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Blood loss associated with radical cystectomy: A prospective, randomized study comparing impact LigaSure vs. stapling device[☆]

Ian M. Thompson III, M.D., Stephen F. Kappa, M.D., M.B.A.^{*}, Todd M. Morgan, M.D., Daniel A. Barocas, M.D., M.P.H., Carl J. Bischoff, M.D., Kirk A. Keegan, M.D., Kelly L. Stratton, M.D., Peter E. Clark, M.D., Matthew J. Resnick, M.D., Joseph A. Smith Jr., M.D., Michael S. Cookson, M.D., and Sam S. Chang, M.D.

Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, TN

Abstract

Objectives—Radical cystectomy (RC) is associated with significant blood loss and transfusion requirement. We performed a prospective, randomized trial to compare blood loss, operative time, and cost using 2 different and commonly employed approaches to tissue ligation and division during RC: mechanical (stapler device) and electrosurgical (heat-sealing device).

Methods and materials—Eighty patients undergoing RC for urothelial bladder carcinoma were randomized to use of either an Endo GIA Stapler or Impact LigaSure device for tissue ligation and division. Primary outcomes were blood loss, operative time, and device costs. Data were analyzed with Wilcoxon rank sum test and Welch 2-sample *t* test.

Results—There were no significant demographic or preoperative differences between the cohorts. Mean estimated blood loss was similar between the electrosurgical (687 ml) and stapler (708 ml) arms ($P = 0.850$). There were no significant differences between cohorts when comparing operative times or transfusion requirement. There was a significant increase in the mean number of adjunctive suture ligatures used in the stapling device arm (3.0 vs. 1.5, $P = 0.047$). Total device costs were significantly lower with the LigaSure compared with the GIA Stapler (\$625.00 vs. \$1490.10, $P < 0.001$). There were no complications attributable to either device.

Conclusions—This prospective, randomized study demonstrates no significant difference in blood loss, transfusion requirement, or safety between mechanical vs. electrosurgical control of the vascular pedicles. The LigaSure device, however, is significantly less costly than the GIA Stapler and required fewer additional measures for hemostasis.

Keywords

Bladder cancer; Cystectomy; Surgical blood loss; Blood transfusion

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^{*}Corresponding author. Tel.: +1-423-9-149-253. stephen.kappa@vanderbilt.edu (S.F. Kappa).

1. Introduction

Blood loss associated with radical cystectomy (RC) has historically concerned urologic surgeons, as it has been significant and oftentimes required blood transfusion in the perioperative period [1–3]. For example, in an earlier series of 297 patients undergoing RC for urothelial carcinoma at our institution, between 1995 and 2000, 30% of patients required a perioperative blood transfusion [4]. Another review of 553 consecutive patients undergoing open RC at our institution between 2000 and 2005 demonstrated median estimated blood loss (EBL) of 600 ml and 38% of patients required blood transfusion either intraoperatively or within the first 30 days of the operation [5].

Previous studies on patients undergoing radical prostatectomy and nephrectomy demonstrated a decreased transfusion requirement associated with modifications in surgical technique [6,7]. Similarly, new surgical techniques and technologies have been developed over the past 10–15 years in an attempt to reduce the significant blood loss associated with RC [4,8–10]. In a prospective, randomized trial, we previously compared the use of a stapling device to that of the more traditional suture ligation technique and examined their effects on operative time, hemostasis, and need for transfusion [11]. This study demonstrated that the use of the stapling device significantly reduced blood loss during RC (362 ml vs. 565 ml, $P = 0.007$) and the perioperative transfusion requirement (34.3–5.7%, $P = 0.006$) for those patients.

More recently, the Impact LigaSure (Covidien Surgical, Boulder, CO) a heat-sealing device has been incorporated in the performance of many open and laparoscopic operative procedures, including RC. However, the beneficial merits of this electrosurgical device on blood loss and transfusion requirement have not been compared directly with the stapling device. Here, we report the first prospective, randomized trial comparing the LigaSure and Endo GIA Stapler (Covidien Surgical, Boulder, CO), specifically examining blood loss, transfusion requirement, and costs, in patients undergoing RC.

2. Materials and methods

Under an institutional review board-approved protocol at Vanderbilt University Medical Center, we prospectively analyzed a cohort of patients scheduled to undergo RC for treating urothelial carcinoma. We randomized patients in a single-blinded fashion to conventional RC with use of the stapling device vs. the electrosurgical device. Eligible patients were extensively counseled preoperatively regarding the potential risks and benefits of study participation, and all patients signed informed consent forms approved by our institutional review board. Patients were randomized on a one-to-one basis to either the stapler or electrosurgical device.

Patient demographics and clinical characteristics were recorded and included American Society of Anesthesiologists classification, clinical stage, and preoperative hematocrit. Open RC was performed with a low-midline incision with wide excision of the bladder and bilateral pelvic lymphadenectomy. The plane between the rectum and bladder was initially established with the use of sharp dissection and electrocautery. In the stapler arm, the

superior, posterior, and lateral pedicles of the bladder were ligated using the stapling device, usually with 2 firings of the stapler per side. In the electrosurgical arm, the Impact LigaSure device was used to divide these same pedicles of the bladder; the only step that differed between the 2 study arms was the single step of ligation and division with the 2 different instruments. Collateral bleeding was controlled with the use of suture ligatures or hemoclips, the numbers of which were recorded for data collection. The remainder of the procedure was performed as previously described [11].

Several intraoperative variables were recorded and analyzed. Time points recorded for this study included skin incision, time of bladder removal, time after bladder removal once hemostasis was achieved, and end of surgery. Total EBL was measured, and the EBL for each of these intervals was also recorded. These estimates were made and agreed upon by the surgeon and anesthesiologist performing the case after considering irrigation fluid used, suction canister volume, and visually assessing surgical sponges at each of these intervals. For those patients randomized to the stapler arm, the number and type (45 vs. 60) of staple loads were recorded. In addition, preoperative and postoperative hematocrits, intraoperative and postoperative blood transfusion requirement, and number of units transfused were determined. Hemoglobin levels were not checked as part of the study. Use of adjunctive hemostasis measures, suture ligatures, and hemoclips was recorded to calculate total intraoperative costs associated with each treatment arm. Intraoperative complications and device malfunctions were also recorded and noted for the study if they were related or possibly related to the stapling device or the LigaSure device.

A power analysis was performed, and it was determined that a total of 80 patients needed to be randomized to detect a significant difference in number of units transfused ($\pi = 0.80$, $P < 0.05$). Alternatively, more than 250 patients would need to be randomized to each arm of the trial to detect a significant difference in EBL.

Patient demographics, preoperative clinical characteristics, operative parameters, outcomes, and costs were all compared with univariate analysis using 2-sample *t* test/ Wilcoxon rank sum test for continuous variables and chi-square test/the Fisher exact test for categorical variables. All tests of significance were 2-tailed with $P < 0.05$ deemed significant. Stata 11.0 (Stata Corporation, College Station, TX) was used for statistical analysis.

3. Results

During the study period between October 2008, and March 2011, 80 patients were enrolled in this randomized trial: 40 to the stapler device arm and 40 to the electro-surgical device arm. At baseline, there were no significant demographic or preoperative clinical differences between the cohorts (Table 1). The mean age for the stapler and electrosurgical arms was 65.8 and 68.5 years, respectively ($P = 0.165$), and the majority of patients in each cohort were men. There were no differences between arms in preoperative comorbidities as measured by American Society of Anesthesiologists classification ($P = 0.134$). The median preoperative hematocrit for the stapler arm was 42 vs. 43 for the LigaSure arm ($P = 0.426$). A total of 10 patients received treatment with neoadjuvant chemotherapy.

No differences in intraoperative outcomes in terms of blood loss or operative time were observed between the 2 study arms, either overall or when broken down into the surgical-time intervals as described earlier. EBL was similar in each cohort with mean of 687 ml in the electrosurgical arm and 708 ml in the stapler arm ($P = 0.850$; Table 2). There were no significant differences between the 2 arms when comparing the mean transfusion requirement (2.9 u vs. 3.4 u, $P = 0.591$) or median operative times (245.5 min for stapler vs. 268 min for electrosurgical, $P = 0.600$). In an exploratory, subset analysis, we excluded patients with baseline anemia, analyzing only those patients with a preoperative hematocrit of 30 or greater. Again, there was no significant difference in EBL or number of units transfused.

When examining the use of hemostatic measures required beyond the devices themselves, there was a significant increase in the median number of adjunctive suture ligatures used in the stapling device arm (3.0 vs. 1.5, $P = 0.047$) (Table 3). There were no complications attributable to either device. Additionally, neither the LigaSure nor the GIA Stapler device mechanically failed during any of the procedures performed. Lastly, the median total device cost was significantly lower with the LigaSure compared with the GIA Stapler (\$625.00 vs. \$1490.10, $P < 0.001$).

4. Discussion

As long as RC remains the preferred treatment option for invasive bladder cancer, urologists would be faced with the task of taking measures to reduce both intraoperative blood loss and subsequent perioperative blood transfusion. We previously reported the beneficial effect of using a stapling device for RC, and this technique was widely adopted at our institution [11]. More recently, our group anecdotally noted improved intraoperative outcomes using the LigaSure device. To test this, we performed this prospective, randomized controlled trial, comparing use of the LigaSure device and more traditional stapling device, and demonstrated no significant difference in blood loss or blood transfusion between these 2 devices. Both devices increase the relative “ease” of the procedure compared with suture ligature, and no significant difference in operative time was found or expected.

Similar studies have recently been conducted comparing LigaSure heat-sealing devices to other hemostatic techniques in various other operations. A trial comparing the LigaSure Precise device to traditional suture ligation in thyroid surgery demonstrated a significant reduction in operative time, the primary end point of the study [12]. In a retrospective review, use of the LigaSure heat-sealing device in low anterior resection for rectal cancer demonstrated reduced operative time and blood loss compared to more traditional hemostatic techniques [13]. Compared to traditional suture ligatures, we previously demonstrated an advantage for the stapling device as well [11]. The LigaSure device did not prove superior to the stapling device for these parameters. While this prospective, randomized controlled trial similarly demonstrated no significant difference in EBL, operative time, or number of units transfused, it did demonstrate a significantly higher use of adjunctive hemostatic measures (suture ligatures) required with the GIA Stapler device.

Importantly, we identified a large difference in intra-operative device costs between the 2 study arms, with the Impact LigaSure being significantly less costly. With all other operative parameters being essentially equal, these findings may support the use of the LigaSure over the traditional stapling device in RC. *Hospital Operating Trends Quarterly* noted a decrease in operating margin for its hospitals from 3.3% to 2.8% between the third quarters of 2009 and 2010 [14]. They also noted that between 2005 and 2010, U.S. hospitals saw nonlabor expenses increase nearly 20% compared to just an 8% growth in labor costs [14]. Perhaps stating the obvious, this article states that if “hospitals could better control nonlabor expenses like supply chain and physician preference items as well as labor expenses, they could enjoy substantial savings” [14]. Such analysis highlights the value of the possible cost savings discovered in this study.

There are several limitations to this study worth noting. The patients in this study did not represent a consecutive cohort of patients undergoing RC at our institution, for several reasons, including increasing use of robotic-assisted RC as well as a separate, ongoing phase 4 prospective, randomized trial for patients undergoing open RC that precluded other synchronous trials. There were 5 different surgeons involved in this study, and transfusion criteria were not established by the study protocol; transfusion was at the surgeon’s discretion. Thus, significant variability may have been present for 1 of the primary end points of the study. In addition, there was no measure or standardization of technique with these devices. For example, it is not known whether each surgeon followed stapler manufacturer’s recommendations for a 20 second plus delay between staple deployment and cutting staple deployment and cutting, which may explain the additional use of ligatures for secondary control in the stapler arm.

Other limitations include that intraoperative data recording was not conducted by the same individual for every case, introducing interobserver variability. There was no minimum hematocrit threshold for admission to the study cohort, and RC patients are often anemic even before their operation. In our practice, all patients hold antiplatelet therapy for at least 7 days prior to the date of operation. During hospitalization for RC, patients receive enoxaparin and sequential compression devices for deep vein thrombosis prophylaxis; however, those with renal insufficiency receive heparin instead of enoxaparin, a difference that was not accounted for during this study. Cost data for the devices used in this study were obtained from the operative supply department at our institution, which may vary from hospital to hospital. Lastly, this study was not designed to collect outcomes data. Despite these points, this was a prospective, randomized trial that found a significant difference in adjunctive suture ligatures and cost between 2 devices commonly used for hemostasis during RC.

While our study design controls for confounders, the results demonstrated no differences in significant cost drivers, such as EBL, operative time, or number of units transfused, and this cost analysis is limited by the small trial size. Caution should be taken in generalizing these findings to other institutions given the unique cost structures and patient populations of high-volume, tertiary care academic medical centers. Additionally, the pricing of these devices can vary significantly by market, further limiting the generalizability of these results. Nevertheless, the cost savings demonstrated in this study suggest consideration of

the use of the LigaSure over the stapling device for patients undergoing RC, and may encourage the study of other cost-savings potential of this device, such as its use instead of staples in the isolation of the bowel segment for urinary diversion.

5. Conclusion

This prospective, randomized study demonstrates no significant difference in blood loss, transfusion requirement, or safety between the LigaSure and GIA Stapler devices. The LigaSure device, however, is significantly less costly than the stapling device and required fewer additional measures for hemostasis. Such savings may prove increasingly important in the current health care environment.

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Table 1

Demographic and preoperative clinical characteristics

Characteristics	GIA Stapler	Impact LigaSure	<i>P</i> value
Total number of patients	40	40	
Mean (SD) age, y	65.8 (9.6)	68.5 (7.9)	0.165
Gender, <i>n</i> (%)			
Male	37 (92.5)	33 (82.5)	0.311
Female	3 (7.5)	7 (17.5)	
ASA class, <i>n</i> (%)			
0–2	4 (10.0)	6 (15.0)	0.134
3	32 (80.0)	34 (85.0)	
4	4 (10.0)	0 (0.0)	
Median (IQR) preoperative hematocrit, %	42 (36.5–44.5)	43 (37.5–45.5)	0.426
Clinical stage, <i>n</i> (%)			
Nonmuscle invasive (cT1)	17 (42.5)	15 (37.5)	0.648
Muscle invasive (cT2)	23 (57.5)	25 (62.5)	
Neoadjuvant chemotherapy, <i>n</i> (%)			
No	36 (90.0)	34 (85.0)	0.737
Yes	4 (10.0)	6 (15.0)	

SD = standard deviation; IQR = interquartile range; ASA = American Society of Anesthesiologists.

Table 2

Operative and pathologic characteristics

Characteristics	GIA Stapler	Impact LigaSure	<i>P</i> value
Median (IQR) operative time, min	245.5 (213–317.5)	268 (222–298)	0.600
Diversion type, <i>n</i> (%)			
Ileal conduit	34 (85.0)	29 (72.5)	0.172
Neobladder	6 (15.0)	11 (27.5)	
Continent cutaneous	0 (0)	0 (0)	
Mean (IQR) estimated blood loss, ml	686.5 (406.1)	707.5 (570.8)	0.850
Perioperative blood transfusion, <i>n</i> (%)			
No	27 (67.5)	27 (67.5)	1.000
Yes	13 (32.5)	13 (32.5)	
Mean (SD) PRBC units transfused, <i>n</i>	2.9 (1.0)	3.4 (2.9)	0.591
Pathologic stage, <i>n</i> (%)			
T0, Ta, Tis, T1	13 (33.3)	17 (42.5)	0.363
T2	11 (28.2)	6 (15.0)	
T3	13 (33.3)	12 (30.0)	
T4	2 (5.1)	5 (12.5)	
Surgical margin, ^a <i>n</i> (%)			
Negative	32 (80.0)	32 (80.0)	0.737
Ureteral/urethral	6 (15.0)	8 (20.0)	
Soft tissue	2 (5.0)	1 (2.5)	

IQR = interquartile range; SD = standard deviation; PRBC = packed red blood cells.

^a One LigaSure patient had both urothelial and soft tissue positive surgical margins, so sum exceeds 100%.

Table 3

Use and overall cost of hemostatic devices

Characteristics	Endo GIA Stapler	Impact LigaSure	<i>P</i> value
Staple loads*			
Type no. 45, median (IQR)	2.5 (2–5)	0 (0–0)	<0.001
Type no. 60, median (IQR)	1.5 (0–2)	0 (0–0)	<0.001
Adjunctive hemostatic measures			
Suture ligatures, median (IQR)	3 (2–5)	1.5 (0–3.5)	0.047
Hemoclips, median (IQR)	2 (0–4)	1 (0–4)	0.285
Overall cost of hemostatic devices, \$, median (IQR)	1490.10 (1376.20–1672.20)	625.00 (625.00–625.00)	<0.001

IQR = interquartile range.