The Effect of Intraluminal Content on the Bursting Strength of Vessels Ligated with the Harmonic ACE and LigaSure V

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Abstract

Purpose: Energy-based surgical devices (ESDs) are critical for maintaining hemostasis during laparoscopy; however, there are no studies that have evaluated the function of ESDs under different physiologic conditions. We evaluated the effect of intraluminal vessel content on bursting pressure (BP) after ligation with two ESDs: the Harmonic ACE and the LigaSure V.

Materials and Methods: Bursting trials were performed on the vasculature of 24 pigs. Blood vessels were distended with blood of different hematocrit concentrations or an albumin solution of varying protein content. The vessel size and BP of each vessel was recorded after ligation with each ESD.

Results: In arteries 0 to 3 mm and veins 0 to 3 mm in size ligated with the Harmonic ACE or the LigaSure V, there were significantly elevated vessel BPs with supraphysiologic intraluminal hematocrits. In arteries and veins ligated with the Harmonic ACE, increasing albumin concentrations also led to increasing BPs, though these maximal BPs were lower than those obtained with supraphysiologic hematocrit levels. Increasing albumin concentrations did not increase the BP of the LigaSure V. Within the ranges tested, there was no decrease in vessel BP associated with anemia.

Conclusion: In small vessels, a supraphysiologic hematocrit increased the BP of both arteries and veins when using the Harmonic ACE or the LigaSure V. With the devices tested, anemia did not seem to affect BP. While factors such as intraluminal protein concentration may play a role with ultrasonic energy devices, the mechanism of the increased BP remains unclear. Better understanding of ESDs will help in the design of future devices.

Introduction

Obtaining and maintaining hemostasis remains a challenge in laparoscopic surgery. Hemostatic techniques typically applied in open surgery such as suture ligation are technically demanding and time-consuming when performed laparoscopically. As such, laparoscopic surgeons have become more dependent on mechanical devices such as clips and staplers, which while effective, are limited to hemostasis in their scope of function and are not cost-effective in many instances.1

The modern era of energy-based surgical devices (ESDs) was engendered by the combined efforts of Harvey Cushing and William T. Bovie, who collaborated to produce the first such device.² Currently, there are several commercially available multi-functional ESDs. Each device possesses unique properties that allow it to dissect, cauterize, seal, and transect vessels and other tissues. Advances in these instruments have focused on the products’ engineering and mechanics. The majority of the technical advances made in the field of ESDs have focused on different energy sources, the pressure applied during sealing, and the architecture of the end-effector. No matter how much the ESDs themselves are optimized, however, they will always remain somewhat limited by a highly variable factor in the equation: the tissue within the jaws of the ESD.

Contrary to data presented by biotechnology companies, our prior studies evaluating the histopathology of vessel sealing have noted that the actual seal created by ESDs maintains much of the vessel tissue’s architecture, and that the material within the lumen of the sealed vessel becomes incorporated into the seal. To our knowledge, there have been no studies evaluating the impact of the luminal contents on the efficacy of ESDs. As such, we evaluated the effects of al-
terating the contents of a vessel at the time of ligation to determine changes in bursting pressures (BPs) using two existing ESDs: the Harmonic ACE® (Ethicon Endosurgery, Cincinnati, OH) and the LigaSure V® (U.S. Surgical, Valleylab, Inc., Boulder CO).

**Materials and Methods**

All experiments were approved by our institutional Animal Protocols Committee. Twenty-four 30- to 35-kg domestic pigs were obtained and were randomly divided into two groups: group 1 Harmonic ACE and group 2 LigaSure V. General endotracheal anesthesia was induced using intramuscular xylazine (2 mg/kg) and ketamine (20 mg/kg) and maintained with inhalational isofluorane (2%–2.5%). Heart rate, blood pressure, and oxygen saturation were measured every 15 minutes. Once adequate general anesthesia was obtained, a laparotomy was performed through a midline incision from the xiphoid process to the pubic symphysis. The inferior incision was then extended bilaterally onto the medial aspects of both hind legs. The small bowel and colon were reflected superiorly to expose the retroperitoneum. Once this was performed, the arterial and venous systems were removed separately so, otherwise the vessel was tied off permanently with a 2-0 silk suture. The entire procedure was repeated in both the arterial and venous systems until the vessels were either too big to seal or there were no vessels remaining.

Once removed, each system was evacuated of all blood through manual compression and light irrigation with normal saline. For each animal, 500 to 800 mL of either a blood or albumin solution was prepared for each animal in groups 1 and 2. Blood (B) solutions were made by extracting blood from the infrahepatic vena cava or the proximal abdominal aorta once the vascular trees were removed. This blood was combined with 10,000 units of heparin to prevent coagulation. Blood was then mixed with normal saline (NS) in one of the following proportions: $\frac{1}{8} B$ with $\frac{7}{8}$ NS, $\frac{1}{4} B$ with $\frac{3}{4}$ NS, $\frac{1}{2} B$ with $\frac{1}{2}$ NS, $\frac{3}{4} B$ with $\frac{1}{4}$ NS, or whole blood. A polycythemic blood sample (labeled 2× blood) was created by allowing the serum to separate from the cells and drawing this serum off. Once mixed, a 5-mL sample of each blood solution was sent for hematocrit. Albumin solutions were made by mixing grade 2 chicken egg white albumin (Sigma-Aldrich, St. Louis, MO) with NS in the following concentrations by weight: 1%, 2%, 4%, and 8%. A 5-mL sample of each of these solutions was also sent to the laboratory for protein content analysis.

Once the particular solution of interest was made, standard intravenous fluid tubing was connected to the superior aorta or inferior vena cava and secured with two 2-0 silk suture ligatures. The air was drawn out of the system with a LeVeen syringe and the system was then lightly re-distended with the chosen solution. Once distended, the peripheral branches which had previously been ligated with suture were re-ligated on the side closer to the LeVeen syringe using either the Harmonic ACE or the LigaSure V. The generators of each ESD were set to the power settings recommended by each manufacturer’s instructions. The Harmonic ACE was set at power levels of 3 and 5, and the LigaSure V was set to 3 power bars. Each vessel was ligated until the stented end fell away or was easily removed.

Upon completion, the LeVeen syringe was refilled as necessary with the chosen blood or albumin solution and the pressure was slowly increased until a sealed vessel was visibly compromised. The diameter of this vessel was measured with the vessel distended to physiologic pressure using a 6-inch dial caliper (Empire, Mukwonago, WI) and the maximum pressure obtained prior to rupture was measured with a digital pressure manometer (DPI 705; GE Druck, Billerica, MA). These parameters were recorded and the vessel was re-ligated with the ESD if there was adequate length to do so, otherwise the vessel was tied off permanently with a 2-0 silk suture. The entire procedure was repeated in both the arterial and venous systems until the vessels were either too big to seal or there were no vessels remaining.

Vessels were stratified by ESD (Harmonic ACE or LigaSure V), vessel type (arteries or veins), vessel diameter (0–3 mm, 3.1–5 mm, 5.1–7 mm, and >7 mm), and intraluminal content as outlined above. If fewer than five bursting pressures were obtained for arteries or veins of a certain diameter at a given dilution, this mean bursting strength was not calculated, and the data were not included and were designated quantity not sufficient (see materials and methods section).

**Table 1.** **Mean Bursting Pressures (in mm Hg) of Vessels Ligated with the Harmonic ACE at Varying Intraluminal Hematocrit Concentrations**

<table>
<thead>
<tr>
<th>Hematocrit</th>
<th>0</th>
<th>4.5</th>
<th>4.9</th>
<th>17.8</th>
<th>26.2</th>
<th>28.2</th>
<th>50.6</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 mm arteries</td>
<td>439.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>313&lt;sup&gt;b,g&lt;/sup&gt;</td>
<td>413.7&lt;sup&gt;c&lt;/sup&gt;</td>
<td>337.2&lt;sup&gt;d,h&lt;/sup&gt;</td>
<td>456.1&lt;sup&gt;e&lt;/sup&gt;</td>
<td>592.2&lt;sup&gt;g,h&lt;/sup&gt;</td>
<td>847.3&lt;sup&gt;a,b,c,d,e,f&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3.1–5 mm arteries</td>
<td>QNS</td>
<td>513.2</td>
<td>326.1</td>
<td>347.5</td>
<td>554.2</td>
<td>453.8</td>
<td>QNS</td>
<td>0.0022</td>
</tr>
<tr>
<td>0–3 mm veins</td>
<td>133.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>157.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>208.7&lt;sup&gt;c&lt;/sup&gt;</td>
<td>153&lt;sup&gt;d&lt;/sup&gt;</td>
<td>219.4&lt;sup&gt;e&lt;/sup&gt;</td>
<td>193.9&lt;sup&gt;f&lt;/sup&gt;</td>
<td>407.4&lt;sup&gt;a,b,c,d,e,f&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<sup>a,b,c,d,e,f,g,h</sup> = Bonferroni correction.

QNS = quantity not sufficient (see materials and methods section).
ficient (QNS). All data were compiled and analyzed with the statistical program Stata (StataCorp, College Station, TX). Mean arterial bursting pressures and mean venous bursting pressures were calculated for each vessel type, size, and intraluminal dilution. ANOVA was used to determine any variance within the groups, and the Bonferroni correction was used to identify the specific cause of variance between each of the dilutions for each ESD, vessel type, and size examined, with \( P \leq 0.05 \) being considered statistically significant.

Results

Results of Harmonic ACE and LigaSure V bursting trials utilizing varying intraluminal hematocrit concentrations are presented in Tables 1 and 2 and Figures 2 and 3. With few exceptions, at sub-physiologic hematocrits both ESDs produced arterial and venous bursting pressures that were equivalent to bursting pressures produced at normal physiologic hematocrit (approximately 28%–30% in the porcine model) for all vessel sizes tested.

In contrast, both the Harmonic ACE and LigaSure bursting trials evaluating the effect of supraphysiologic hematocrit levels resulted in significantly increased bursting pressures for all vessels tested (Table 3 and Figs. 4 and 5). For example, arteries 0 to 3 mm in size that were ligated with the Harmonic ACE produced a mean bursting pressure of 592 mm Hg at physiologic hematocrit. At a supraphysiologic hematocrit (50%), the mean bursting pressures were 43% higher, having increased to 847 mm Hg. Only the arteries 0 to 3 mm in size ligated with the LigaSure V did not exhibit an increase in bursting pressure at a supraphysiologic hematocrit.

Unlike the hematocrit trials, the results of the albumin trials were more device-specific. For all arterial trials with the LigaSure V, there were no significant changes in bursting pressures. For small veins (0–3 mm), while there was no increase in bursting pressure with supraphysiologic albumin levels, there was a decrease in bursting pressure at the lowest (1%) albumin concentration evaluated.

In contrast to the LigaSure V, arterial trials performed with the Harmonic ACE at varying albumin concentrations showed stable bursting pressures at and below physiologic albumin concentrations (not a decrease as was seen with the LigaSure V), and a trend toward increased bursting pressures when trials were performed with a supraphysiologic albumin concentration. There was a similar trend noted with venous trials, but the increase in bursting pressure at the supraphysiologic albumin concentration tested was much more pronounced when compared to the arterial trials.

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### Table 2. Mean Bursting Pressures (in mm Hg) of Vessels Ligated with the LigaSure V at Varying Intraluminal Hematocrit Concentrations

<table>
<thead>
<tr>
<th>Hematocrit (%)</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>18</th>
<th>21.8</th>
<th>31.3</th>
<th>49.1</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 mm arteries</td>
<td>482</td>
<td>359.7&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>480.5</td>
<td>342&lt;sup&gt;b,e&lt;/sup&gt;</td>
<td>633&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>672&lt;sup&gt;a,e&lt;/sup&gt;</td>
<td>573.1</td>
<td>0.034</td>
</tr>
<tr>
<td>3.1–5 mm arteries</td>
<td>QNS</td>
<td>464&lt;sup&gt;c,f&lt;/sup&gt;</td>
<td>321&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>209&lt;sup&gt;b,c,d,f&lt;/sup&gt;</td>
<td>579&lt;sup&gt;c,d&lt;/sup&gt;</td>
<td>491&lt;sup&gt;e,f&lt;/sup&gt;</td>
<td>717&lt;sup&gt;a,b,c,e&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>0–3 mm veins</td>
<td>QNS</td>
<td>QNS</td>
<td>QNS</td>
<td>209&lt;sup&gt;c&lt;/sup&gt;</td>
<td>QNS</td>
<td>144.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>573&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<sup>a,b,c,d,e,f,g,h</sup> = Bonferroni correction.
QNS = quantity not sufficient (see materials and methods section).

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![FIG. 2. Graph depicting the mean bursting pressures of arteries ligated at varying intraluminal hematocrit concentrations.](image2)

![FIG. 3. Graph depicting the mean bursting pressures of veins ligated at varying intraluminal hematocrit concentrations.](image3)
Despite dramatic improvements and recent innovations in ESDs, hemostasis remains a challenge in laparoscopy. The challenges of intracorporeal suturing have made ESDs a mainstay in the laparoscopist’s hemostatic armamentarium. There are a number of ESDs that are clinically available. Contemporary ESDs are generally based on monopolar, bipolar, or ultrasonic energy platforms, and have a wide spectrum of efficacy, efficiency, and safety.

There is no question that on occasion, ESDs fail to either obtain or maintain hemostasis, and thus manufacturers have focused a considerable amount of time and energy on improving their devices to optimize their function. Companies have upgraded their end-effector design, jaw pressure distribution, ergonomics, and energy delivery mechanisms to allow instruments to transect larger vessels more quickly than their predecessors. However, despite these innovations, little attention has been paid to what may be an equally important component of the vessel-sealing equation: the material within the jaws of the device. Indeed, even with the most well-engineered ESDs, the tissue being ligated constitutes another uncontrolled and extremely heterogeneous variable that has not been well considered or evaluated, but likely has a tremendous impact on the ability of an ESD to seal vessels.

Despite the importance of the tissue characteristics in vessel sealing, the tissues themselves have largely been ignored, and to our knowledge this aspect of vessel sealing has not previously been analyzed. Indeed, many authors studying vessel sealing have not even separately evaluated arteries and veins, which are clearly very different in their tissue architecture and content. Vessel differences are clinically relevant, with several groups reporting that the size and type of vessel create a significant difference in bursting pressures, with larger vessels and veins bursting at lower pressures.3–5

### Table 3. Mean Bursting Pressures (in mm Hg) of Vessels Ligated with the LigaSure V or Harmonic ACE at Varying Intraluminal Albumin Concentrations

<table>
<thead>
<tr>
<th>Protein</th>
<th>Normal saline</th>
<th>1% albumin</th>
<th>2% albumin</th>
<th>4% albumin</th>
<th>8% albumin</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 mm arteries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LigaSure V</td>
<td>482</td>
<td>504.74</td>
<td>599</td>
<td>696.7</td>
<td>637.5</td>
<td>Insignificant</td>
</tr>
<tr>
<td>3–5 mm arteries</td>
<td>QNS</td>
<td>509.7</td>
<td>554.9</td>
<td>582.1</td>
<td>641.5</td>
<td>Insignificant</td>
</tr>
<tr>
<td>LigaSure V</td>
<td>QNS</td>
<td>192.62</td>
<td>349.7</td>
<td>370.69</td>
<td>311.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>0–3 mm veins</td>
<td>QNS</td>
<td>355.2</td>
<td>474.5</td>
<td>353.1†</td>
<td>593.4a,b</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Harmonic ACE</td>
<td>439.5</td>
<td>355.2</td>
<td>474.5</td>
<td>353.1†</td>
<td>593.4a,b</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>0–3 mm veins</td>
<td>133.3b</td>
<td>159.3c</td>
<td>196.5</td>
<td>105.4a</td>
<td>295.0a,b,c</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Harmonic ACE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a,b,c,d,e,f,g,h = Bonferroni correction.
QNS = quantity not sufficient (see materials and methods section).

**Discussion**

**FIG. 4.** Graph depicting the mean bursting pressures of arteries ligated at varying intraluminal albumin concentrations.

**FIG. 5.** Graph depicting the mean bursting pressures of veins ligated at varying intraluminal albumin concentrations.
There are, however, a number of other clinical settings in which the importance of the tissue itself has been well characterized. It has long been recognized and commonly acknowledged that extrinsic factors can affect anastomoses. Bowel anastomoses can be negatively impacted by radiation, stool contamination, immune status, and other factors extrinsic to the actual anastomosis.\(^6\) Buchmiller-Crair and co-workers performed small and large intestinal anastomoses in rabbits both with and without anemia.\(^7\) Their group found that anemia significantly decreased anastomotic strength at 2 weeks and altered the wound healing response. Xie and colleagues demonstrated that the use of an intraluminal albumin-coated stent in the ureter increased the bursting strength of a soldered ureteral anastomosis compared to using solder alone.\(^8\)

To our knowledge, the current study is the first to demonstrate that the contents of a blood vessel at the time that it is sealed can impact the quality of the seal produced. Our data indicate that in arteries 0 to 3 mm and veins 0 to 3 mm in size ligated with the Harmonic ACE, and in veins 0 to 3 mm and arteries 3 to 5 mm in size ligated with the LigaSure V, supraphysiologic hematocrits create a significantly stronger seal. The mechanisms for this are unclear but are likely multi-modal and complex, depending on vessel type and the type of ESD used. Ligation of vessels containing polycythemic blood may be reinforced by cellular or intracellular factors that are lysed as the vessel is sealed. Alternatively, extracellular molecules may play a pivotal role.

It does appear that increasing albumin concentrations may play a small role in increased vessel bursting pressures when a Harmonic ACE is used. The maximal mean bursting pressures obtained with 8% albumin, however, are much lower than those obtained with polycythemic blood, and thus albumin is most likely not the sole contributing factor to this phenomenon. In contrast, when the LigaSure V is utilized, arterial seals do not appear to be impacted by changes in albumin concentration, while venous seals do appear to have higher bursting pressures at higher albumin concentrations. Again, the causes of this phenomenon are likely multi-factorial and complex, but one possible explanation for this difference may be the make-up of the vessel wall. Arterial walls, which are significantly more muscular than venous walls, may have enough protein content in them to negate any effect that intraluminal albumin may contribute. Venous walls, however, which are thin and have a lower protein content, may be more heavily reliant upon the protein within the lumen.

Regarding relevance to a clinical setting, the current study represents the first effort to document that the efficacy of ESDs may not be significantly diminished by anemia, a condition commonly found in the operating room. Though the pressures at which failures occurred in this study were higher than those pressures seen in a normal clinical setting, we know that ESDs do occasionally fail, even in small vessels, and that optimizing the efficiency and efficacy of these devices is the only way to improve our ability to perform safe and effective surgery with these instruments.

As the complexity of laparoscopic cases grows in scope, the need for safe and effective hemostatic ESDs will grow as well. While there has been significant innovation in ESDs in recent years, there is still tremendous potential for these devices that has not been realized. While further experiments are warranted before drawing any definitive conclusions, the current study is the first to document that as an alternative to merely changing the mechanics of a device, manipulation of intraluminal content and the patient’s own physiologic status may be able to supplement an ESDs ability to obtain and maintain hemostasis in the clinical setting.

**Conclusion**

In small vessels, polycythemic blood increased the bursting pressure in both arteries and veins when using either the Harmonic ACE or the LigaSure V. Alterations in the albumin content of the vessels has a more variable device- and vessel-specific (arterial v. venous) effect on bursting pressure. The exact mechanism of increased bursting pressure at supraphysiologic hematocrits is likely complex and warrants further study to optimize the utilization of current devices and help develop novel devices in the future.

**References**


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**Abbreviations Used**

B = blood
BP = bursting pressure
ESD = energy-based surgical device
NS = normal saline
QNS = quantity not sufficient.
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