Efficacy of the Opened Legs Position for Protecting Against Postoperative Rhabdomyolysis after Robot-Assisted Radical Prostatectomy: A Propensity Score-Matched Analysis of Perioperative Outcomes

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Running head: Rhabdomyolysis after Robot Assisted Radical Prostatectomy

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Abstract

Objectives: The aim of the present study was to clarify the relationships of intraoperative surgical position with the incidence of postoperative rhabdomyolysis and with postoperative renal function to safely perform robot-assisted radical prostatectomy (RARP).

Methods: The participants in the present study were 276 consecutive patients who underwent RARP at our institutions between 2013 and 2020; 130 cases were performed in the opened legs position and 146 cases in the lithotomy position with a steep 23-25-degree head-down position. Rhabdomyolysis was defined as CK values greater than 1000 IU/L. Propensity score matching including age, BMI, presence of comorbidities, preoperative CK, preoperative eGFR, and PSA was performed, resulting in a matched cohort of 146 patients (opened legs position group n=73; lithotomy position group n=73).

Results: After propensity score matching, CK values on the first day after surgery were significantly lower in the opened legs position group than in the lithotomy position group (opened legs position group: lithotomy position group = 246.9 ± 114.9 IU/L: 558.2 ± 114.9 IU/L, P = 0.034). There were significantly fewer patients diagnosed with postoperative rhabdomyolysis in the opened legs position group (opened legs position group: lithotomy position group = 0% (0/73): 9.6% (7/73), P < 0.001). In addition, fluid replacement volume was significantly less in the opened legs position group (opened legs position group: lithotomy position group = 5747 ± 180 mL: 6349 ± 0176 mL, P = 0.018).

Conclusions: To prevent rhabdomyolysis after surgery, RARP should be performed in the opened legs position.

Keywords: creatine kinase; opened legs position; lithotomy position; robot-assisted radical prostatectomy; rhabdomyolysis

INTRODUCTION

Robotic surgery has been one of the surgical options in the urological field since 2000 (1). Robot-assisted radical prostatectomy (RARP) has become the gold standard surgical treatment for localized prostate cancer, owing to its decreased complications and earlier rehabilitation compared to the open approach (2). However, compared to open radical prostatectomy, RARP is ordinarily performed in an exaggerated lithotomy position with a steep 23-25-degree head-down. As a result, there have been several reports of rhabdomyolysis after surgery (3) (4). In this position, weight and compression could occur on the lower legs, buttocks, and lower back leading to local circulatory disturbances of these areas. Consequently, rhabdomyolysis due to ischemia of muscle tissue could occur after surgery performed with the patient in an exaggerated lithotomy position (5).

Rhabdomyolysis is a rare but serious complication of surgery. The pathological mechanism of rhabdomyolysis considered to be as follows. Inflow of myoglobin into the vascular flow and discharge of creatinine kinase (CK) are induced by skeletal muscle damage (6) (7). The renal tubules are then occluded by these enzymes, leading to acute renal failure (6) (7). Acute renal failure usually occurs when CK values exceed 1,000-5,000 IU/L despite definitive criteria for the diagnosis of rhabdomyolysis (8) (9) (10) (11). Thus, fluid replacement therapy and increase hospital stay might be needed to improve rhabdomyolysis (12). Furthermore, in the worst case scenario, there is a risk of death after the occurrence of rhabdomyolysis (13). Therefore, prophylaxis of rhabdomyolysis is considered extremely valuable.

In recent years, there have been several facilities that perform RARP without an exaggerated lithotomy position to reduce the burden on the lower buttocks and lower legs during surgery (14). Although Kog et al. reported that complication rates during RARP were almost identical between the opened legs position using a split-leg table during RARP and the exaggerated lithotomy position (15), no reports have investige the effect of intraoperative position during RARP on muscle breakdown. To safely perform RARP, the aim of the present study was to clarify the relationships of the intraoperative surgical position with the occurrence rate of postoperative rhabdomyolysis and with postoperative renal function.

MATERIALS AND METHODS

Study cohort

The participants in the present study were 276 consecutive patients who underwent RARP at our institutions between 2013 and 2020; 130 cases were performed in the opened legs positionand 146 cases in the lithotomy position with a steep 23-25-degree head-down position. The study protocols were approved by the ethics committee of our institutions. Informed consent was obtained from all patients before the study. This study was performed in accordance with the Declaration of Helsinki. In the present study, because postoperative renal function was evaluated, patients with end-stage renal disease were excluded.

Study design

The present study was a multi-institutional, retrospective, propensity score-matched (PSM) investigation comparing patients in the lithotomy position group and patients in the opened legs position group. Console time, postoperative CK, postoperative renal function, the presence of rhabdomyolysis after RARP, fluid replacement volume, duration of fluid replacement, and the duration of urethral catheter insertion were also evaluated. Fluid replacement volume, duration of fluid replacement, and the duration of urethral catheter insertion were at the physicians' discretion.

Operative technique

In the opened legs position group, RARP was performed using the da Vinci Xi Surgical System® (Intuitive Surgical, Sunnyvale, CA, USA) via the transperitoneal approach at one institution. The patient was laid horizontally with the face and torso facing up, and the legs were placed on a split-leg table (Figure 1A). Softnurse®

(Muranaka Iryoki Co., Tokyo, Japan) was matted on the surgical table for body pressure dispersion. In the lithotomy position group, RARP was performed using the da Vinci Si Surgical System via the transperitoneal approach. The lithotomy position involves the patient lying on the back with legs flexed 90 degrees at the hips. The patient's knees are bent at 70 to 90 degrees, and padded footrests attached to the table support the legs. The lithotomy position was maintained using a lithotomy position device, Levitator® (Mizuho Medical Industry Co, Tokyo, Japan) and Allen HUG-U-VAC® (Muranaka Iryoki Co., Tokyo, Japan) (Figure 1B). In both groups, the steep Trendelenburg position was in the range of 23°-25° as necessary for adequate visualization in both surgical positions. In addition, the surgical procedures of RARP were identical in the lithotomy position group and the opened legs position group. Briefly, all cases underwent combined posterior and anterior intraperitoneal approaches and early exposure of the seminal vesicles and vasa deferentia. The pneumoperitoneum pressure during RARP was kept at 12 mmH_2O, it was kept at 15mmH_2O only when the dorsal vascular complex was transected. After removal of the prostate, anastomosis between the urethra and bladder started with the Rocco technique for posterior reconstruction of Denonvilliers' fascia (16) (17), followed by Van Velthoven's stitch (18) using a running, double-armed barbed 3-0 polyglyconate suture (V-LOC®; Covidien, Mansfield, MA, USA). Integrity of the urethrovesical anastomosis was confirmed intraoperatively with intravesical instillation of 150 ml of sterile saline.

RARP in the opened legs position was performed by five surgeons, and RARP in the lithotomy position was performed by three surgeons. In the opened legs position group, M.T. performed 55cases, N.H. performed 4 cases, S.I. performed 44 cases, R.F. performed 15 cases, H.M. performed 12 cases. In the lithotomy position group, Y.K. performed 79 cases, S.O. performed 56 cases, N.H. performed 11 cases. However, in both institutions, RARP was performed under the supervision of the most experienced surgeons (M.T., Y.K.). In addition, N.H. confirmed that the operating procedures at both facilities were almost identical. Thus, differences in surgical procedures would have little effect on postoperative CK values.

Investigation of parameters

To investigate the factors related to the development of rhabdomyolysis after RARP, perioperative parameters were collected from the electronic health record system at our institutions. Age, height, weight, CK, serum creatinine, eGFR, presence of hypertension (HT), and diabetes mellitus (DM), and PSA were investigated as preoperative parameters. Console time was defined as the time from docking the robot to undocking the robot. Serum creatinine, CK and eGFR levels were measured before RARP and on postoperative day 1. Rhabdomyolysis was defined as a CK level on postoperative day 1 after RARP > 1000 IU/L (19) (20).

Propensity score -matched and statistical analysis

To rule out significant differences in baseline characteristics, i.e., age, body mass index, preoperative CK, preoperative eGFR, console time, a propensity score was calculated using multivariate logistic models on the basis of patients' characteristics and other clinical data that were significantly different in the whole cohort. One-to-one greedy nearest-neighbor matching within one-quarter of the standard deviation of the estimated propensity was performed to create comparable cohorts (caliper 0.2). Patients in the lithotomy position group were then matched with patients in the opened legs position group. Continuous variables are presented as means ± standard deviation. The two-sample *t*-test for continuous variables and Fisher's exact test for categorical valuables were used. *P*-values <0.05 were considered significant. Analysis was performed with JMP version 11.0 software (SAS, Cary, NC, USA).

RESULTS

Baseline patients' characteristics

Baseline characteristics including primary assessment measures are shown in Table 1. The baseline patients' characteristics were not comparable between the lithotomy position group and the opened legs position group, since the following clinical data were significantly different: age (opened legs position group : lithotomy position group = 68.3 ± 0.4 y : 65.9 ± 0.4 y, $P < 0.001$), preoperative CK (opened legs position group : lithotomy position group = 108.6 ± 5.5 IU/L : 131.9 ± 5.2 IU/L, $P = 0.002$), preoperative eGFR (opened legs position group : lithotomy position group = 66.1 ± 11.3 mL/min : 73.5 ± 13.6 mL/min, $P < 0.001$), and console time (opened legs position group : lithotomy position group = 198.6 ± 61.1 min : 156.4 ± 32.5 min, $P < 0.001$). After propensity score-matching based on these data, there were no significant differences in patients' characteristics (Table 1). Thus, 73 patients in the opened legs group and 73 patients in the lithotomy position group were matched for further investigation.

Comparison of postoperative parameters

CK values on the first day after surgery were significantly lower in the opened legs position group than the lithotomy position group (opened legs position group : lithotomy position group = 246.9 ± 114.9 IU/L : 558.2 ± 114.9 IU/L, $P = 0.034$) (Figure 2). There were significantly fewer patients diagnosed with postoperative rhabdomyolysis in the opened legs position group than in the lithotomy position group (opened legs position group: lithotomy position group = 0% (0/73): 9.6% (7/73), $P < 0.001$) (Figure 3). There were 0 cases of subjective symptoms of compartment syndrome such as pain, paresthesia, and cold feeling of skeletal muscle in the opened legs position group. In the lithotomy position group, swelling of the right lower leg was identified in 1 case. In addition, fluid replacement volume was significantly low in the opened legs position group than in the lithotomy position group (opened legs position group: lithotomy position group = 5747 ± 180 mL: 6349 ± 0176 mL, P = 0.018) (Figure 4). However, there was no significant difference in the duration of fluid replacement between the two groups (opened legs position group: lithotomy position group = 3.1 ± 0.1 days: 3.2 ± 0.1 days, P = 0.715). The duration of urethral catheter placement was not significantly different between the two groups (opened legs position group: lithotomy position group = 6.4 ± 0.3 days: 6.9 ± 0.3 day, P = 0.24). Moreover, no significant difference in postoperative renal function was observed between the two groups (opened legs position group: lithotomy position group = 74.4 ± 1.8 mL/min: 73.0 ± 1.8 mL/min, P = 0.589). The detailed clinical courses of rhabdomyolysis in the opened legs position and lithotomy position groups are shown in Table 2.

Discussion

With the progression of minimally invasive surgery, RARP has been selected as one of the treatment options for localized prostate cancer (21). From the nationwide database in the United States, position-related complications, e.g., rhabdomyolysis, compartment syndrome, neuropathies in the lower extremities and so on, were less commonly reported after RARP (22). To the present, evaluation of rhabdomyolysis after RARP was only performed with the patient in the lithotomy position during the surgery (23) (24). Onagi et al. reported that rhabdomyolysis after RARP performed in the lithotomy position was observed in 6.1% of patients (3). Thus, research investigating the difference in the occurrence rate of rhabdomyolysis between the opened legs position and the lithotomy position was needed. In the present study using a propensity score-matched analysis, the CK values after surgery were significantly lower in the opened legs position group than in the lithotomy position group. Thus, rhabdomyolysis occurred significantly less in the opened legs position group. This is the first report to demonstrate the efficacy of the opened legs position for preventing rhabdomyolysis after RARP compared with the lithotomy position.

The reason why there was more rhabdomyolysis in the lithotomy position with steep head down than in the opened legs position with steep head down was as follows. In the lithotomy position, a small circulation disorder occurred in the lower extremities due to the flexure of the hip and knee joints and the pressure on of the lower extremities owing to the lithotomy position device (3). This led to damage of the skeletal muscles and nerves in the lower extremities because of the increased pressure in the compartment of the lower extremities. In addition, because the vertical distance between the lower extremities and the heart increased in the surgery with the head-down position, blood flow in the lower extremities decreased in this surgical position (25). Moreover, it was possible that patients slipped in the direction of the head in the head-down position during the surgery (26). Slippage of the head might accelerate the compression of the lower extremities by the lithotomy position device. Therefore, in the lithotomy position with steep head-down, not only the pressure on the lower extremities by the lithotomy position device itself, but also the disturbance of blood flow and slippage in the direction of the head by the steep head-down position might together induce rhabdomyolysis. On the other hand, although the disturbance of blood flow in the lower extremities and slippage of the body in the direction of the head by the steep head-down position might also occur in the opened legs position with steep head-down, there might be fewer patients with rhabdomyolysis in the opened legs position group because the pressure of the lower extremities could be prevented without using a lithotomy position device.

In the present study, the incidence of postoperative rhabdomyolysis was 9.6% of lithotomy position group after propensity score matching. This appears to be a complication rate. On the other hand, Gelpi-Hammerschmidt et al. compared laparotomy, laparoscopic surgery, and robotic surgery in renal tumor surgery, and included cases other than those with the patient in the lithotomy position (12). In that study, 0.001% of all cases developed postoperative severe rhabdomyolysis (Clavien grade III-IV). However, the definition of rhabdomyolysis was completely different between the present study and the study conducted by Gelpii-Hammerschmidt et al. The definition of rhabdomyolysis in the present study was a value of CK greater than 1000 IU/L and most cases did not require treatment. Therefore, the difference in the degree of the rhabdomyolysis between the present study in the study conducted by Gelpii-Hammerschmidt et al. was thought to be related to the difference in definitions.

In the present study, there was no significant difference in postoperative renal function between the two groups. One of the reasons for this was that appropriate fluid replacement therapy might have been performed for the increased CK after surgery because significantly more fluid replacement volume was administered in the lithotomy position group in which CK values were significantly higher than in the opened legs position group. Another reason for this difference was that there were a few patients (opened legs position group: lithotomy position group = 0% (0/130): 0.7% (1/146)) with severe rhabdomyolysis defined by CK values greater than 5000 IU/L (27) in the present cohort. Thus, no difference in postoperative renal function was observed between the two groups.

There were five limitations in the present study. First, the present study was retrospective. However, propensity score matching was carried out to reduce selection bias because there were significant differences in patients' characteristics and console time, which could have affected the perioperative outcomes. Second, CK was measured only once after surgery. Several CK measurements after surgery could show the severity and/or changes in rhabdomyolysis after RARP. Third, another study demonstrated that serum CPK and serum AST levels showed a positive correlation (23), although preoperative liver function was not evaluated in the present study. Thus, liver function during the perioperative period might affect the postoperative CK value. However, there might be few patients with severe liver dysfunction affecting postoperative CK values in both groups, because preoperative liver function of all patients was checked by an anesthesiologist. Fourth, regarding the statistical analyses of propensity score matching, the 'one-to-one greedy nearest neighbor matching' used in this study may result in poor match quality because it is a 'top-down' model. Finally, the present results may reflect the learning curve. This was a multicenter study involving two facilities, in which, RARP was separately performed in the opened legs position and the lithotomy position. Both were serial cases from the first case, and no randomization was performed. Therefore, each facility included cases on the learning curve. During the learning curve in RARP, operation time and, the rate of a positive surgical margin may be affected (28), but these have been shown to decrease with each case performed (28). However, the main purpose of this study was to examine the occurrence frequency of rhabdomyolysis due by position. In the present study, since there was a significant difference in the operation time between the two groups, the occurrence frequency of rhabdomyolysis was examined by matching the operation time with a propensity score. Therefore, the present results are not considered a learning curve artifact, but as ongoing risks in RARP.

In conclusion, in the present study, rhabdomyolysis occurred significantly less often in the opened legs position group than in the lithotomy position group. In addition, more fluid replacement volume was needed in the lithotomy position group. In order to prevent rhabdomyolysis and decrease the volume of fluid replacement therapy, RARP should be performed in the opened legs position.

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None

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICAL CONSIDERATION

• Approval of the research protocol by an Institutional Reviewer Board:

The study protocols were approved by the ethics committee of our institutions: number is H20-09-002.

• Informed Consent:

Informed consent was obtained from all patients before the study.

• Registry and the Registration No. of the study/trial: N/A

• Animal Studies: N/A

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LEGENDS

Figure 1: Typical photograph of the surgical position

A) Opened legs position with a steep 23-25-degree head down

B) Lithotomy position with a steep 23-25-degree head down

Figure 2: Serum creatine kinase levels on postoperative day 1 in propensity-matched patients in the opened legs position and lithotomy position groups*P<0.05

Figure 3: Postoperative rhabdomyolysis in propensity-matched patients in the opened legs position and lithotomy position groups*P<0.05

Figure 4: Fluid replacement volume after surgery in propensity-matched patients in the opened legs position and lithotomy position groups*P<0.05

ABBREVIATIONS

RARP, robot-assisted radical prostatectomy

BMI, body mass index

CK, creatine kinase

eGFR, preoperative estimated glomerular filtration rate

PSA, prostate-specific antigen

HT, hypertension

DM, diabetes mellitus

AKI, acute kidney injury

Table 1 Characteristics of the population before and after matching

	Before matching			After matching		
	Opened legs position	Lithotomy position	p	Opened legs position	Lithotomy position	p
Number of patients	130	146		73	73	
Age (years)	68.3 ± 4.7	65.9 ± 5.1	<0.001*	67.6 ±0.58	67.5 ± 0.58	0.91
BMI (kg/m^2)	23.7 ± 2.3	24.1 ± 2.4	0.19	23.5 ± 0.29	23.5 ± 0.29	0.91
HT (n)	62 (48%)	62 (47%)	0.97	36 (49%)	33 (45%)	0.62
DM (n)	18 (14%)	21 (14%)	0.90	12 (16%)	8 (11%)	0.34
Preoperative CK (IU/L)	108.6 ± 5.5	131.9 ± 5.2	0.002*	116.2 ± 6.0	108.3 ± 6.0	0.35
Preoperative eGFR (mL/min)	66.1 ± 11.3	73.5 ± 13.6	<0.001*	68.9 ± 1.3	69.8 ± 1.3	0.64
PSA (ng/mL)	9.3 ± 0.7	10.6 ± 0.6	0.18	8.9 ± 0.9	11.0 ± 0.9	0.11
pT2a (n)	24 (18%)	42 (29%)	0.05*	11 (15%)	17 (23%)	0.29
pT2b (n)	5 (4%)	12 (8%)	0.2	4(5%)	10 (14%)	0.16
pT2c (n)	70 (54%)	63 (43%)	0.07*	38 (52%)	31 (42%)	0.32
pT3a (n)	24 (18%)	25 (17%)	0.87	17 (23%)	13 (18%)	0.54
pT3b (n)	7 (5%)	4 (3%)	0.36	3 (4%)	2 (3%)	1.0
Console time (min)	198.6 ± 61.1	156.4 ± 32.5	<0.001*	170.0 ± 3.9	170.0 ± 3.9	0.94
Rhabdomyolysis (n)	4 (0.03%)	9 (0.06%)	0.27	0 (0%)	7 (9.6%)	0.013*
Length of stay (days)	14.0 ± 0.3	8.6 ± 0.2	<0.001*	13.7 ± 0.3	8.4 ± 0.3	<0.001*
postoperative Gleason sum	7.27 ± 0.1	7.1 ± 0.1	0.21	7.3 ± 0.1	7.2 ± 0.1	0.28
Estimation blood loss (mL)	184 ± 19	302 ±18	<0.001*	157 ± 27	319 ±27	<0.001*
30-day complications (n)	13 (10%)	20(14%)	0.36	6 (8%)	9 (12%)	0.59

BMI body mass index, HT hypertension, DM diabetes mellitus, eGFR estimated glomerular filtration rate
mean ± SD or the number of patients (%), *$p < 0.05$

Table 2 The treatment course of rhabdomyolysis cases in the opened legs position group and lithotomy position group

Case no.	Clavien grade	CK values on the first day after surgery (IU/L)	Days of fluid replacement therapy (days)	Amount of fluid replacement volume (ml)
Opened legs position group				
4	I	2315	4	5700
7	I	1320	4	6100
14	I	1414	4	7100
74	I	1167	3	5100
Lithotomy position group				
2	I	1329	4	7500
27	I	3002	3	6000
50	I	1145	3	6000
77	I	2383	3	6000
79	I	4674	3	6000
88	I	2412	3	6000
89	I	10628	5	12000
91	I	1664	3	6000
109	I	1445	3	6000

Figure 1

A)

B)

Figure 2

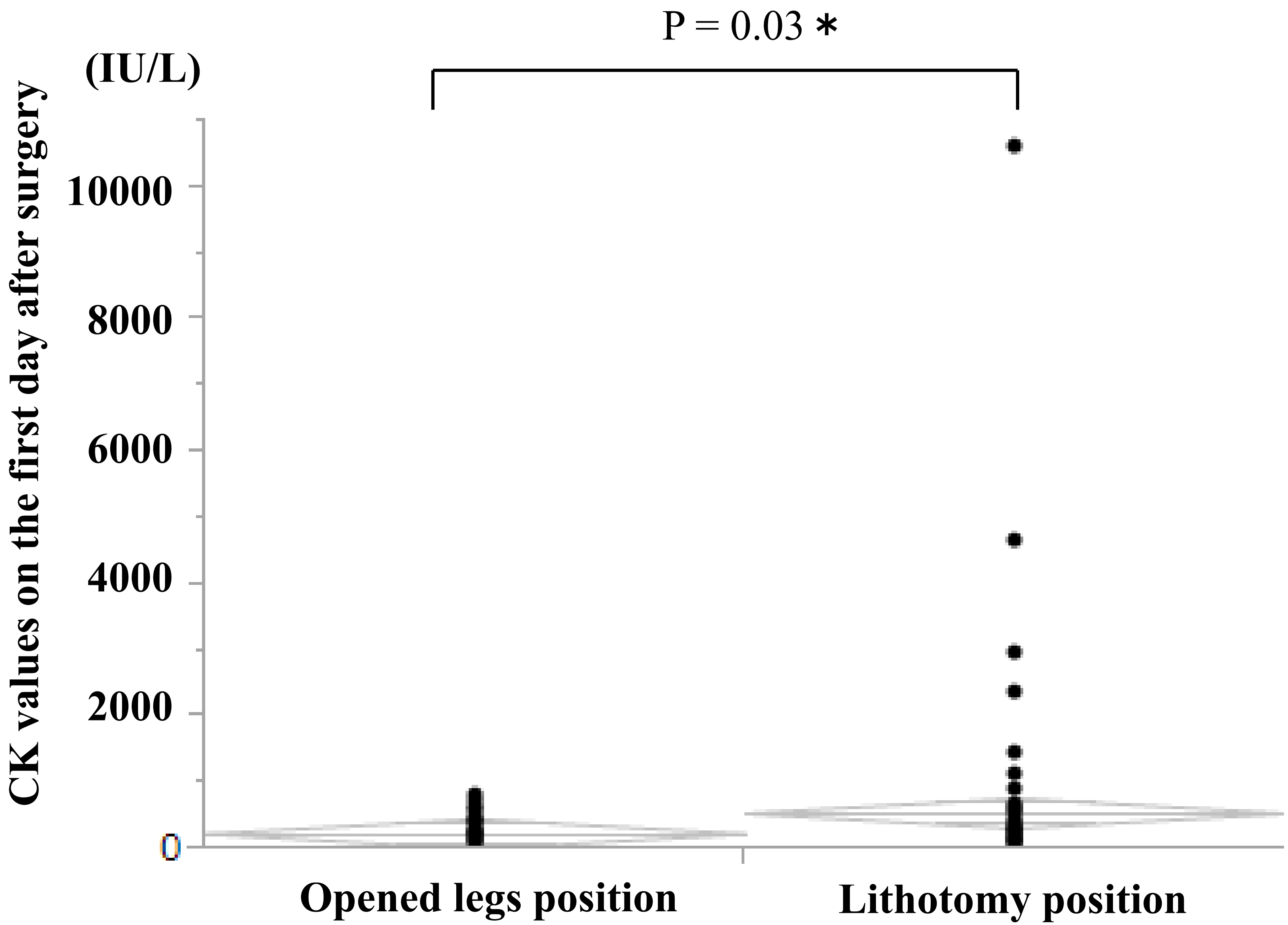
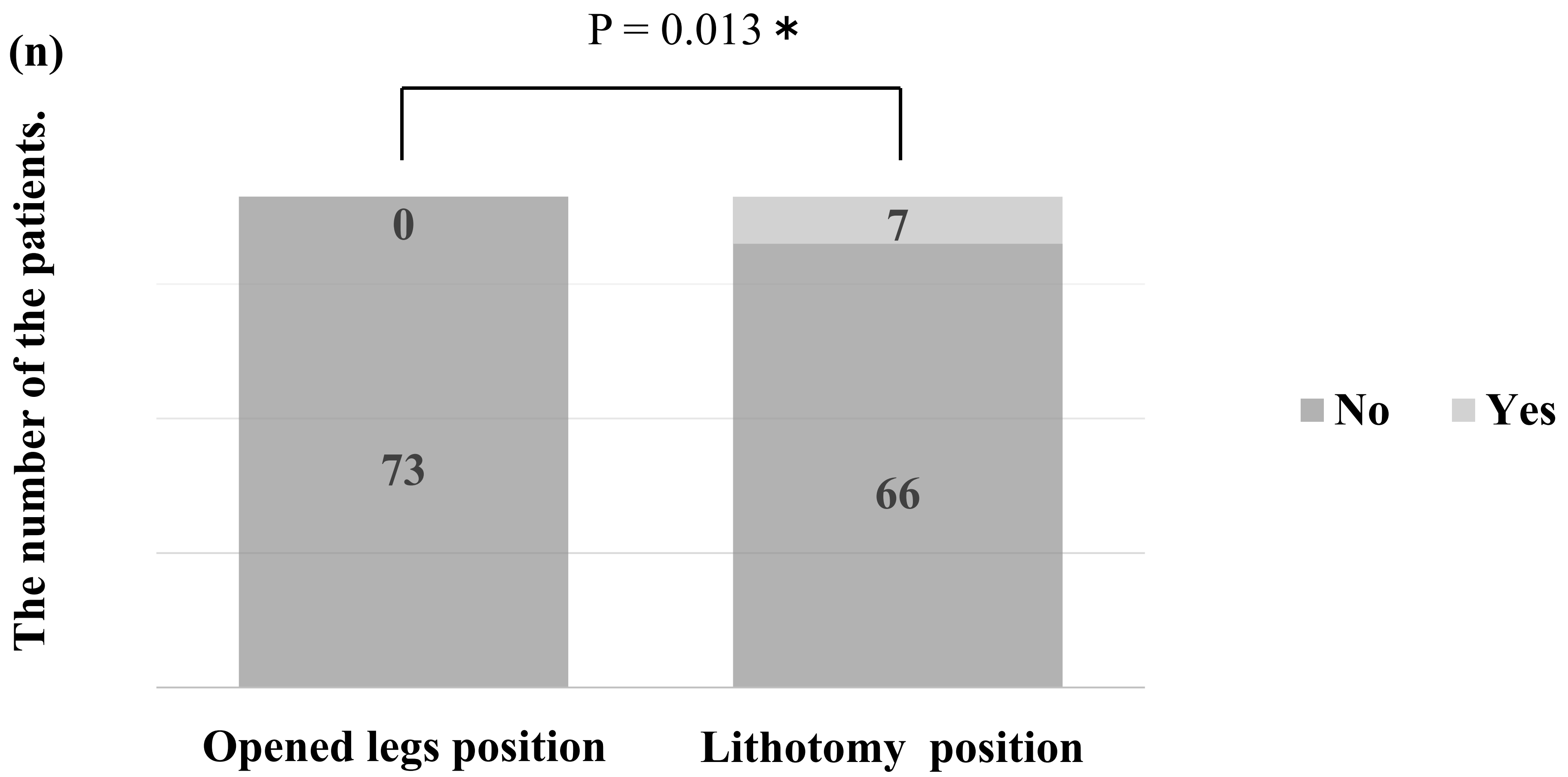
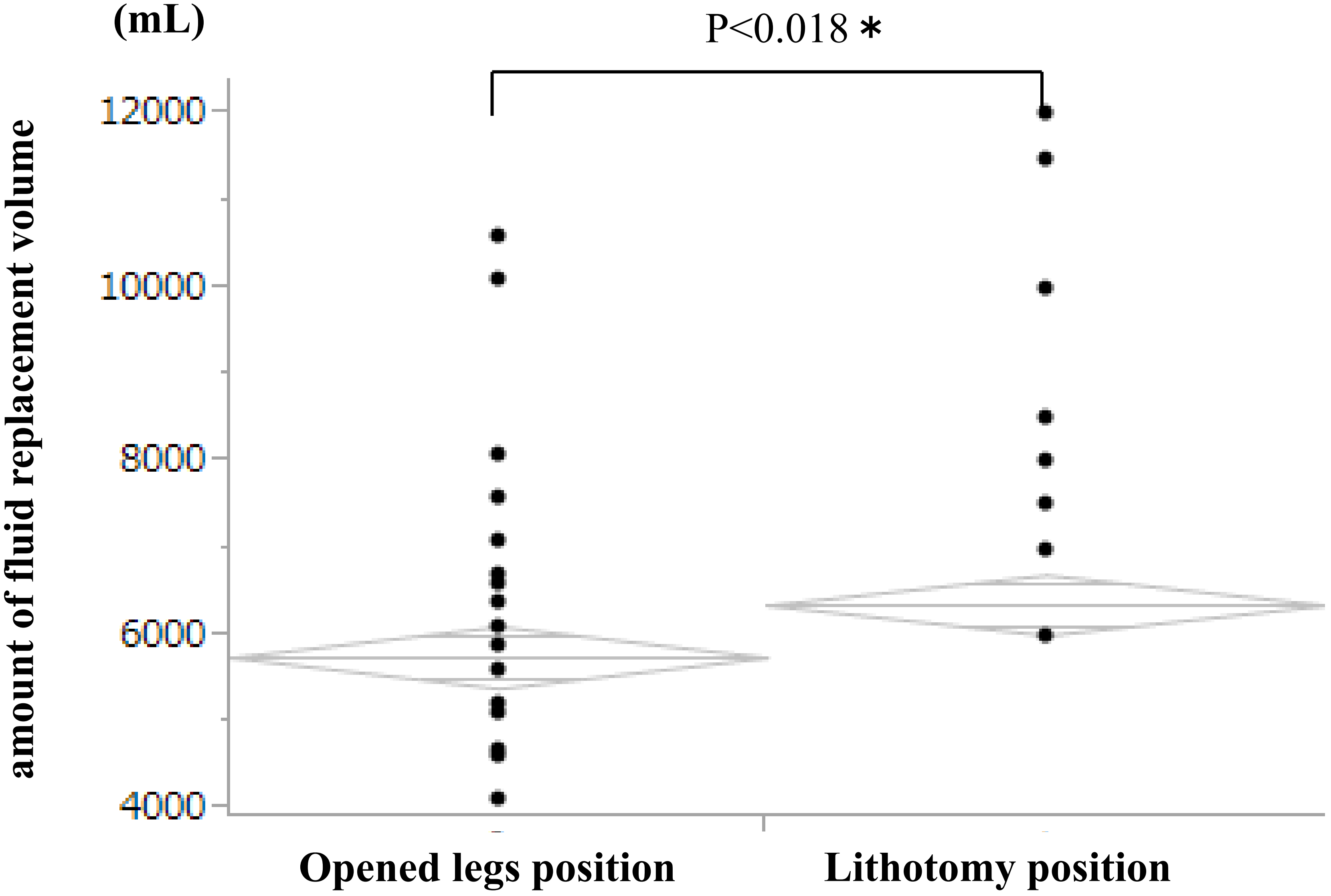

P = 0.03 *
(IU/L)
CK values on the first day after surgery
10000
8000
6000
4000
2000
0
Opened legs position
Lithotomy position

Figure 3



P = 0.013 *
(n)
The number of the patients.
0
73
7
66
Opened legs position
Lithotomy position
No
Yes

Figure 4



(mL)
P<0.018 *
amount of fluid replacement volume
12000
10000
8000
6000
4000
Opened legs position
Lithotomy position