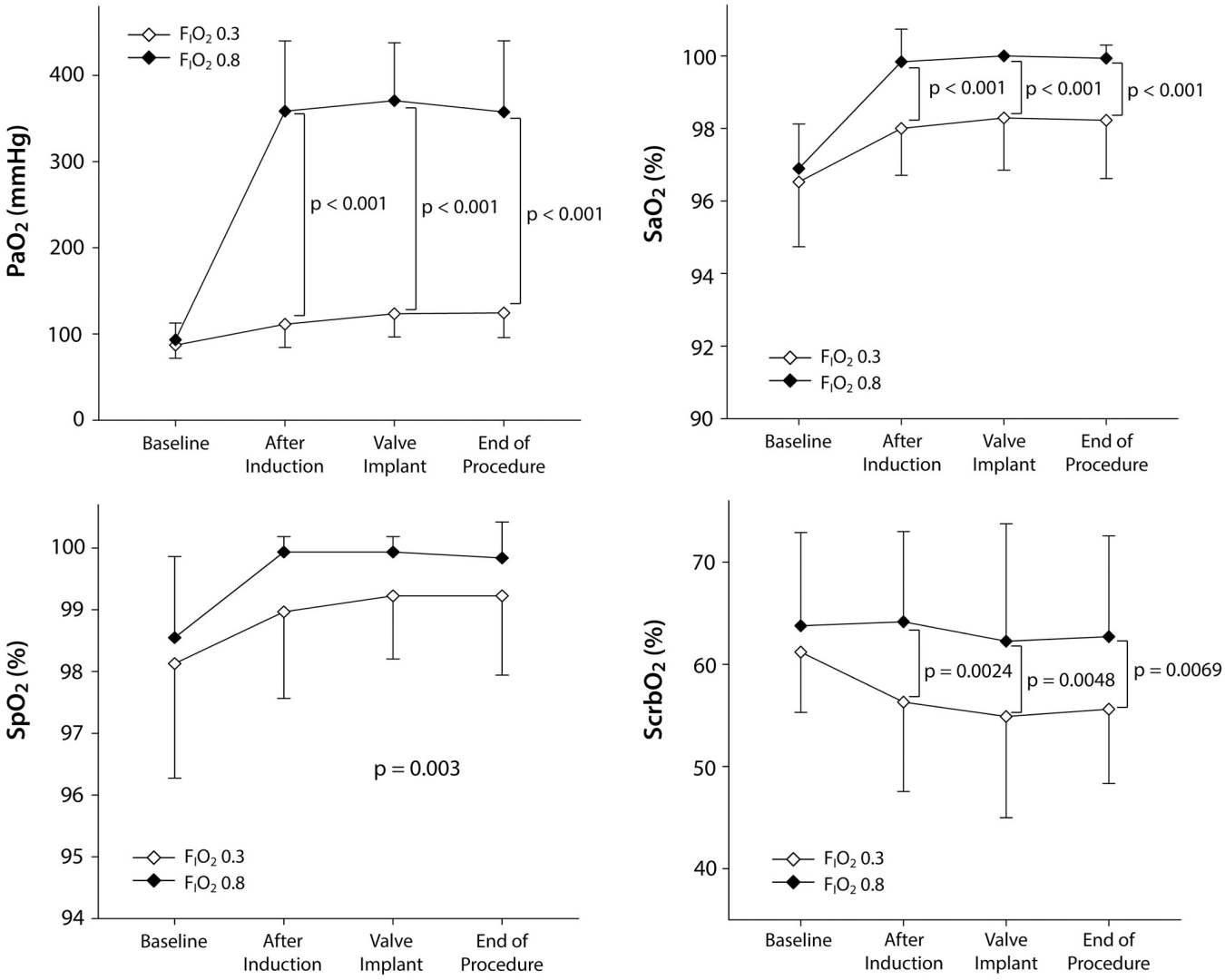

Fig 2. Changes in arterial oxygenation, pulse oxygen saturation, and cerebral oximetry in patients receiving a fraction of inspired oxygen of 0.3 or 0.8 during transcatheter aortic valve implantation. F_IO_2, fraction of inspired oxygen; PaO_2, arterial partial pressure of oxygen; SaO_2, arterial oxygen saturation; SpO_2, pulse oxygen saturation; $ScrbO_2$, mean cerebral oxygen saturation.

https://doi.org/10.1371/journal.pone.0281232.g002

frequent in the F_IO_2 0.3 group. There was no difference in other periprocedural outcomes between the groups.

Myocardial injury after TAVI

Even after successful TAVI, the cardiac biomarkers cTnI and CK-MB showed post-procedure increases despite prompt relief of transvalvular pressure overload, and periprocedural myocardial injury occurred along with transient deterioration in myocardial function [22]. Significant deterioration in the myocardial performance index, which implies both systolic and diastolic dysfunction, was observed immediately following TAVI [22]. New myocardial late enhancement with an ischemic pattern, indicating myocardial damage, was detected on cardiac magnetic resonance images following both balloon-expandable and self-expandable valve implantation [23].

Table 3. Postprocedural variables in patients received fraction of inspired oxygen 0.3 or 0.8 during transfemoral transcatheter aortic valve implantation.

	F_IO_2 0.3 (n = 31)	F_IO_2 0.8 (n = 31)	p value
Echocardiographic data (at discharge)			
LV EF, %	63 (60–67)	65 (62–69)	0.140
AV area, cm^2	1.8 (1.5–2.1)	1.6 (1.3–1.9)	0.126
AV peak velocity, m/s	2.2 ± 0.4	2.3 ± 0.5	0.350
AV mean pressure gradient, mmHg	10 (6–13)	11 (8–14)	0.386
LVIDd, mm	45 (42–48)	45 (43–47)	0.854
LVIDs, mm	27 (25–31)	27 (25–30)	0.685
Stroke volume, mL	74 ± 24	71 ± 17	0.538
Pulmonary complications			
Reintubation	0	0	
Prolonged mechanical ventilation	0	0	
Pneumonia	1 (3%)	1 (3%)	> 0.999
Peak creatinine within 7 days, mg/dL	0.87 (0.77–0.99)	0.89 (0.74–1.16)	0.508
Peak hs-CRP within 72 h, mg/dL	3.71 ± 2.21 4.14 (1.56–5.22)	4.38 ± 3.23 4.25 (2.01–5.84)	0.393 0.694
AKI within 7 days	11 (36%)	13 (42%)	0.602
$AKI_{creatinine}$	0 (0%)	3 (10%)	0.238
$AKI_{urine\ output}$	11 (36%)	12 (39%)	0.793
AKR within 48 h	20 (65%)	12 (39%)	0.042
Both AKI and AKR	7 (23%)	3 (10%)	0.167
New conduction abnormality	15 (48%)	11 (36%)	0.303
PPM insertion	3 (10%)	4 (13%)	> 0.999
Stroke	1 (3%)	1 (3%)	> 0.999
Myocardial infarction	0	0	
In-hospital mortality	0	0	
Post-procedural hospital length of stay, days	6 (5–7)	5 (5–7)	0.403

Values are median (interquartile range), mean ± SD, or n (%). AKI was defined as an increase in serum creatinine ≥ 1.5 times the baseline level or by ≥ 0.3 mg/dL (≥ 26.5 μmol/L) for [$AKI_{creatinine}$], or urine output < 0.5 mL/kg/h for ≥ 6 h within 7 days for [$AKI_{urine\ output}$].

AKI, acute kidney injury; AKR, acute kidney recovery; AV, aortic valve; EF, ejection fraction; F_IO_2, fraction of inspired oxygen; LV, left ventricular; LVIDd, left ventricular internal diameter end diastole; LVIDs, left ventricular internal diameter end systole; PPM, permanent pacemaker.

https://doi.org/10.1371/journal.pone.0281232.t003

Table 4. Results of linear mixed models for repeated measures of cardiac biomarkers for 72 h following procedure.

Cardiac biomarker	Model with group*time interaction		Model with main effects	
	Effect	Overall p value	Overall p value	Mean difference (95% CI)
hs-cTnI	Group	0.125	0.125	0.299 (-0.085 to 0.683)
	Time	< 0.001	< 0.001	
	Group*time (interaction)	0.200	-	
CK-MB	Group	0.084	0.084	1.131 (-0.182 to 2.807)
	Time	< 0.001	< 0.001	
	Group*time (interaction)	0.096	-	

CI, confidence interval; CK-MB, creatine kinase-myocardial band; hs-cTnI, high-sensitivity cardiac troponin I.

https://doi.org/10.1371/journal.pone.0281232.t004

Transient LV dysfunction and injury following TAVI seems to be partly influenced by procedural aspects of transcatheter valve deployment [24]. Procedure-related mechanical trauma during TAVI, including during balloon valvuloplasty, valve positioning, and prosthesis delivery, also plays a substantial role in myocardial damage [25]. Rapid ventricular pacing is used to temporarily reduce the LV output during pre-implantation balloon valvuloplasty and balloon-expandable valve implantation, and for post-implantation ballooning to reduce paravalvular leakage. Rapid ventricular pacing transiently reduces microvascular tissue perfusion and the flow index in small- and medium-sized vessels, and induces partial microcirculatory arrest and delayed recovery of microflow [26]. Subsequently, ventricular stunning and subsequent dysfunction may occur [24].

Hyperoxia and myocardial injury

The role of oxidative stress in reperfusion injury is relatively well established. Abrupt oxidative reactions following reperfusion produce reactive oxygen species (ROS) from cardiomyocytes and endothelial cells, which amplifies local inflammatory responses and leads to a vicious cycle of ROS production [27]. The biological mechanism underlying the adverse effects of hyperoxia is related to the generation of ROS, specifically the superoxide anion, which has a negative impact on coronary blood flow and LV distensibility [28]. Hyperoxia can exacerbate oxidative stress and thereby worsen coronary vasoconstriction and myocardial injury. Interestingly, hyperoxic reperfusion limited myocardial necrosis in rodents with cardiovascular risk factors more so than in a normoxemic reperfusion group, while the reverse occurred in healthy rodents [27]. Similarly, in a preliminary canine MI model, administering 100% oxygen had beneficial effects on the myocardium by reducing myocardial infarct size and improving the EF after reperfusion compared to room-air ventilation [29].

However, in the AVOID trial, patients presenting with acute MI were randomized to receive oxygen 8 L/min via face mask or ambient air, and oxygen treatment increased myocardial injury and infarct size in patients without hypoxia [30]. In patients admitted to the intensive care unit (ICU), conservative use of oxygen, which aimed to maintain arterial oxygen tension within the physiological range, reduced ICU mortality compared to conventional use of oxygen [31]. In the large randomized DETO2X-AMI study, there was no difference in 1-year mortality or the peak cardiac troponin level between patients with suspected MI who received supplemental oxygen versus ambient air [32]. During general anesthesia for major non-cardiac surgery, there was no difference in myocardial injury—assessed using the AUC for high-sensitive troponin in the first 3 postoperative days—between F_IO_2 0.3 and 0.8 administered intraoperatively and for 2 h after surgery [3]. In the ICU-ROX study, conservative use of F_IO_2 ($\leq$0.21) during mechanical ventilation in adult ICU patients resulted in no difference in the number of ventilator-free days compared to standard administration of F_IO_2 [33]. In a more recent nationwide registry trial, high oxygen supplementation (6–8 L/min by face mask) resulted in no significant difference in the 30-day or 1-year mortality rate in patients with suspected acute coronary syndrome compared to low oxygen treatment [34].

Myocardial injury and clinical outcomes after TAVI

Cardiac biomarkers elevation following surgery or intervention result from perioperative hemodynamic stress, inflammation, or oxygen supply and demand imbalance [35]. Periprocedural myocardial injury following TAVI was associated with a significantly increased risk of poor short- and long-term clinical outcomes, including 30-day and 1-year mortality, neurological events, and postprocedural permanent pacemaker implantation [36].

Table 5. Sensitivity analysis results for primary and secondary outcomes.

	Final analysis dataset (n = 62) p value	ITT dataset (n = 72) p value
Primary outcome		
AUC for serum hs-cTnI in the first 72 h post-TAVI	0.107	0.114
Secondary outcomes		
AUC for CK-MB in the first 72 h post-TAVI	0.132	0.093
Peak hs-cTnI in the first 72 h post-TAVI	0.051	0.185
Peak CK-MB in the first 72 h post-TAVI	0.159	0.105

AUC, area under the curve; CK-MB, creatine kinase-myocardial band; hs-cTnI, high-sensitivity cardiac troponin I; ITT, intention-to-treat.

https://doi.org/10.1371/journal.pone.0281232.t005

In our study, high oxygen tension during TAVI tended to increase the release of cardiac biomarkers in the first 72 h post-TAVI compared to the low oxygen tension group, but the difference was not significant. There was no clinical impact of the level of intraoperative oxygen tension during TAVI, except that recovery of kidney function was more common in the low- compared to the high-F_IO_2 group.

Acute kidney recovery

Acute kidney recovery, which is a relatively recently described phenomenon, has been observed more frequently than AKI after both TAVI and surgical aortic valve replacement (SAVR) [37]. Following TAVI or SAVR, normalization of the aortic valve area, prompt relief of the trans-aortic pressure gradient, and normalization of post-stenotic flow abnormality occur. Regarding renal blood flow, a rapid increase in cardiac output and reduced LV afterload may cause abrupt hemodynamic changes in the early postprocedural period, such as renal congestion. In a recent prospective registry analysis, both AKI and AKR early after TAVI were independent predictors of cardiovascular mortality [38]. In our study cohort, 10 of the 62 (16%) patients met the criteria for both AKI and AKR during the study period (Table 5). Rapid changes in renal hemodynamics could have occurred in these groups, and both post-TAVI AKI and AKR may reflect a cardiorenal aspect of the extra-cardiac damage characterizing severe AS. Further studies are required to assess the relationship between renal circulatory changes and clinical outcomes in AS patients following TAVI.

Study limitations

This study has some limitations. First, it was a single-center trial with limited number of included patients, and was only powered for one surrogate cardiac biomarker, hs-cTnI. To evaluate the effects of deteriorated power and bias on study data, we performed sensitivity analysis by using bootstrap inference for multiple imputation in the intention-to-treat dataset. Although we observed a trend toward reduced hs-cTnI release and better postprocedural kidney recovery, we cannot definitely conclude that arterial oxygenation is beneficial for patients undergoing TAVI in terms of periprocedural myocardial and renal protection. Second, we included patients undergoing general anesthesia for transfemoral TAVI in this study. However, many patients undergo TAVI under conscious sedation or even local anesthesia, unless they are at very high periprocedural risk due to severely compromised cardiopulmonary function or the inability to maintain a stable supine position, for example. Although conscious sedation is increasingly provided to patients undergoing transfemoral TAVI than general anesthesia [39], anesthetic protocol is determined considering patients' comorbidity and

practitioners' preference and based on the institutional practice. As many centers, including ours, perform TAVI under general anesthesia [39], our results may contribute to establishing oxygen treatment strategy in this practical context. Future investigators could compare the oxygenation strategies of minimal supplemental oxygen and no supplemental oxygen, as in the treatment of acute MI patients without hypoxia, in terms of the likelihood of avoiding unnecessary periprocedural oxidative stress and protecting multiple organ systems, in patients undergoing TAVI under conscious sedation or local anesthesia. Third, we included relatively low-risk patients; we excluded those who were already hypoxemic or required supplemental oxygen, and those with acute coronary syndrome or renal failure. In high-risk patients with severe LV dysfunction or poor oxygenation, however, different supplemental oxygen strategies may have a differential impact on myocardial injury and other clinical outcomes. Therefore, further studies are required of high-risk patients, who may be more suitable candidates for TAVI. Lastly, there is lack of control subjects undergoing SAVR in evaluating oxygenation and perioprocedural myocardial injury in this study. As it is beyond the primary aim of the present study, future studies can be conducted regarding periprocedural oxygen content and myocardial injury in patients undergoing TAVI vs. SAVR.

Conclusions

In conclusion, the F_IO_2 level did not have a significant effect on periprocedural myocardial injury following TAVI with general anesthesia. However, considering the marginal results, a benefit of low F_IO_2 during TAVI could not be ruled out.

Supporting information

S1 Checklist. CONSORT 2010 checklist of information to include when reporting a randomised trial*.
(DOC)

S1 Fig. Intraprocedural changes in hemodynamic variables and hematocrit in patients received a fraction of inspired oxygen of 0.3 or 0.8 during transcatheter aortic valve impalntation. HR, heart rate; MBP, mean blood pressure; SBP, systolic blood pressure.
(TIF)

S2 Fig. Changes in cardiac biomarkers in the first 72 h in patients including five patients who were excluded from the main analysis due to pre-procedural elevation of cardiac biomarkers after randomization and received a fraction of inspired oxygen of 0.3 or 0.8 during transcatheter aortic valve implantation. AUC, area under the curve; CK-MB, creatine kinase-myocardial band; hs-cTnI, high sensitivity cardiac troponin I; TAVI, transcatheter aortic valve implantation.
(TIF)

S1 File.
(DOCX)

S2 File.
(PDF)

Acknowledgments

The authors gratefully acknowledge Sun-Young Jung, a statistician, who is collaborating with our institution, for her assistance in the statistical analysis and invaluable advice and

comments. We also thank to the Medical Research Collaborating Center of Seoul National University Hospital for their dedicated support and advice concerning the statistical analyses.

Author Contributions

Conceptualization: Youn Joung Cho, Hyo-Soo Kim, Yunseok Jeon.

Data curation: Cheun Hyeon, Seohee Lee.

Formal analysis: Youn Joung Cho.

Investigation: Karam Nam, Jae-Woo Ju, Jung-Kyu Han.

Methodology: Youn Joung Cho, Karam Nam, Jeehoon Kang, Jung-Kyu Han.

Project administration: Karam Nam, Hyo-Soo Kim.

Resources: Cheun Hyeon, Jae-Woo Ju.

Software: Seohee Lee, Jae-Woo Ju.

Supervision: Seohee Lee, Jeehoon Kang, Jung-Kyu Han, Hyo-Soo Kim, Yunseok Jeon.

Validation: Jeehoon Kang.

Visualization: Cheun Hyeon.

Writing – original draft: Youn Joung Cho.

Writing – review & editing: Yunseok Jeon.

References

1. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis 2016; 16: e288–e303. https://doi.org/10.1016/S1473-3099(16)30402-9 PMID: 27816414
2. Fasquel C, Huet O, Ozier Y, Quesnel C, Garnier M. Effects of intraoperative high versus low inspiratory oxygen fraction (FiO2) on patient's outcome: A systematic review of evidence from the last 20 years. Anaesth Crit Care Pain Med 2020; 39: 847–858. https://doi.org/10.1016/j.accpm.2020.07.019 PMID: 33038560
3. Holse C, Aasvang EK, Vester-Andersen M, Rasmussen LS, Wetterslev J, Christensen R, et al. Hyperoxia and Antioxidants for Myocardial Injury in Noncardiac Surgery: A 2 x 2 Factorial, Blinded, Randomized Clinical Trial. Anesthesiology 2022; 136: 408–419. https://doi.org/10.1097/ALN.0000000000004117 PMID: 35120193
4. Damiani E, Donati A, Girardis M. Oxygen in the critically ill: friend or foe? Curr Opin Anaesthesiol 2018; 31: 129–135. https://doi.org/10.1097/ACO.0000000000000559 PMID: 29334496
5. Cabello JB, Burls A, Emparanza JI, Bayliss SE, Quinn T. Oxygen therapy for acute myocardial infarction. Cochrane Database Syst Rev 2016; 12: CD007160. https://doi.org/10.1002/14651858.CD007160.pub4 PMID: 27991651
6. Hafner C, Wu J, Tiboldi A, Hess M, Mitulovic G, Kaun C, et al. Hyperoxia Induces Inflammation and Cytotoxicity in Human Adult Cardiac Myocytes. Shock 2017; 47: 436–444. https://doi.org/10.1097/SHK.0000000000000740 PMID: 27648689
7. Carrabba N, Valenti R, Migliorini A, Vergara R, Parodi G, Antoniucci D. Prognostic value of myocardial injury following transcatheter aortic valve implantation. Am J Cardiol 2013; 111: 1475–1481. https://doi.org/10.1016/j.amjcard.2013.01.301 PMID: 23465097
8. van Waes JA, Grobben RB, Nathoe HM, Kemperman H, de Borst GJ, Peelen LM, et al. One-Year Mortality, Causes of Death, and Cardiac Interventions in Patients with Postoperative Myocardial Injury. Anesth Analg 2016; 123: 29–37. https://doi.org/10.1213/ANE.0000000000001313 PMID: 27111647
9. Vasireddi SK, Pivato E, Soltero-Mariscal E, Chava R, James LO, Gunzler D, et al. Postoperative Myocardial Injury in Patients Classified as Low Risk Preoperatively Is Associated With a Particularly Increased Risk of Long-Term Mortality After Noncardiac Surgery. J Am Heart Assoc 2021; 10: e019379. https://doi.org/10.1161/JAHA.120.019379 PMID: 34151588

10. van Waes JA, Nathoe HM, de Graaff JC, Kemperman H, de Borst GJ, Peelen LM, et al. Myocardial injury after noncardiac surgery and its association with short-term mortality. Circulation 2013; 127: 2264–2271. https://doi.org/10.1161/CIRCULATIONAHA.113.002128 PMID: 23667270

11. Barbash IM, Dvir D, Ben-Dor I, Badr S, Okubagzi P, Torguson R, et al. Prevalence and effect of myocardial injury after transcatheter aortic valve replacement. Am J Cardiol 2013; 111: 1337–1343. https://doi.org/10.1016/j.amjcard.2012.12.059 PMID: 23415511

12. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014; 129: e521–643. https://doi.org/10.1161/CIR.0000000000000031 PMID: 24589853

13. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017; 135, e1159–e1195. https://doi.org/10.1161/CIR.0000000000000503 PMID: 28298458

14. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006; 145: 247–254. https://doi.org/10.7326/0003-4819-145-4-200608150-00004 PMID: 16908915

15. Delanaye P, Mariat C. The applicability of eGFR equations to different populations. Nat Rev Nephrol 2013; 9: 513–522. https://doi.org/10.1038/nrneph.2013.143 PMID: 23856996

16. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012; 120: c179–184. https://doi.org/10.1159/000339789 PMID: 22890468

17. Azarbal A, Malenka DJ, Huang YL, Ross CS, Solomon RJ, DeVries JT, et al. Recovery of Kidney Dysfunction After Transcatheter Aortic Valve Implantation (from the Northern New England Cardiovascular Disease Study Group). Am J Cardiol 2019; 123: 426–433. https://doi.org/10.1016/j.amjcard.2018.10.042 PMID: 30522749

18. Azarbal A, Leadholm KL, Ashikaga T, Solomon RJ, Dauerman HL. Frequency and Prognostic Significance of Acute Kidney Recovery in Patients Who Underwent Transcatheter Aortic Valve Implantation. Am J Cardiol 2018; 121: 634–641. https://doi.org/10.1016/j.amjcard.2017.11.043 PMID: 29329828

19. Nijenhuis VJ, Peper J, Vorselaars VMM, Swaans MJ, De Kroon T, Van der Heyden JAS, et al. Prognostic Value of Improved Kidney Function After Transcatheter Aortic Valve Implantation for Aortic Stenosis. Am J Cardiol 2018; 121: 1239–1245. https://doi.org/10.1016/j.amjcard.2018.01.049 PMID: 29525062

20. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. Eur Heart J 2012; 33: 2403–2418. https://doi.org/10.1093/eurheartj/ehs255 PMID: 23026477

21. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008; 36: 309–332. https://doi.org/10.1016/j.ajic.2008.03.002 PMID: 18538699

22. Dworakowski R, Wendler O, Bhan A, Smith L, Pearson P, Alcock E, et al. Successful transcatheter aortic valve implantation (TAVI) is associated with transient left ventricular dysfunction. Heart 2012; 98: 1641–1646. https://doi.org/10.1136/heartjnl-2012-302505 PMID: 22914532

23. Kim WK, Rolf A, Liebetrau C, Van Linden A, Blumenstein J, Kempfert J, et al. Detection of myocardial injury by CMR after transcatheter aortic valve replacement. J Am Coll Cardiol 2014; 64: 349–357. https://doi.org/10.1016/j.jacc.2014.03.052 PMID: 25060368

24. Sarraf M, Burkhoff D, Brener MI. First-in-Man 4-Chamber Pressure-Volume Analysis During Transcatheter Aortic Valve Replacement for Bicuspid Aortic Valve Disease. JACC Case Rep 2021; 3: 77–81. https://doi.org/10.1016/j.jaccas.2020.11.041 PMID: 34317473

25. Kim WK, Liebetrau C, van Linden A, Blumenstein J, Gaede L, Hamm CW, et al. Myocardial injury associated with transcatheter aortic valve implantation (TAVI). Clin Res Cardiol 2016; 105: 379–387. https://doi.org/10.1007/s00392-015-0949-6 PMID: 26670909

26. Selle A, Figulla HR, Ferrari M, Rademacher W, Goebel B, Hamadanchi A, et al. Impact of rapid ventricular pacing during TAVI on microvascular tissue perfusion. Clin Res Cardiol 2014; 103: 902–911. https://doi.org/10.1007/s00392-014-0728-9 PMID: 24898704

27. Acheampong A, Melot C, Benjelloun M, Cheval M, Reye F, Delporte C, et al. Effects of hyperoxia and cardiovascular risk factors on myocardial ischaemia-reperfusion injury: a randomized, sham-controlled parallel study. Exp Physiol 2021; 106: 1249–1262. https://doi.org/10.1113/EP089320 PMID: 33660345

28. Mak S, Azevedo ER, Liu PP, Newton GE. Effect of hyperoxia on left ventricular function and filling pressures in patients with and without congestive heart failure. Chest 2001; 120: 467–473. https://doi.org/10.1378/chest.120.2.467 PMID: 11502645

29. Kelly RF, Hursey TL, Parrillo JE, Schaer GL. Effect of 100% oxygen administration on infarct size and left ventricular function in a canine model of myocardial infarction and reperfusion. Am Heart J 1995; 130: 957–965. https://doi.org/10.1016/0002-8703(95)90194-9 PMID: 7484756

30. Stub D, Smith K, Bernard S, Nehme Z, Stephenson M, Bray JE, et al. Air Versus Oxygen in ST-Segment-Elevation Myocardial Infarction. Circulation 2015; 131: 2143–2150. https://doi.org/10.1161/CIRCULATIONAHA.114.014494 PMID: 26002889

31. Girardis M, Busani S, Damiani E, Donati A, Rinaldi L, Marudi A, et al. Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit: The Oxygen-ICU Randomized Clinical Trial. JAMA 2016; 316: 1583–1589. https://doi.org/10.1001/jama.2016.11993 PMID: 27706466

32. Hofmann R, James SK, Jernberg T, Lindahl B, Erlinge D, Witt N, et al. Oxygen Therapy in Suspected Acute Myocardial Infarction. N Engl J Med 2017; 377: 1240–1249. https://doi.org/10.1056/NEJMoa1706222 PMID: 28844200

33. ICU-ROX Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group, Mackle D, Bellomo R, Bailey M, Beasley R, Deane A, et al. Conservative Oxygen Therapy during Mechanical Ventilation in the ICU. N Engl J Med 2020; 382: 989–998. https://doi.org/10.1056/NEJMoa1903297 PMID: 31613432

34. Stewart RAH, Jones P, Dicker B, Jiang Y, Smith T, Swain A, et al. High flow oxygen and risk of mortality in patients with a suspected acute coronary syndrome: pragmatic, cluster randomised, crossover trial. BMJ 2021; 372: n355. https://doi.org/10.1136/bmj.n355 PMID: 33653685

35. Buse GL, Matot I. Pro-Con Debate: Cardiac Troponin Measurement as Part of Routine Follow-up of Myocardial Damage Following Noncardiac Surgery. Anesth Analg 2022; 134: 257–265. https://doi.org/10.1213/ANE.0000000000005714 PMID: 35030121

36. Michail M, Cameron JN, Nerlekar N, Ihdayhid AR, McCormick LM, Gooley R, et al. Periprocedural Myocardial Injury Predicts Short- and Long-Term Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement. Circ Cardiovasc Interv 2018; 11: e007106. https://doi.org/10.1161/CIRCINTERVENTIONS.118.007106 PMID: 30571209

37. Lahoud R, Butzel DW, Parsee A, Huang YL, Solomon RJ, DeVries JT, et al. Acute Kidney Recovery in Patients Who Underwent Transcatheter Versus Surgical Aortic Valve Replacement (from the Northern New England Cardiovascular Disease Study Group). Am J Cardiol 2020; 125: 788–794. https://doi.org/10.1016/j.amjcard.2019.11.024 PMID: 31924319

38. Peillex M, Marchandot B, Matsushita K, Prinz E, Hess S, Reydel A, et al. Acute kidney injury and acute kidney recovery following Transcatheter Aortic Valve Replacement. PLoS One 2021; 16: e0255806. https://doi.org/10.1371/journal.pone.0255806 PMID: 34375346

39. Sammour Y, Kerrigan J, Banerjee K, Gajulapalli RD, Lak H, Chawla S, et al. Comparing outcomes of general anesthesia and monitored anesthesia care during transcatheter aortic valve replacement: The Cleveland Clinic Foundation experience. Catheter Cardiovasc Interv 2021; 98: E436–E443. https://doi.org/10.1002/ccd.29496 PMID: 33512085