Effect of Pneumoperitoneum on Renal Resistive Index and Renal Function in Patients Who Have Undergone Laparoscopic Living Donor Nephrectomy: A Pilot Study

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ABSTRACT

Introduction. The use of low-pressure pneumoperitoneum during laparoscopic living donor nephrectomy (LLDN) was assumed to cause less renal damage compared to high-pressure pneumoperitoneum. This study aims to evaluate the effect of low vs high-pressure pneumoperitoneum during LLDN on renal function and renal resistive index (RRI), which has never been done before.

Materials and Methods. The subjects were divided into 2 groups, low-pressure (8–10 mmHg) and high-pressure pneumoperitoneum (12–14 mmHg). The RRI, serum creatinine, and estimated glomerular filtration rate were measured during the perioperative period.

Results. A total of 45 samples were analyzed in this study: 17 subjects in the low-pressure pneumoperitoneum group and 28 subjects in the high-pressure group. RRI levels remained within the normal range ($<.80$) with no significant difference observed between the 2 groups ($P>.05$) before surgery, intraoperatively, or post-surgery. The preoperative and postoperative serum creatinine and glomerular filtration rate were similar in both groups.

Conclusions. The use of low-pressure pneumoperitoneum had no benefit compared to high-pressure pneumoperitoneum in preserving RRI and function in LLDN.

LIVING kidney donation is one way to overcome the deficit of kidneys needed worldwide. As it involves healthy individuals who must undergo major surgery, the safety of the kidney donors is essential. In most countries, the gold standard surgery to procure living donor kidney is the laparoscopic living donor nephrectomy (LLDN) [1]. LLDN has several advantages over open-donor nephrectomy, including shorter length of hospital stay, earlier return to normal physical function, reduced use of analgesics, and less scarring. Pneumoperitoneum during liver donor nephrectomy does not appear to have an adverse impact on early graft reperfusion and there were more donors in the open group who had abnormal renal resistive index (RRI) values [2–4].

LLDN requires the use of pneumoperitoneum to create working space and obtain adequate surgical exposure between intraabdominal organs and the abdominal wall [5]. Several studies have reported adverse effects with the use of pneumoperitoneum [6,7]. Pneumoperitoneum leads to elevated intra-abdominal pressure, which reduces renal blood flow to 60% of normal values [8]. This is the result of the mechanical compression of renal vein and cortical hypoperfusion. Furthermore, increased renin activity induces afferent and efferent vasoconstriction [9]. Several animal studies have shown that pneumoperitoneum increases the production of antidiuretic hormone [4]. Wever et al's meta-analysis of animal studies showed that pneumoperitoneum increases intra-operative serum creatinine (SCr) and decreases urine output [10].

The severity of renal damage was measured using SCr and glomerular filtration rate (GFR). In an animal study conducted by Abassi et al, GFR decreased after 1 hour of insufflation, using 14 mmHg pneumoperitoneum pressure

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Table 1. Patients' Demographic Characteristics

Demographic Characteristics	Low-Pressure Pneumoperitoneum (n = 17)	High-Pressure Pneumoperitoneum (n = 28)
Age (y)	29 (23–52)	32.5 (21–58)
Sex		
Male	12 (70.6%)	16 (57.1%)
Female	5 (29.4%)	12 (42.9%)
Donors' BMI (kg/m^2)	21.8 (17.57–23.90)	22.01 (15.60–39.20)
Recipients' BMI (kg/m^2)	24.76 (14.60–30.10)	22.20 (16.8–38.00)

Abbreviation: BMI, body mass index.

[11]. Deterioration of GFR and urine output was observed with pneumoperitoneum pressures above 10 mmHg, based on the previous study [8]. This GFR decrease was temporary and returned to a normal range after 60 minutes of pneumoperitoneum release [12]; however, this transient renal damage was suspected of altering allograft function after transplantation [8].

Renal function during pneumoperitoneum was influenced by the pressure level [8,9]. The standard pneumoperitoneum pressure used frequently in clinical settings was 12–14 mmHg [5]. In an animal study conducted by Bishara et al, postoperative GFR declined significantly in the 14 mmHg pressure pneumoperitoneum group compared to preoperative levels [12]. This decline was not observed the in 7 mmHg pressure pneumoperitoneum group [12]. Low-pressure pneumoperitoneum, described as 6–10 mmHg, caused less renal damage compared to high-pressure pneumoperitoneum. This damage had no clinical implications in healthy patients [5], although it may have a worse impact on patients with preexisting renal impairment [10].

Another method used for the routine evaluation of renal allografts in many centers is the RRI, a noninvasive method that uses Doppler ultrasonography to analyze intrarenal arterial waveforms in renal transplantation [13]. RRI is used to measure renal function, renal vascular resistance, and renal artery stenosis [14]. It is a good diagnostic tool to assess renal blood flow alterations [15] in transplant and native kidneys [16]. An increased level of RRI is a predictor of worse renal outcomes [14]. RRI level is also associated with chronic histologic destruction in renal allografts [17] and can be used to predict patient death after transplantation [16]. RRI has been used for routine evaluation in renal transplantation; however, a study about the effects of pneumoperitoneum in RRI has never been conducted. Previous studies about the advantage of using low-pressure compared to high-pressure pneumoperitoneum in preserving renal function in LLDN are not sufficient. A new study is needed to establish a strong recommendation for the use of low-pressure pneumoperitoneum during LLDN [5].

MATERIAL AND METHODS

Subjects

This prospective pilot study was approved by the FKUI (*Faculty of Medicine Universitas Indonesia*) Research Ethical Committee (registration number 0236/UN2.F1/ETIK/2018). Before the subject's enrollment began, each subject had consented through signed informed consent. The subjects enrolled were kidney donor patients scheduled to undergo LLDN at Cipto Mangunkusumo National Hospital, Jakarta, Indonesia, between January and July 2018. The demographic characteristics of the subjects were recorded. The patients were divided into 2 groups: Group 1, who received low-pressure (8–10 mmHg) pneumoperitoneum (22 subjects); and Group 2, who received high-pressure (12–14 mmHg) pneumoperitoneum (23 subjects).

Outcomes

The RRI, creatinine, and estimated GFR (eGFR) were measured several times perioperatively. RRI was assessed 5 times: before insufflation (bilateral kidneys), 1 hour post-insufflation (donor's kidney), 3 hours post-insufflation (donor's kidney), after surgery (remaining kidney), and 24 hours post-surgery (remaining kidney). Creatinine and eGFR were measured before and after surgery.

RRI Measurement

The RRI measurement was performed by an operator from the radiology and urology departments. The patients were hydrated and put in the left lateral decubitus position. RRI was measured using

Table 2. Comparison of the Renal Resistive Index

Time of Measurement	Renal Resistive Index		*P*
	8–10 mmHg Group	12–14 mmHg Group	
Pre-op (right kidney)*	.68 ± .03	.66 ± .04	.257
Pre-op (left kidney)*	.65 ± .04	.67 ± .04	.107
1 hour post-insufflation*	.69 ± .072	.69 ± .03	.603
3 hours post-insufflation†	.67 (.61-.73)	.68 (.61-.79)	.869
Post-operation†	.69 (.60-.73)	.69 (.60-.80)	.897
24 hours post-operation*	.65 ± .04	.70 ± .04	<.001

*Student's *t*-test analysis, mean ± standard deviation.
†Mann-Whitney analysis, median (minimum-maximum).

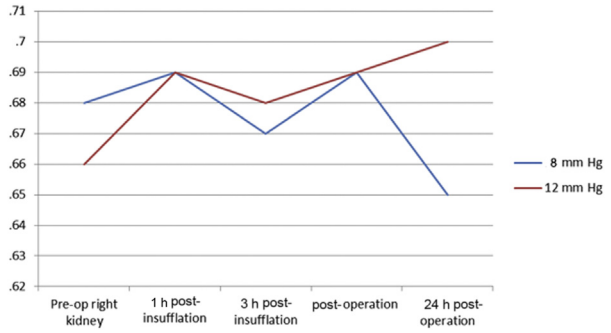

Fig 1. Renal resistive index.

Doppler ultrasonography with a 3.5–5 MHz convex probe and Doppler vascular mode on the living donor's bilateral renal artery. The formula for RRI is based on Doppler flow velocity, as follows:

RRI = (Peak systolic velocity − End diastolic velocity)/(Peak systolic velocity)

Creatinine-Based Estimated Glomerular Filtration Rate

eGFR was calculated using the following formula:

$$eGFR = 175 \times (SCr) - 1.154 \times (age) - .203 \times .742 \text{ [if female]}$$

Statistical Analysis

The independent Student's t test and the Mann-Whitney U test were used to compare the mean difference of RRI between the 2 groups. The RRI value was further classified based on the cut-off median value and analyzed using the χ^2 test. The mean difference in creatinine and eGFR levels between the 2 groups were analyzed using the paired parametric Student's t test.

RESULTS

A total of 45 subjects were analyzed in this study. Nevertheless, intraoperative adjustments of pneumoperitoneum pressure were made due to bleeding and the need for better visualization. These adjustments caused the donor numbers to be unevenly distributed (there were 17 subjects in Group 1 and 28 subjects in Group 2). The median age was 29 (23–52) years old in Group 1 and 32.5 (21–58) years old in Group 2. The BMIs in Groups 1 and 2 were 21.8 (17.57–23.90) and 22.01 (15.60–39.20), respectively. The demographic characteristics of the subjects are described in Table 1.

There was no significant difference in RRI between Group 1 and Group 2 (.68 ± .03 vs .66 ± .04, $P = .257$ in the right kidney, .65 ± .04 and .67 ± .04, $P = .107$ in the left kidney). No significant difference in RRI was found between the groups 1 hour post-insufflation, 3 hours post-insufflation, and post-operation ($P = .603$, $P = .869$, and $P = .897$, respectively). At 24 hours post-surgery, there was a statistically significant difference between Group 1 and Group 2 (.65 ± .04 vs .70 ± .04; $P < .001$). However, RRI levels remained within the normal range. The RRI results for the 2 groups are presented in Table 2 and Figure 1.

Table 3. Comparison Between Renal Resistive Index 24 Hours Post-surgery With Pneumoperitoneum

	Renal Resistive Index			
Pneumoperitoneum Pressure	≤.67	>.67	Total	*P*
8–10 mmHg	12 (70.6%)	5 (29.4%)	17 (100%)	.012*
12–14 mmHg	8 (28.6%)	20 (71.4%)	28 (100%)	
Total	20 (44%)	25 (55.6%)	45 (100%)	

*χ^2analysis.

The RRI results were further analyzed based on the cut-off (median) value of .67 at 24 hours post-surgery. The proportion of patients with an RRI level over .67 were higher in the high-pressure pneumoperitoneum group than in the low-pressure pneumoperitoneum group (20 vs 5, $P = .012$, respectively). The RRI results based on the median value cutoff are presented in Table 3.

There was no significant decrease of GFR and SCr in either group (Table 4). The eGFR levels for Group 1 was 110.59 ± 16.56 preoperatively and 107.50 ± 17.90 postoperatively ($P = .244$). The eGFR levels for Group 2 was 112.60 ± 12.93 preoperatively and 110.66 ± 12.64 postoperative ($P = .266$). The SCr values for Group 1 were .81 ± .15 pre-surgery and .84 ± .16 post-surgery ($P = .163$). The SCr values for Group 2 were .76 ± .14 pre-surgery and .78 ± .15 post-surgery ($P = .212$).

DISCUSSION

This is the first study to compare RRI in low-pressure vs high-pressure pneumoperitoneum in renal transplantation. Pneumoperitoneum is associated with significant direct and indirect effects on renal physiology based on pressure level [6]. The mechanism is associated with increased intra-abdominal pressure during pneumoperitoneum that compresses renal parenchyma and veins [18]. This compression causes transient renal dysfunction due to the decrease in renal blood flow. Reduced renal perfusion activates the renin-angiotensin-aldosterone system, which further decreases blood flow [19]. In particular, at a pressure over 10 mmHg, pneumoperitoneum has been shown to produce reduced renal dysfunction and transient oliguria [20,21]. Demyttenaere et al conducted a systematic review of the effects of pneumoperitoneum on renal perfusion and function; they observed that 17 of 20 studies demonstrated a reduction in renal blood flow associated with pneumoperitoneum, while 20 of 25 studies showed a decrease of renal function [22].

This study compares the effects of low-pressure and high-pressure pneumoperitoneum during laparoscopic surgery on RRI and function. A similar study was conducted by Warlé et al using a lower pressure level (7 mmHg) vs standard pressure pneumoperitoneum [23]. Patients in the low-pressure pneumoperitoneum group had a higher urine output (23 mL/h vs 11 mL/h, $P = .041$), while difficulty and blood loss were similar in both groups [23]. Based on the previous study, low-pressure pneumoperitoneum requires a longer skin-to-skin surgery time than standard-pressure pneumoperitoneum [2]. Low-pressure pneumoperitoneum also impaired surgeons' view of the surgery area, making it hard for them to perform complex procedures such as

Table 4. Comparison of eGFR and SCr Levels

Pressure	eGFR (mL/min/1.73m^2)			SCr (mg/dL)		
	Pre-op	Post-op	P^*	Pre-op	Post-op	P^*
8–10 mmHg	110.59 ± 16.56	107.50 ± 17.90	.244	.81 ± .15	.84 ± .16	.163
12–14 mmHg	112.60 ± 12.93	110.66 ± 12.64	.266	.76 ± .14	.78 ± .15	.212

Abbreviations: eGFR, estimated glomerular filtration rate; SCr, serum creatinine.
*Paired Student's *t*-test analysis, mean ± standard deviation.

nephrectomy for this group, especially in complicated cases with multiple vessels and abundant perirenal fat [2].

No abnormalities in RRI levels (less than .8)were found in this study in any measurement. RRI was affected by peripheral arterial resistance, compliance, and hemodynamics [14]. Intrarenal factors (e.g. transplant rejection, severe acute tubular necrosis, and graft nephritis), extrarenal factors (e.g. ureteric obstruction, vascular obstruction/stenosis/compression, and large perinephric collection compressing the allograft), and systemic factors (e.g. hypotension, patient age, and heart rate) were found to influence RRI levels [14]. The increase of RRI in the early postoperative period (the first 24 hours) indicated a vascular complication [24]. Mortality at 3, 12, and 24 months were significantly more likely in patients with an RRI level over .8 after renal transplantation [16]. RRI levels were associated with postoperative GFR level. Patients with a higher RRI had a 50% higher risk of GFR reduction [16]. No association was found between renal RRI and SCr [17].

There was no significant difference in eGFR or SCr between the 2 groups, which is consistent with another study [23]. Hawasli et al compared SCr levels between low-pressure and high-pressure pneumoperitoneum and found that there was no difference in SCr levels between the 2 groups on the first day after surgery [25]; however, it is a delayed indicator of acute renal injury. It is also influenced by many non-renal factors, such as muscle mass, muscle metabolism, diet, medications, and hydration status [26]. Therefore, another method to assess renal function more accurately is required.

For approximately 90% of the patients who underwent low-pressure pneumoperitoneum, the pressure was set to 8 mmHg; for high-pressure pneumoperitoneum it was set to 12 mmHg. However, adjustments of about 2 mmHg were made due to difficulties such as bleeding; therefore, for 10% of the operation time, the pneumoperitoneum pressure was 10 mmHg (low-pressure pneumoperitoneum) or 14 mmHg (high-pressure pneumoperitoneum).

This study was subject to several limitations. The length of surgery between the 2 pneumoperitoneum groups was not analyzed, although the duration of operation is one of the factors that influences renal function.

CONCLUSIONS

Based on our study, we conclude that the use of low-pressure pneumoperitoneum had no benefit compared to high-pressure pneumoperitoneum in preserving RRI and function. Further studies are required to investigate long-term RRI and function based on pneumoperitoneum pressure levels in LLDN.

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