En bloc ligation of renal vessels is safe and reduces duration of surgery

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ABSTRACT

INTRODUCTION: Conventionally, individual ligation of the renal vessels with clips is performed during laparoscopic nephrectomy (LN). Concomitant ligation of the vessels is not a standard procedure due to an expected risk of stapler dysfunction and the development of arteriovenous fistulas (AVF). Using the EndoGIA stapler 45/2.5 mm, we compared en bloc ligation with individual ligation during LN and nephroureterectomy (LNU) with a special focus on the development of AVF and technique safety.

METHODS: This was a retrospective study of all patients undergoing LN or LNU at the Department of Urology, Roskilde Hospital, Denmark, between January 2010 and April 2014. The follow-up period was minimum six months.

RESULTS: A total of 228 patients underwent LN and 56 patients underwent LNU. In the LN group, 77 patients underwent en bloc ligation. The mean surgical time was significantly reduced to 89 minutes in the en bloc group compared to 109 minutes in the conventional group (p = 0.0001). The difference remained significant with multivariate analysis. In the LNU group, seven patients underwent en bloc ligation. There was no significant difference between conventional ligation and en bloc ligation with respect to surgical time in either the univariate or the multivariate analyses. None of the patients needed blood transfusion. With a mean follow-up of 13.5 months, no AVF were found.

CONCLUSIONS: En bloc ligation appears to be safe and can reduce the surgical time during LN without increased risk of blood transfusion and without development of AVF. Further studies are needed to assess any advantages associated with use of the method during LNU.

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Conventionally, individual ligation of the renal artery and vein with clips is performed during laparoscopic nephrectomy (LN). Concomitant ligation of the vessels (en bloc ligation) is not a standard procedure due to an expected risk of stapler dysfunction [1, 2] and the development of arteriovenous fistulas (AVF) [3]. However, recent studies suggest that en bloc ligation may be a safe procedure that offers a reduction in surgical time as well as a lower blood loss without evidence of an increased risk of the development of AVF [4] compared with the conventional technique.

The aim of the present study was to compare en bloc ligation, using the EndoGIA stapler (**Figure 1**) 45/2.5 mm (Covidien Inc, Mansfield, MA), with conventional individual ligation with Hem-o-lok clips during LN and laparoscopic nephroureterectomy (LNU) regarding surgical time, blood transfusions and the development of AVF.

METHODS

A retrospective chart review of 284 consecutive patients undergoing either LN or LNU between January 2010 and April 2014 was performed in December 2014. The study was approved by the Danish Data Protection Agency in accordance with Danish law. For the en bloc ligation, the EndoGIA stapler (Covidien Inc, Mansfield, MA) 45/2.5 mm was used. For the conventional method, Hem-o-lok clips were used. All operations were performed by three certified urologists; the method of ligation depended on the surgeon's preference in each individual case.

Demographic data were collected including age, gender ±, indication for surgery, surgical method (conventional hand-assisted laparoscopy or robot-assisted laparoscopy), method of ligation, blood loss, blood transfusions, follow-up time, perioperative complications, post-operative complications, conversion to open surgery and any evidence of post-operative AVF development.

All patients had a minimum follow-up period of six months or more with computed tomography (CT) as dictated by their original diagnosis (based on recommendations from the Danish Urological Cancer Group guidelines) [5] and clinical evaluations for AVF development. AVF was suspected in case of presence of abdominal bruit, diastolic hypertension, congestive heart failure, flank pain and tachycardia [3, 4, 6]. Such symptoms prompted additional abdominal CTs.

! ABBREVIATIONS

AVF = arteriovenous fistulas
BMI = body mass index
CT = computed tomography
LN = laparoscopic nephrectomy
LNU = laparoscopic nephroureterectomy
SAS = Statistical Analysis System

ORIGINAL ARTICLE

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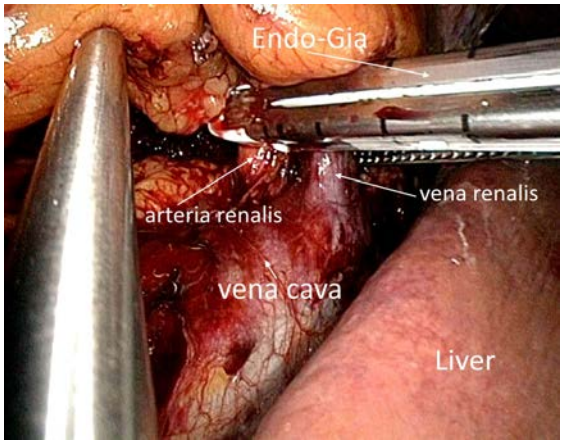
FIGURE 1

The EndoGIA stapler.



Post-operative complications were assessed by the Clavien Dindo Classification [7] and divided into complications related to the ligation technique (perioperative bleeding, post-operative bleeding in the renal field, dysfunction of the ligation technique and the development of AVF) or complications not related to the ligation technique.

Statistical analyses were performed with the Statistical Analysis System (SAS) version 9.2, software package for windows (Institute Inc., Cary, NC, USA). In the univariate analyses, continuous variables were compared using Students t-test. Categorical variables were compared using the chi-squared test or Fisher's exact test. Multivariate analyses were performed using multiple linear regression and multivariate logistical regression models. A p-value < 0.05 was considered statistically significant.

Operation technique

The patient was placed in the left or right lateral decubitus position. Initial access to the peritoneal cavity was obtained via the Hasson technique. Next, three accessory 12-mm trocars were placed on the left side, and one 5-mm plus three 12-mm trocars were placed on the right side; the 5-mm trocar was used to support the liver. All trocars were inserted under visual control, and 10-15 ml bupivacain (2.5 mg/ml) was permeated to all trocar incisions. The colon and spleen were dissected from the left kidney; and the colon, duodenum and liver from the right kidney. The ureter was dissected and traced to the renal pelvis, and the dissection was continued towards the renal vessels. With the conventional technique, the renal artery and vein were dissected carefully and secured with two Hem-o-lok clips, centrally. During the en bloc technique, the renal vessels were secured with EndoGIA 45/2.5 mm without further dissection. The dissection of the kidney continued cranially and laterally in both techniques. In case of nephroureterectomy, the ureter was dissected and traced towards the bladder. Finally, the kidney was placed in an endo-bag and removed through a 7-10 cm incision.

Trial registration: not relevant.

RESULTS

A total of 174 (61%) men and 110 (39%) women were included; 228 patients underwent LN and 56 patients underwent LNU. The mean age for the entire group was 64 years (range: 16-87 years), and the mean follow-up time was 13.5 months (range: 6-50 months). Overall, 243 procedures were performed as conventional laparoscopy (74 of these included hand assistance) and 41 procedures were performed with robot-assisted surgery. Overall, 77% of patients in the en bloc group had at least one CT.

Laparoscopic nephrectomy

The indication for LN was renal masses in 179 patients (79%) and chronic inflammatory disease in 49 patients (21%) (**Table 1**). The en bloc technique was performed in 77 patients (34%) and the conventional technique was performed in 151 (66%) patients. The procedure was performed as LN in 136 (60%), hand-assisted LN in 72 (32%) and as a robot-assisted procedure in 20 (8%).

In the univariate analysis, there was a significant difference in mean operating time with 89 minutes (95% confidence interval (CI): 81-97 minutes) in the en bloc group versus 109 minutes (95% CI: 103-115 minutes) in the conventional group ($p < 0.0001$). The difference remained significant in multivariate analysis after controlling for age, gender, indication for surgery, surgical method, surgeon, tumour size, body mass index (BMI) and blood transfusions (< 24 minutes) (95% CI: < 12 – < 37 minutes), $p < 0.0001$).

Blood loss was significantly lower in the conventional group with a mean 50 ml (95% CI: 29-71 ml) than in in the en bloc group where it was mean 117 ml (95% CI: 74-160 ml), ($p = 0.006$). Controlling for age, gender, indication for surgery, surgical method, tumour size, BMI and surgeon in a multivariate analysis, we found that the difference remained significant with an estimated increase in blood loss in the en bloc group of 90 ml (95% CI: 19-161 ml) ($p = 0.01$). Three patients received blood transfusions in the en bloc group compared with one in the conventional group. The difference was not significant in either univariate ($p = 0.11$) or multivariate analyses ($p = 0.17$).

The univariate analysis showed a significant difference in the mean tumour size with 69.8 cm (95% CI: 64-75 cm) in the en bloc group versus 57 cm (95% CI: 52-63

cm) in the conventional group (p < 0.003). The mean BMI in the en bloc group was 27.9 kg/m^2 (95% CI: 26-29 kg/m^2); in the conventional group, the mean BMI of 27.1 kg/m^2 (95% CI: 26-28 kg/m^2), (p = 0.4). The distribution of the histological outcome between the groups was significantly different (Table 1).

No complications were related to the ligation technique in the en bloc group, whereas one operation was converted into open nephrectomy in the conventional ligation group due to bleeding. A total of three patients in the en bloc group and five patients in the conventional group suffered complications unrelated to the ligation technique with a Clavien score > 2. Only one incidence of intraoperative EndoGIA failure was reported (the knife of the EndoGIA instrument did not drive through the whole tissue). This failure did not result in complications as the knife was immediately replaced with a new one.

The mean follow-up period was 13 months (range: 6-50 months). A total of 59 patients in the en bloc group and 128 patients in the conventional group had at least one CT in the follow-up period. The remaining patients did not receive a CT, either because the indication for surgery was benign or because the pathology showed no evidence of malignancy. There was neither radiological nor clinical evidence of AVF development in either group.

Laparoscopic nephroureterectomy

Indications for LNU included urothelial cell carcinoma of the upper urinary tract in 47 patients and benign diseases in nine patients. The en bloc technique was performed in seven patients (13%) and the conventional technique was performed in 49 patients (87%).

The procedure was performed as LNU in 33 (59%), as hand-assisted procedure in two (3%) and as robot-assisted procedure in 21 (38%).

Univariate analysis showed was no significant difference in the mean operating time, with 159 minutes (95% CI: 129-189 minutes) in the en bloc group versus 172 minutes (95% CI: 157-188 minutes) in the conventional group (p = 0.36). However, in the multivariate analysis, the difference reached statistical significance with a difference of 43 minutes (95% CI: 4-81 minutes) (p = 0.03) in favour of the en bloc technique.

No significant difference in the mean blood loss was observed with 79 ml (95% CI: 20-137 ml) versus 91 ml (95% CI: 40-142 ml) (p = 0.73) in the en bloc and the conventional group, respectively. Likewise, no difference in blood loss was observed between the groups in multivariate analysis (p = 0.71). None of the patients received blood transfusions.

No significant difference in BMI was observed; mean 25 kg/m^2 (95% CI: 21-28 kg/m^2) in the en bloc group versus a mean of 27 kg/m^2 (95% CI: 26-28 kg/m^2)

TABLE 1

The demographic distribution of per- and post-operative outcome after nephrectomy.

	En bloc	Clips	p-value[a]
Patients, n	77	151	
Age, yrs, mean	65	62	0.10
Gender, male/female, n	46/31	91/60	0.06
Knife time, min., mean	89	109	0.0001
Bleeding, ml, mean	117	50	0.0001
Blood transfusions, n	3	1	0.11
Post-operative in-hospital stay, days, mean	2.5	2	0.11
Complications, Clavien Dindo classification > 2, n	3	5	1.00
Stapler dysfunctions, n	1	–	–
Radiographic follow-ups, n	59	128	–
Follow-up, months, mean	9.5	15	–
AVF, n	0	0	–
Pathological feature, n (%)			< 0.0001
Renal cell carcinoma	64 (83.1)	87 (57.6)	
Oncocytoma	7 (9.1)	9 (6.0)	
Angiomyolipom	2 (2.6)	1 (0.7)	
Renal cystic disease	0	9 (6.0)	
Chronic inflammatory disease	4 (5.2)	45 (29.8)	
T-stage, n (%)			0.049
T1a	11 (17.2)	20 (23.0)	
T1b	18 (28.1)	35 (40.2)	
T2	11 (17.2)	16 (18.4)	
T3	24 (37.5)	16 (18.4)	

AVF = arteriovenous fistulas.
a) p < 0.05 is considered significant.

TABLE 2

The demographic distribution of per- and post-operative outcome after nephroureterectomy.

	En bloc	Clips	p-value[a]
Patients, n	7	49	
Age, yrs, mean	67	70	0.95
Gender, male/female, n	4/3	33/16	0.28
Operation time, min., mean	159	172	0.79
Bleeding, ml, mean	79	91	0.36
Blood transfusions, n	0	0	–
Post-operative in-hospital stay, days, mean	4	5	0.32
Complications, Clavien Dindo classification > 2, n	0	8	0.58
Stapler dysfunctions, n	0	0	–
Radiographic follow-ups, n	6	40	–
Follow-up, months, mean	11	17	–
AVF, n	0	0	–
T-stage, n (%)			0.83
Ta	3 (42.86)	22 (44.90)	
T1	1 (14.29)	7 (14.29)	
T2	1 (14.29)	7 (14.29)	
T3	2 (28.57)	12 (24.49)	
T4	0	1 (2.04)	

AVF = arteriovenous fistulas.
a) p < 0.05 is considered significant.

in the conventional group (p = 0.18). No significant differences in the distribution of histological outcome between the groups were found (**Table 2**).

No perioperative complications were related to the ligation technique in either group. In the conventional group, eight patients suffered post-operative complications with a Clavien score > 2 not related to the ligation technique, whereas no such complications were reported in the en bloc group.

The mean follow-up time in the group was 16 months (range: 6-48 months). A total of six patients in the en bloc group and 40 patients in the conventional group had at least one CT in the follow-up period. No evidence of development of AVF was seen in either group.

DISCUSSION

The development of AVF is rare and has been reported in a small number of case reports [8]. In 1985, Lacombe et al published a series of 62 cases of AVFs associated with nephrectomies, but unfortunately the ligation technique was not described in 48 of the cases, and 57 of the 62 patients had undergone nephrectomy for infectious, inflammatory or traumatic reasons. The interval between surgery and development of an AVF ranges widely from five months to 40 years with a mean of 15 years [3]. Furthermore, the en bloc technique is widely used in thoracic surgery, gynaecologic surgery and laparoscopic splenectomy, using stapler, and there was no evidence of development of AVF [9-11].

A randomised study has compared en bloc ligation and individual ligation in laparoscopic radical nephrectomy for renal cell carcinoma [12]. The study showed a statistically lower knife time and lower estimated blood loss in the en bloc group. No evidence of AVF was found in either group. We reproduced this finding in our study, but not regarding the estimated blood loss. Larger tumour size and the significant increase in frequency of T3 tumours (38%) in the en bloc group may explain the difficulty of the procedure which can lead to increased blood loss.

The mechanism to develop AVF may be infection, inflammation or the technique of en bloc ligation [13-15]. In our cohort, four patients underwent en bloc technique due to inflammatory renal disease without the development of AVF. These results are in accordance with other literature [4, 6, 12, 16-18]. This development of AVF may be due to the difference in the en bloc ligation technique in the past and today. According to the old method, the renal vessels were forcibly occluded together by couple suture, where at least one of them drives through the vessels and may create ischaemic damage to the vessels, whereas the en bloc technique required that the vessels close by multiple lines staples.

Moreover, dissection of the perinephric tissue between the renal artery and the vein during conventional technique can lead to erosion of the wall of renal vessels, which may increase the risk of development of renal artery aneurysms and subsequently the formation of AVF. According to this theory, the use of stapler may prevent the formation of AVF, especially because no human case reports of an AVF after en bloc ligation with titanium staplers has been published to date [19].

Limitations on the use of EndoGIA include a wide renal vascular pedicle as well as the presence of enlarged lymph nodes in the field, which may result in closure failure of the EndoGIA. The EndoGIA failure rate in our cohort was 1/84 (1.2%), which is similar to that reported in other studies, namely between 0.2 and 1.8%. Most of the stapler challenges are preventable and can be avoided with careful application and recognition [1, 2, 6].

In the LN group and the LNU group, the knife time was reduced significantly with the en bloc technique, as also been reported in previous studies [4]. Despite this, it is important to note that our study may include a learning curve effect. Thus, the use of en bloc ligation of the renal vascular pedicle was not a standard procedure in our department prior to the current series of patients. In addition, the use of the ligation technique was based on the surgeon's preference in each individual case. This means that the EndoGIA stapler may, in some cases, have been used out of necessity to secure the renal vascular pedicle in challenging cases associated with perioperative bleeding.

Therefore, the higher blood loss in the en bloc group could be due to selection bias; this also applies to the increase in the tumour size and high frequency of T3 tumours in the en bloc group.

The limitations of this study include its retrospective and non-randomised design and the relatively short follow-up period. In addition, some of the patients had no radiographic follow-up.

En bloc ligation appears to be safe and capable of reducing surgical time during LN without increasing the risk of blood transfusions or the development of AVF. To date, no human case reports of an AVF after en bloc ligation with titanium staplers have been published. Further randomised studies are needed to assess advantages and possible drawbacks to en bloc ligation of the renal vessels during LN and LNU.

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