Effects of Total Intravenous Anesthesia with Propofol Versus Inhalational Anesthesia with Sevoflurane on Postoperative Quality of Life and Postoperative Delirium in Patients Undergoing Total Knee Arthroplasty: A Randomized, Controlled, Double-Blinded Clinical Trial

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Research article

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Abstract

Background: The widespread use of total knee arthroplasty(TKA) to treat patients who suffer knee osteoarthritis(KOA) has led to a number of postoperative problems, including the recovery of postoperative quality of life and postoperative delirium(POD). Both problems could cause profound damages to patients and their families. This study assessed and compared the effects of total intravenous anesthesia with propofol versus inhalational anesthesia (sevoflurane) on postoperative quality of life and POD in patients who underwent TKA.

Methods: One hundred and fifty patients American Society of Anesthesiologists(ASA) I-III were assessed for inclusion in this study, and randomly divided into inhalational anesthesia with sevoflurane group(group S), and total intravenous anesthesia with propofol group(group P). The primary outcome was postoperative quality of life and secondary outcome was POD.

Results: The quality of life at the first month after surgery in group S was better than that in group P(P=0.02). However, there was no significant difference in quality of life between the two groups at 1 day before surgery, 1 day after surgery, 3 days after surgery, 7 days after surgery and 3 months after surgery. In group P, 19 patients (31.1%) had no anxiety/depression problems, 40 patients (65.6%) had moderate problems, and 2 patients (3.3%) had severe problems.In group S, 37 patients (60.6%) had no problems in anxiety/depression, 23 patients (37.7%) had moderate problems, and 1 patient had severe problems (1.7%). These two outcomes had significant differences (P=0.005) .The incidence of POD within 3 days after surgery was 24.6% (15/61) in group P and 36.1% (22/61) in group S. There was no significant difference in the incidence of POD between the two groups (P=0.17).

Conclusions: Group S patients have a better quality of life at the first month after surgery in comparison with those in group P regarding anxiety/depression. However, there were no significant differences in the quality of lives between the two groups at 1 day before surgery, 1 day after surgery, 3 days after surgery, 7 days after surgery, and 3 months after surgery. There was also no significant difference in POD. Thus, we concluded that both anesthetic technologies could be extensively used for TKA.

Trial registration: This trial was registered at the Chinese Clinical Trial Registry (ChiCRT-IOR-17012428). Date of Registration: 21 Aug. 2017.

Background

There are many risk factors for knee osteoarthritis(KOA), but the major risk factors are age and obesity. As the population ages and obesity rates rise, It is inevitable that the incidence of KOA is increasing[1]. Total knee arthroplasty has been extensively used since the 1970s and it has improved quality of life in patients with end-stage arthritis. Therefore TKA is now regarded as an effective and economical treatment for end-stage knee arthritis[2, 3].

Traditionally, more attention has been paid to the indicators of local pain and limb function recovery after TKA than to the quality of life of patients. With the general improvement of health requirements, traditional health evaluation indicators such as morbidity, mortality and life expectancy have been unable to fully assess the health. When the concept of quality of life was proposed, the medical model gradually changed to the bio-psycho-social medical model. Accordingly, the purpose of clinical treatment of diseases no longer limited to the improvement of the survival rate and extension of the survival time of patients, but more importantly, the improvement of the quality of life of patients[4, 5]. Additionally, the postoperative delirium (POD) is also a common complication after TKA [6, 7]. Delirium is a brain disorder with an acute onset and a specific volatility. The main clinical manifestations were acute disturbances of the consciousness, inattention, confusion of thinking, and mental state fluctuations. At the international level, healthcare professionals have emphasized delirium as a primary public health question because it is significantly related with delayed recovery and excessive use of medical resources[8]. Therefore, our primary outcome is quality of life after TKA, and the secondary outcome is POD.

Propofol is a typical short-lived intravenous anesthetic, with advantages of quick onset, quick recovery, low-incidence of postoperative nausea, and vomiting. Sevoflurane is a representative compound of the new class of volatile anesthetics, and has the advantages of low-blood/gas distribution coefficient, precise control of anesthetic depth, and minor influences on the cardiovascular system[9]. Propofol and sevoflurane are two general anesthesia maintenance drugs with different mechanisms of action. The influences of the different maintenance anesthesia strategies on the postoperative quality of life and POD may be different. Studies confirmed that sevoflurane induced apoptosis and increased amyloid protein levels in patients. These changes are characteristic in Alzheimer disease. However, propofol did not enhance amyloidosis in pheochromox cells[10]. Saporito et al. also indicated that propofol had neuroprotective effects [11]. However, subject to experimental conditions, and considering that these findings were revealed, it is still uncertain on whether these effects were the same in patients. We hypothesized that owing to the different mechanisms and effects of propofol and sevoflurane on patients, these two anesthetic approaches may have different impacts on the postoperative quality of life and POD. Therefore, we performed prospective randomized clinical trials to compare the effects of sevoflurane or propofol anesthesia on the postoperative quality of life and POD in patients who underwent TKA.

Methods

Trial design and participants

This study was conducted between July 2017 and June 2019 at the First Affiliated Hospital of Anhui Medical University. This manuscript adheres to the applicable CONSORT guidelines. It was registered at http://www.chictr.org.cn/index.aspx (registration number: ChiCRT-IOR-17012428). and it has been approved (approval number: PJ2019-16-08) by the Institutional Ethics Committee (First Affiliated Hospital of Anhui Medical University Ethics Committee). All the patients provided written informed consents. We enrolled 150 patients (American Society of Anesthesiologists, ASA grades I to III, ages 40–75, male or

female, weight 45–100 kg), who had been scheduled for elective TKA for the first time between July 1, 2017 and June 1, 2019. Patients with dementia, central nervous system disease or psychosis, inability to walk independently before surgery, inability to complete cognitive function tests, and allergy to anesthetics, were excluded. Additionally, if the Mini-Mental State Examination scores did not meet the corresponding standard (illiterate > 17 points, primary b > 20 points, secondary, and above mean educational levels > 23 points), these patients were excluded.

Patients were randomly divided into two groups (Groups S and P) to receive sevoflurane or propofol combined with a peripheral nerve block.

Conduct Of Anesthesia

All enrolled patients were monitored with standard techniques (noninvasive assessment of blood pressure, bispectral index, oxygen saturation, pulse oximetry, electrocardiography) when they arrived in the operating room. Nerve stimulator-guided combined with ultrasound-guided femoral nerve and sciatic nerve blocks were administered in both groups. After preoxgenation, patients were induced with etomidate 0.2 mg/kg, sufentanil 0.5 ug/kg, cisatracurium 0.2 mg/kg, and laryngeal mask airways (LMAs) were inserted. Patients were mechanically ventilated by an anesthesia ventilator with tidal volumes in the range of 6–8 ml/kg, respiratory rates in the range of 10–12 /min, and were adjusted to maintain the end-tidal CO_2 ($EtCO_2$) between 30–40 mmHg. In the P group, propofol was continually pumped to maintain the depth of anesthesia, and in the S group, sevoflurane was continually inhaled during the operation. The BIS value was maintained in the range of 40–60. Propofol and sevoflurane were adjusted according to the BIS value. Cisatracurium (0.5 mg/kg) was intermittently administered to both groups to maintain muscle relaxation. Vasoactive agents were used to maintain the intraoperative hemodynamic fluctuations that did not exceed 20% of the basal value. Flurbiprofen (100 mg) and azasetron (10 mg) were injected intravenously 30 min before the end of surgery, and LMA was removed after patients reached extubation conditions.

Postoperative quality of life and POD were assessed by using the EuroQol five-dimensional (EQ-5D) scale and confusion assessment method (CAM), respectively. The EQ-5D score was recorded on the first day before surgery, first day after surgery, third day, seventh day, first month, and on the third month. The EQ-5D score represents the health status of the interviewee. This scale includes five dimensions: mobility, self-care, usual activities, pain discomfort, and anxiety or depression. The higher the score is, the better the quality of life is. Conversely, the lower the score is, the worse the quality of life is. The incidence of delirium was assessed daily during the first 3 days after surgery (5:00 pm–7:00 pm).

Statistical Analyses

We used the software PASS (version 11.0) to calculate the sample size. Based on previous research, we assumed that the internal investigation correlation of the patients preoperatively and postoperative (6

months) was 0.60 (moderate correlation). According to the preliminary experimental results, the calculated EQ-5D cross-sectional score standard deviation of each point in time was 0.17, the maximum set inspection alpha level was 0.8, and $P < 0.05$ was considered statistically significant. In this study, a long-term followup was conducted after surgery, and there was a certain shedding rate. Accordingly, we increased the sample size to 65 in each group.

The SPSS software (version 20.0) was used for the statistical analyses. Measurement data were expressed as mean ± standard deviations, and repeated measurement analysis of variance was used for comparison between groups. Non-normal distribution measurement data were represented by the median (M) and interquartile spacing (IQR), and were compared by the rank sum test. Enumeration data were expressed in cases or (%), and the comparison between groups was performed by the chi-square test.

Results

A total of 150 patients who underwent unilateral TKA were enrolled. Ten patients with severe cardiopulmonary disease or kidney failure, three who underwent repeated TKA (two times), two who were also participating in other studies, and five who withdrew temporarily from the study, were excluded. A total of 130 eligible patients were assigned randomly into two groups, and each group included 65 patients. In group P, two patients were required to terminate the study after surgery, and another two patients had incomplete postoperative followup data. In group S, one patient was excluded owing to the surgical refusal, two patients were excluded owing to incomplete followup data, and one patient died unexpectedly within 3 months after surgery. A total of 122 patients were included in the two groups (Fig. 1). There were no significant differences in patient characteristics among the two groups (Table 1).

Table 1
Baseline Characteristics

Variable	Group S(n = 61)	Group P(n = 61)	P value
Age (year)	62.7 ± 7.9	65.1 ± 6.9	
Male/Female	13/48	13/48	0.08
BMI(kg/m2)	25.6 ± 3.3	26.5 ± 5.1	0.22
ASA physical status(I/II/III)	2/56/3	3/54/4	0.83
Duration of anesthesia (min)	116.0 ± 16.4	117.1 ± 16.2	0.56
Duration of surgery (min)	84.7 ± 13.9	89.6 ± 16.2	0.08
Data are expressed as mean ± standard deviation. ASA, American Society of Anesthesiologists. BMI, Body Mass Index. Group S, Group sevoflurane; Group P, Group propofol.			

The primary outcome in group S was better than that in group P ($P = 0.02$) at the first month after surgery. However, there was no significant difference in quality of life between the two groups 1 day before surgery, 1 day after surgery, 3 days after surgery, 7 days after surgery, and 3 months after surgery

(Table 2). In group P, 19 patients (31.1%) had no anxiety/depression problems, 40 patients (65.6%) had some problems, and two patients (3.3%) had severe problems. In group S, 37 patients (60.6%) had no anxiety/depression problems, 23 patients (37.7%) had moderate problems, and 1 patient had severe problems (1.7%). These two outcomes had significant differences ($P = 0.005$) (Table 2).

Table 2
A multidimensional comparison of life quality 1 month after surgery

		No problems	Moderate problems	Severe problems	P value
Mobility	P	16 (26.2)	45 (73.8)	0(0)	0.165
	S	24(39.3)	36 (59.0)	1(1.7)	
Self-care	P	43(70.5)	18 (29.5)	0(0)	0.08
	S	51(83.7)	10 (16.3)	0(0)	
Usual activities	P	57(93.4)	4(6.6)	0(0)	1
	S	58(95.1)	3(4.9)	0(0)	
Pain/discomfort	P	35(57.4)	25(40.9)	1(1.7)	0.362
	S	41(67.2)	20(32.8)	0(0)	
Anxiety/depression[a]	P	19(31.1)	40(65.6)	2(3.3)	0.005
	S	37(60.6)	23(37.7)	1(1.7)	

[a] Compared with group S, $P < 0.05$ (Group S, sevoflurane; Group P, propofol).

The incidence of POD within 3 days after surgery was 24.6% (15/61) in group P and 36.1% (22/61) in group S. There were no significant differences in the POD incidence rates between the two groups ($P = 0.17$) (Fig. 3).

Discussion

TKA with severe postoperative pain, limited limb movement, and reduced daily life moving ability, has a serious impact on the patients' quality of life after surgery.

Naal et al. followed up 233 patients who underwent TKA and found that at 3, 6, and 12 months after surgery, patients improved gradually over time at 3, 6, and 12 months after surgery, and recovered and reached the optimal level at 12 months. Before surgery, and at 3, 6, and 12 months after surgery. Shim et al. used the EQ-5D scale to evaluate 721 patients who underwent TKA. The results showed that period that yielded maximum improvement were the first 3 months after surgery, and that the changes were minor within the period that spanned 3 to 6 months after surgery [12]. Most of the studies found that the

quality of life in the first 3 months after TKA was significantly changed. Thus, our study focused on the changes in the early postoperative period, and conducted high-density studies during this period.

In our study, we used the EQ-5D scale to evaluate the quality of life for patients who underwent TKA with different anesthesia methods. We tried to find a better anesthetic approach to improve patients' quality of life after TKA. We found that the quality of life in group S was better than that in group P at the first month after surgery. Furthermore, in the first month after TKA, we compared the dimensions of the two groups 1 month after surgery, and the results showed that there were statistically significant differences regarding anxiety or depression. Most of the current studies showed that depression or anxiety was closely related to the quality of life, and patients who experienced depression or anxiety before surgery were expected to have a lower quality of life. In these studies, depression or anxiety was treated as an independent variable, and the quality of life as a dependent variable[13, 14]. However, contrary to previously reported results, Hajek et al. proposed that depression or anxiety were associated with an increased decline in the quality of life, and showed that physical dysfunction and the loss of the ability to move in daily life were risk factors for depression or anxiety[15].Therefore, the relationship between depression/anxiety and quality of life is complex. While depression or anxiety can have a negative impact on the quality of life, they can also be a manifestation of an impaired quality of life. The difference between the two groups regarding anxiety or depression one month after surgery was a sign of an impaired quality of life. However, there was no significant difference in quality of life between the two groups 1 day before surgery, 1 day after surgery, 3 days after surgery, 7 days after surgery, and 3 months after surgery.

Following joint arthroplasty surgery, 6–41% of patients exhibited delirium [16–20]. The reported incidence of POD is different owing to differences in the diagnostic criteria, the population under study, and the methods of postoperative monitoring for delirium [21–23]. In this study, the incidence rates of POD after TKA in groups P and S were 24.6% and 36.1%, respectively, with no statistical differences. This is consistent with some of the current findings on POD. Stacie et al. found that patients who received total intravenous anesthesia during surgery demonstrated lower levels for all stress markers compared with patients who received sevoflurane, but no POD differences[24]. Another study also reported that the incidence rates of POD in patients who underwent off pump-CABG did not exhibit differences for patients who received propofol-based anesthesia versus sevoflurane [25]. Lurati et al. followed 385 patients who underwent major noncardiac surgery to compare the incidence of myocardial ischemia and POD. Neither group reduced the incidence of myocardial ischemia and delirium[26]. However, there are also many studies that differ from us. Koji et al. compared 30 patients in the sevoflurane group and 29 in the propofol group and found that propofol anesthesia was associated with a lower incidence of POD in elderly patients[27].

Our study has several limitations. First of all, we evaluated POD within 3 days after surgery. Correspondingly, cases after 3 days may have been missed. It is recommended that the assessment ought to be conducted within the first 7 days after surgery or discharge the patients from the hospital. Secondly, continuous peripheral nerve block was not used for postoperative analgesia. Thirdly, as a

preliminarily observational study, the sample size of this study was relatively small, and the results still need to be confirmed by a randomized controlled study with a larger sample.

Conclusion

Group S yielded a better quality of life at the first month after surgery in comparison with group P, particularly as it pertains to anxiety/depression. However, there was no significant difference in the quality of life between the two groups 1 day before surgery, 1 day after surgery, 3 days after surgery, 7 days after surgery, and 3 months after surgery. There was also no significant difference in POD. Thus, we conclude that both anesthetic technologies could be extensively used for TKA.

Abbreviations

ASA
American Society of Anesthesiologists; TKA:total knee arthroplasty; KOA:knee osteoarthritis; POD:postoperative delirium; EtCO2:end-tidal CO2;
EQ-5D
EuroQol five-dimensional scale; CAM:Confusion Assessment Method;
LMA
laryngeal mask airway; BIS:bispectral index; BIM:body mass index.

Declarations

Ethics approval and consent to participate:

This trial was approved by the ethics committee of the First Affiliated Hospital of Anhui Medical University(approval number:PJ2019-16-08). All patients provided written informed consent.

Consent for publication:

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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This study is supported by Natural Science Foundation of China(81701073). The founder have significant influence on the study design but did not analyze the datas.

Author contributions:

HS and XSL designed this study and wrote the manuscript. YXF performed the experiments. GHX assisted with data analysis. XSL revised the final manuscript. All the authors contributed to the final version of the manuscript.

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Figures

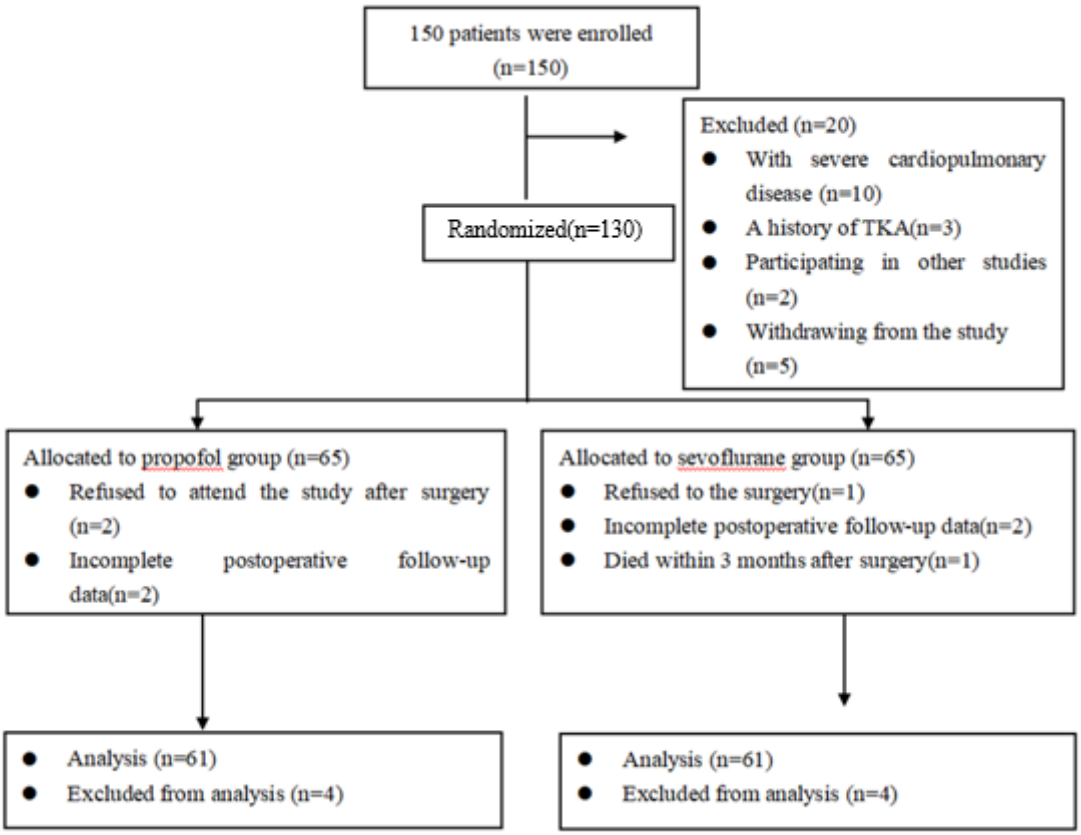

Figure 1

Consort flow chart that outlines the patient assignments and treatment protocols. Patients were allocated into two groups (Groups S and P) to receive propofol or sevoflurane to maintain the depth of anesthesia respectively following a computer-generated randomization code.

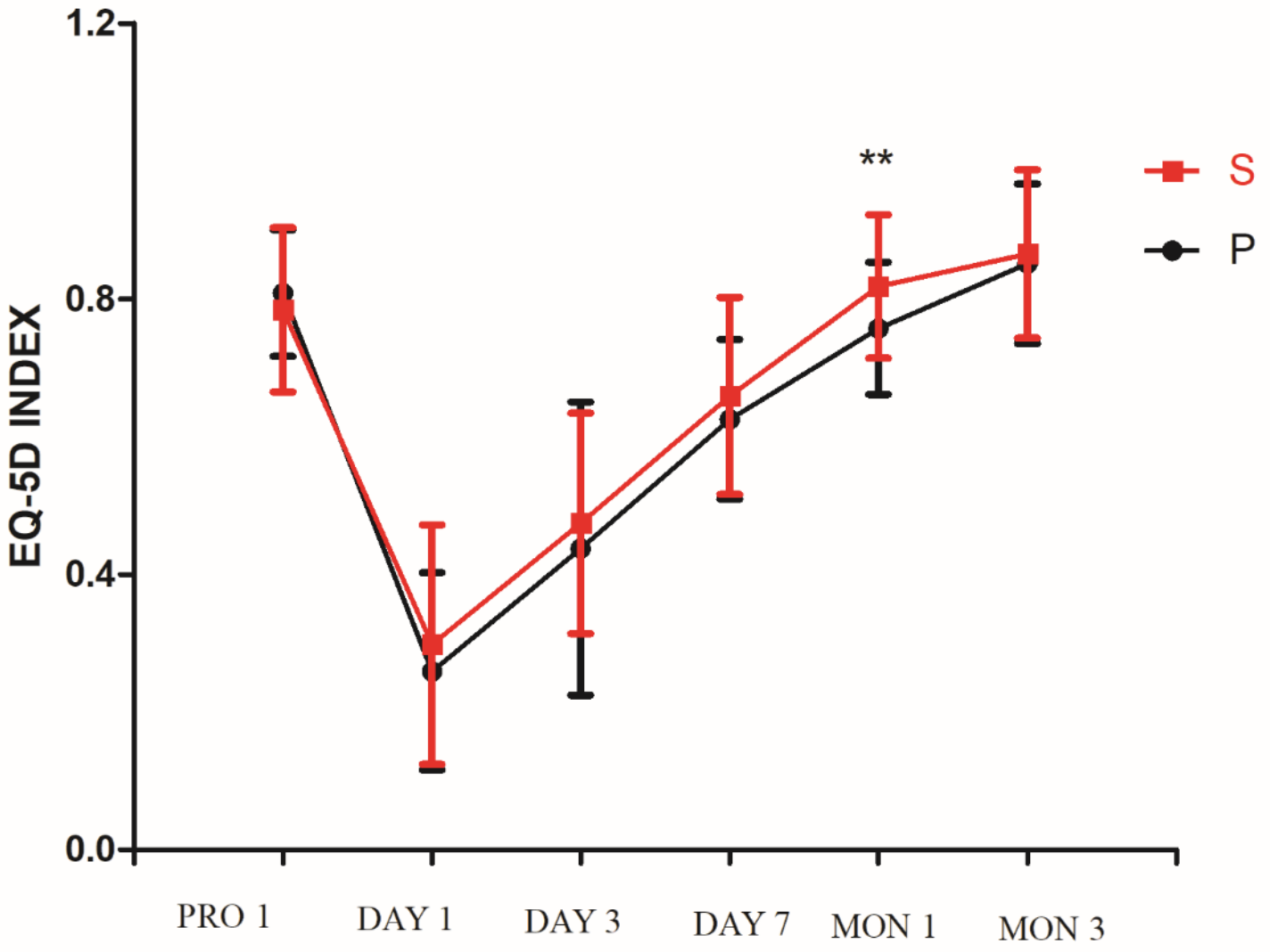

Figure 2

Comparison of quality of life between the two groups at 1 month after surgery **There were significant differences in the quality of life between the two groups at the first month after surgery (P = 0.02) (Group S, sevoflurane; Group P, propofol).

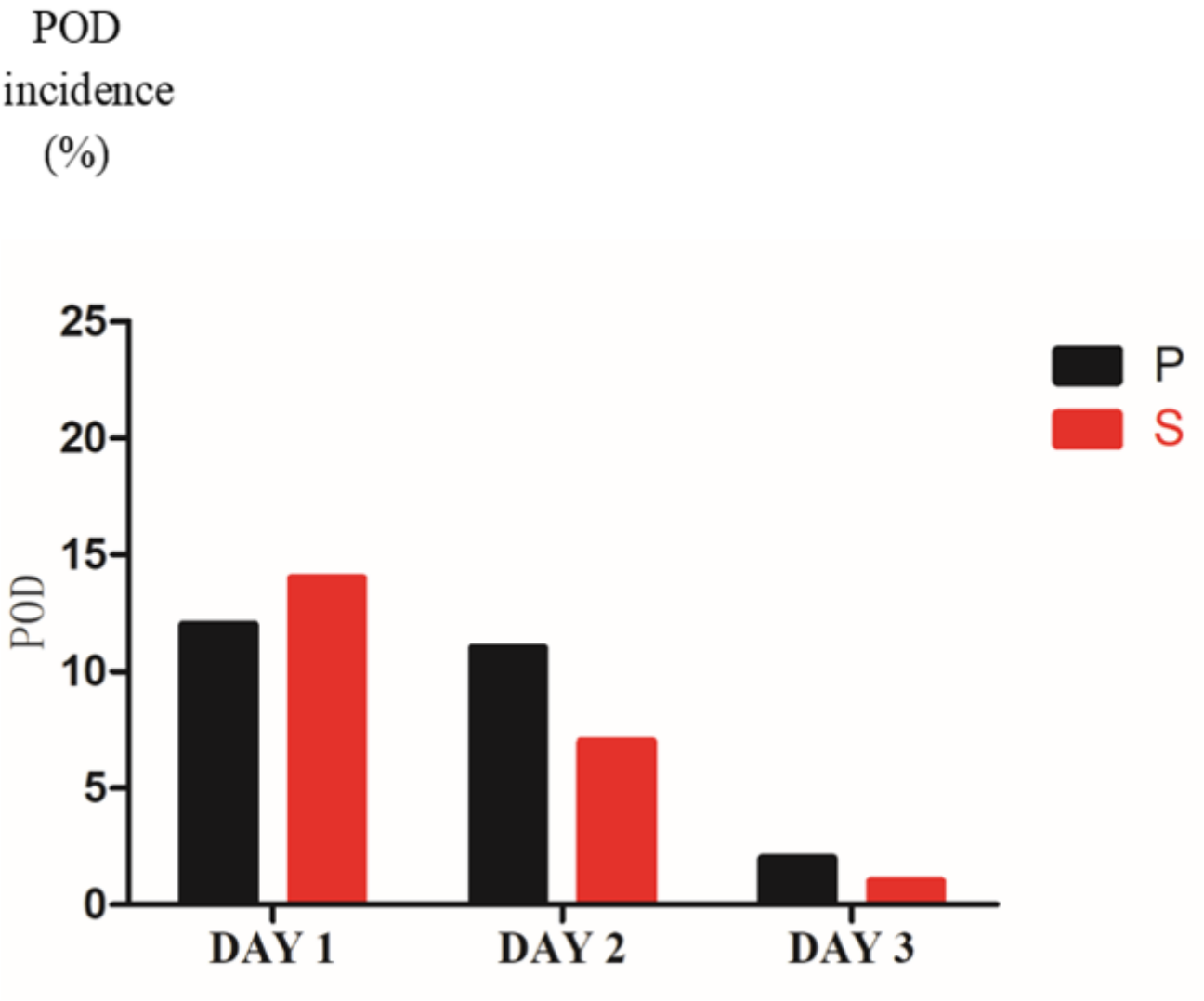

Figure 3

Comparison of POD within 3 days after surgery between the two groups Group S, sevoflurane; Group P, propofol.

Supplementary Files

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- CONSORT2010Checklist1.doc