

BioGlue Surgical Adhesive as a Thermal Reflector During Laparoscopic Cryoablation: Effect on Iceball Size and Ablation Zone Diameter

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ABSTRACT

Background and Objectives: Cryoablation represents an alternative for treating small renal cortical neoplasms (RCN). Previously, we demonstrated that applying BioGlue during cryoablation diminished bleeding and incidentally noted that the iceballs seemed larger than those in controls. We examined the effects of BioGlue as a thermal insulator of cryoablated tissue to determine its effect on iceball size.

Methods: Laparoscopic cryoablation (LCA) was performed in 6 female pigs (24 ablations) by using a single 1.47-mm cryoablation probe. One pole of each kidney was randomly treated with BioGlue prior to ablation, while the contralateral pole was the untreated control. The size of the iceball was measured using laparoscopic ultrasound. The tissue ablation zone was measured grossly after the specimens were harvested. We also documented the amount of bleeding on a subjective scale.

Results: There were no differences in the diameters of the iceballs between the BioGlue and control groups when measured with laparoscopic ultrasound ($P=.85$). Similarly, the ablation zones on gross measurement were not significantly different ($P=.47$). No difference occurred in the amount of subjective bleeding.

Conclusions: In a porcine model, the application of BioGlue prior to LCA does not appear to increase the size of the iceball generated. No change was observed in the amount of subjective bleeding as a result of using BioGlue.

Key Words: Laparoscopic cryoablation, Small renal mass, Kidney cancer.

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INTRODUCTION

Laparoscopic cryoablation (LCA) is a minimally invasive treatment alternative for select patients with a small renal cortical neoplasm (RCN).¹ The laparoscopic approach requires mobilization of the kidney and adequate visualization of the surface of the tumor. These maneuvers allow the surgeon to precisely place the cryoablation probes under direct vision followed by confirmation of placement using laparoscopic intraoperative ultrasound. Additionally, the active monitoring of the iceball can be performed with ultrasound guidance and is an advantage of cryoablation compared to other forms of ablation.

Although the complication rates with cryoablation are low, the risk of parenchymal fracture and subsequent hemorrhage increase with the size of the tumor.² Our prior *in vivo* porcine evaluation³ showed that the use of a surgical adhesive (BioGlue®, Cryolife, Inc., Kennesaw, GA) limits renal parenchymal cracking and bleeding during LCA. We observed in that study that the size of the iceballs treated with BioGlue were subjectively larger than iceballs in control ablation sites. We hypothesized that BioGlue acts as a thermal insulator and reflects cold energy to the surface of the parenchyma, leading to a larger iceball and area of tissue ablation. In this study, we examined the insulation effects of BioGlue on the size of iceball formation and ablation zone diameter during LCA in a porcine kidney. We also attempted to confirm BioGlue's ability to reduce renal parenchymal cracking and subsequent bleeding.

MATERIALS AND METHODS

A pilot study was performed in an *in vivo* porcine kidney model using 6 female Yorkshire pigs. The study was approved by our institutional review board (IRB) and Institutional Animal Care and Use Committee (IACUC). The pigs were anesthetized using a mixture of xylazine, ketamine, and atropine. The animals were intubated and ventilated with 1% to 3% isoflurane anesthesia. Each pig was then positioned in a modified flank position and secured. A Veress needle was used to insufflate the abdomen to a pressure of 15mm Hg, and 3 laparoscopic trocars (Ethicon Endosurgery, Cincinnati, OH) were then placed

in a standard configuration to triangulate the kidney. The kidney was mobilized in the retroperitoneum and the capsule was exposed. The renal hilum was also adequately dissected so that it could be accessed in an emergency situation. A single 1.47-mm IceRod (Galil Medical Inc., Arden Hills, MN) was used to create lesions in both the upper and lower pole of each kidney. Each needle was deployed under direct vision and placed at a depth of 2cm within the parenchyma.

Following IceRod placement, 5-mL BioGlue surgical adhesive was placed randomly on one pole of each kidney by using a 27-inch laparoscopic BioGlue tip applicator (Cryolife, Inc., Kennesaw, GA). The opposite pole of each kidney served as the control. A randomization schedule was used to determine which renal pole received treatment with BioGlue and which was to be used as the control. Care was taken to limit the spread of BioGlue so that the majority was confined to the renal ablation site and not surrounding tissues. The adhesive was allowed to dry and seal for 2 minutes before the first cryoablation cycle was begun. A double freeze thaw cycle was performed using the Precise System (Galil Medical Inc., Arden Hills, MN). Freeze cycles were performed for 10 minutes and alternated with 2 active thaw cycles lasting 3 minutes each. After the second thaw cycle, the IceRods were removed under direct vision, and the ablation sites were monitored for 5 minutes for bleeding. The iceball created was measured using a standard laparoscopic ultrasound probe (BK Medical Systems Inc, Peabody, MA) at the end of each freeze cycle. The largest measurements were taken in 2 dimensions. Visual evidence of bleeding was documented on a scale of bleeding severity (absent, mild, moderate, severe). The animals were then euthanized by using Euthasol, and the kidneys were harvested through a midline incision. The specimens were sectioned, and the ablation sites were grossly measured in 2 dimensions and recorded to determine the size of the ablation zone. Data were analyzed using the unpaired Student *t* test and Fisher exact test where appropriate. All data were analyzed using Stata version 9 (Stata Corp., College Station, TX).

RESULTS

There were 24 ablations performed (12 BioGlue and 12 control). The mean pig weight was 22.1kg (range, 21.0 to 24.0). The average iceball diameter measured with laparoscopic ultrasound was 2.54cm (range, 2.5 to 2.8) in control lesions and 2.60cm (range, 1.5 to 3.4) for ablation sites treated with BioGlue. There was no statistically sig-

nificant difference between the 2 measurements ($P = .85$). The ablation site diameters on gross pathology revealed a mean diameter of 1.97cm (range, 1.2 to 3.5) for control sites and 2.30cm (range, 1.2 to 3.6) for BioGlue treated lesions. Similarly, the average ablation zone diameters on harvested specimens did not differ significantly between the groups ($P = .47$).

In the control group, there were 7 (58.3%) ablations in which bleeding was described as “none” and 5 (42.0%) were described as “mild” bleeding. The BioGlue group demonstrated 5 (45.5%) ablations with no hemorrhage and 6 (55.0%) with mild blood loss, subjectively. Neither group had evidence of subjective moderate or severe hemorrhage.

DISCUSSION

The treatment for small RCN includes surgical extirpation, renal ablation, and active surveillance. While extirpation is the gold standard for managing these tumors, certain patients are categorized as high-surgical risk or wish to avoid surgery.⁴ Cryotherapy appears to have lower rates of local recurrence compared to radiofrequency ablation and can provide a precise and minimally invasive method of treating renal masses <3cm.⁴ Methods to improve the area of ablation could increase the availability of cryotherapy to a larger patient population.

BioGlue is a surgical adhesive that spontaneously forms strong covalent bonds in approximately 20 seconds to 30 seconds after application. It is a combination of albumin and glutaraldehyde that is mixed and applied in a single delivery system. The maximal strength of the adhesive is reached in approximately 2 minutes. BioGlue is not a hemostatic agent and does not influence the clotting cascade; however, it has been shown in a number of human and animal studies to effectively maintain hemostasis during open or laparoscopic partial nephrectomy alone or in combination with suturing or other hemostatic agents.^{6–8}

Efforts to increase the size of the cryoablation lesion have largely focused on manipulating the duration or number of freeze thaw cycles.^{9–11} In addition, renal arterial clamping during cryoablation has been studied as a way to reduce the heat sink phenomenon and decrease the size of ablation diameter. Campbell and colleagues found that arterial clamping did not significantly affect the size of the ablation zone.¹² Collyer and coworkers¹³ examined the effects of intrarenal cooling during LCA with arterial and venous clamping. They observed that the diameter of the

iceball created increases with arterial and venous clamping, but that the area of necrosis was no different when compared to that in controls.

BioGlue has been used during LCA in a porcine model to minimize the risk of bleeding and renal fracture.³ Additionally, it was observed that the size of the iceballs created with BioGlue applied to the surface were larger in size. We believed that this increase in iceball diameter also translated into a larger area of tissue ablation.

In the current study, we evaluated the size of the iceballs after cryoablation with and without the application of BioGlue and found that there was no difference in either the size of the iceball or in the area of coagulative necrosis on gross measurement. Our findings could be related to the position of the IceRods in that they were placed at a depth of 2cm. Therefore, at this depth they would be treating only endophytic tumors and would be subject to a great heat sink effect. The surface application of BioGlue may not have any impact on tumors at this depth, because it is unable to insulate against the loss of heat from the surface of the kidney. In contrast, tumors that are mesophytic and exophytic are further from any heat sink effect. BioGlue is more likely to adequately insulate heat loss at this level and result in a larger diameter iceball and ablation zone. In addition, the number of IceRods used at this depth (2cm) would have impacted the temperature. In our initial study,³ our observation of larger iceball diameters with BioGlue occurred when using 3 IceRods compared to 1 IceRod used in this study.

We did not observe any significant difference in the amount of parenchymal bleeding between the BioGlue and controlled ablations. This was in contrast to our previous study, which demonstrated a decrease in the number of tumor fractures and severity of bleeding.³ We believe that this was likely due to the number of IceRods used, because 3 cryoprobes would have created larger iceballs, which are known to be at higher risk for fracture and bleeding relative to smaller iceballs.¹⁴ The lack of hemostatic difference noted in the current study was likely simply the result of the minimal overall bleeding that we noted.

Limitations in this study include the small number of cryoablations performed, the inability to replicate exophytic tumors, and the smaller number of IceRods used during the ablations. The type of probe may have also influenced our results, because a probe that creates a larger more oblong iceball would have been closer to the surface of the kidney. Therefore, the BioGlue shell

may have had more of an insulation effect and may have led to an increase in ablation zone diameter. Additionally, we did not record the time to maximum iceball size. The freeze cycles performed were 10 minutes in length, and only one measurement of the iceball diameter was obtained using the ultrasound at the 10-minute time period. Sequential measurements over time would have been helpful to determine the actual time to maximum iceball diameter. This would have given some evidence that BioGlue provided insulation value with a surface application.

CONCLUSION

The application of BioGlue surgical adhesive did not influence the diameter of the iceball formation during LCA compared with control ablations in a porcine model. Cryoprobe type, number, and placement affect the size, shape, and location of iceball formation. Additional studies must be performed to determine the insulation effect of BioGlue during cryoablation.

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