SCIENTIFIC PAPER

# Evaluation of Microporous Polysaccharide Hemospheres for Parenchymal Hemostasis During Laparoscopic Partial Nephrectomy in the Porcine Model

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## ABSTRACT

**Objectives:** We evaluated the efficacy of Microporous Polysaccharide Hemospheres (MPH) for parenchymal hemostasis during laparoscopic partial nephrectomy (LPN) in the porcine model.

**Methods:** Six female farm pigs underwent a transperitoneal right lower-pole LPN during occlusion of the renal hilum. Renal parenchyma was excised using cold Endoshears. MPH was applied to the defect and the hilar clamp released. Animals were kept alive for one week. Before sacrifice, left LPN was similarly performed using MPH. Study variables included blood loss, number of MPH applications, hilar clamp time, hemostasis time, perioperative complications, and abnormalities noted at sacrifice.

**Results:** Hemostasis was achieved in all kidneys solely by using MPH. The average excised specimen represented 5.6% (range, 3.6 to 8.5) of renal weight. Mean hilar clamp and hemostatic times were 12.8 minutes (range, 6 to 18) and 2 minutes (range, 1 to 3), respectively. Hemostasis occurred after one MPH application in 8 kidneys (67%). In 3 kidneys, additional MPH powder was required to treat minor residual bleeding. In the remaining kidney, a second standard MPH application was required for hemostasis. No operative complications were encountered. No hematomas or residual MPH was found at necropsy; however, small urinomas were found in 2 of 6 kidneys.

**Conclusions:** In the experimental porcine model, this initial study suggests that MPH provides effective parenchymal hemostasis during laparoscopic resection of an exophytic kidney lesion.

**Key Words:** Laparoscopy, Nephron-sparing surgery, Microporous Polysaccharide Hemospheres, Hemostasis, Renal tumor.

## INTRODUCTION

Hemostasis remains one of the most important technical concerns associated with laparoscopic partial nephrectomy (LPN). Controlling hemostasis during LPN can effectively be performed by using bolsters and sutures in a similar fashion as in open partial nephrectomy; however, this technique can be time-consuming and challenging.[1] Several hemostatic agents and technical adjuncts have been evaluated in an attempt to simplify LPN, yet an optimal alternative approach has not been realized.[2–9]

Microporous Polysaccharide Hemospheres (MPH, Medafor Pharmaceutical Inc., Minneapolis, MN, USA) are made entirely from purified plant starch[10] that activates the clotting cascade via a unique mechanism that hyperconcentrates platelets and coagulation proteins.

Previously, a randomized study comparing MPH versus conventional surgical techniques confirmed the efficacy of this new hemostatic agent in achieving rapid and durable hemostasis during open partial nephrectomy in the porcine model.[10] However, the technical issues of laparoscopic cases present greater challenges in achieving hemostasis than in open cases, mainly in applying the agent accurately and whether the agent will be able to stop bleeding without the benefit of open techniques (ie, applying pressure). Thus, the goal of this pilot study is to evaluate the feasibility of MPH for controlling parenchy-

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mal bleeding during partial nephrectomy in a laparoscopic environment.

## METHODS

After approval of the study protocol by the Institutional Animal Care and Use Committee, laparoscopic transperitoneal lower-pole partial nephrectomies were performed in 8 Yorkshire white female pigs weighing 32.1 kg to 40 kg. Following development and refinement of the laparoscopic MPH application technique on the initial 2 animals, 6 pigs underwent our experimental protocol.

Following induction of general anesthesia, right-sided LPN was performed using a standard 4-port transperitoneal approach in a flank position. The peritoneal cavity was insufflated to 15 mm Hg. After mobilization of the kidney, the renal artery and vein were occluded with a laparoscopic bulldog clamp. Renal parenchyma from the inferior pole of the kidney was then excised using cold Endoshears. The defect was circular in shape, 2 cm in diameter, and 1cm in depth, thereby simulating the excision of a small exophytic renal mass.

Two grams of MPH were applied directly to the wound surface using a custom laparoscopic applicator **(Figures 1 and 2)**, taking care to keep the resection bed dry. Following MPH application, the vascular clamp was immediately removed and pneumoperitoneum at 15mm Hg was maintained for 3 minutes. If hemostasis was achieved after 3 minutes, the pneumoperitoneum was released.

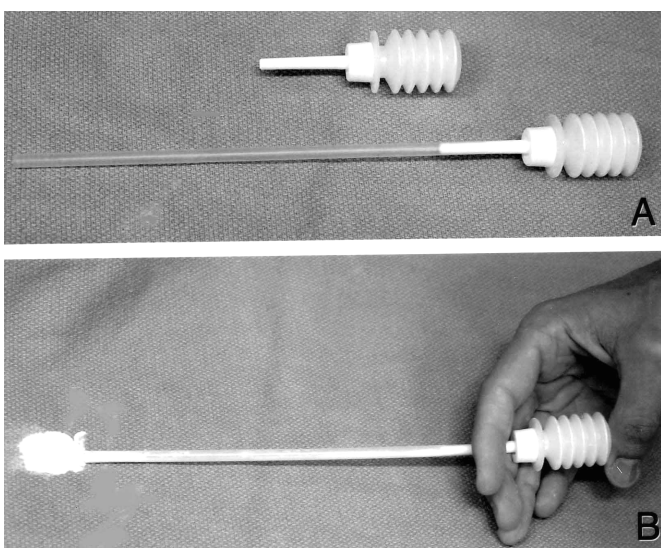


**Figure 1.** Laparoscopic microporous polysaccharide hemospheres applicator loaded on the microporous polysaccharide hemospheres custom applicator.

Every 10 minutes thereafter, intraperitoneal pressure was reinstated to 15 mm Hg to completely visualize the resection bed for bleeding. This observation period of periodic insufflation lasted for approximately 30 minutes following initial MPH application. If major rebleeding occurred, another standard MPH application (2.0 grams) was performed in the same manner. In case of mild residual bleeding, additional MPH (1.0 gram) was applied to the oozing area without reclamping. If more than 2 total MPH applications were required, the attempt was considered a failure. At the end of the observation period, the renal specimen was removed through an existing port site, and the posterior peritoneum was closed. After surgery, the animals were observed twice daily to monitor their general well being and for any evidence of surgical complications.

One week later, each pig underwent the same procedure on the contralateral kidney. The right kidney was also examined in situ for evidence of delayed bleeding, hematoma, and adverse treatment effects to associated tissues. Each animal was then sacrificed and both kidneys removed. The right kidneys were used as a chronic phase cohort to study pathologic changes after one week of healing.

MPH efficacy was evaluated using the following variables: blood loss (quantitated from the suction canister), number of required MPH applications, hilar clamp time, hemostasis time, resected and remnant renal weights, perioperative complications, and presence of residual MPH on right (chronic phase) kidneys. Hilar clamp time was defined as the duration of renal artery and renal vein occlusion during LPN. Hemostatic time was defined as the time needed to achieve hemostasis with the first MPH application after the bulldog clamp had been removed. For animals requiring additional MPH applications, data on hemostatic time were not recorded and therefore were excluded from the final data analysis. The presence of residual MPH on right kidneys was evaluated grossly and histologically with hematoxylin and eosin staining performed on paraffin-embedded sections containing the resection edge and neighboring renal parenchyma. All data were summarized using descriptive statistics and performed with JMP4 software (SAS Institute Inc., Cary, NC, USA).

## RESULTS

Successful hemostasis was achieved in all 12 kidneys solely by using MPH **(Table 1)**. Hemostasis was attained after one MPH application in 8 of 12 kidneys (67%). In 3 treated kidneys, a small amount of additional MPH (1.0

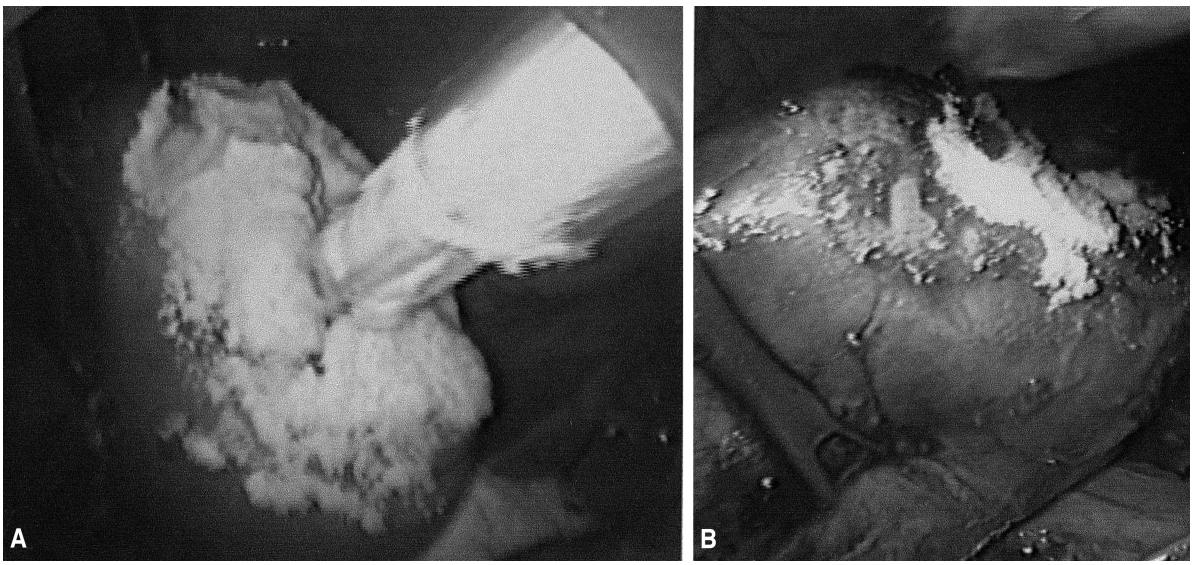


**Figure 2.** Macroscopic appearance of exposed renal parenchyma during (A) and 30 minutes after (B) the microporous polysaccharide hemospheres application.

**Table 1.**
Study Variables (N = 12 Kidneys)

| | Mean | Range |
|---|---|---|
| Hilar clamp time (min) | 12.8 | 6–18 |
| Hemostatic time (min) | 2 | 1–3 |
| Specimen weight (g) | 5.84 | 3.4–10.3 |
| Remnant kidney weight (g) | 96.7 | 77.7–111.4 |
| % Resected kidney | 5.6 | 3.6–8.5 |

gram) was required for minor residual bleeding. In the remaining kidney, an additional standard 2.0-gram MPH application was required to control residual central bleeding with an overall 50-mL blood loss. Once complete hemostasis had been achieved, no acute rebleeding was noted for any kidney during the 30-minute observation period.

Aside from the one LPN associated with a 50-mL blood loss, remaining LPN procedures were associated with negligible blood loss. No intraoperative complications were encountered, nor did gross violations of the collecting system occur.

After one week of follow-up, no gross residual MPH was found at necropsy among the chronic treatment kidneys. Likewise, no evidence of MPH was found microscopically at the wound surface **(Figure 3)**. In 2 of 6 (33%) chronic phase kidneys, however, small urinomas (each <2 cm in greatest diameter) were found at necropsy, and these represented the only postoperative complications in the protocol. In each case, the urinoma was located in a retroperitoneal position, and the animal was entirely asymptomatic before sacrifice.

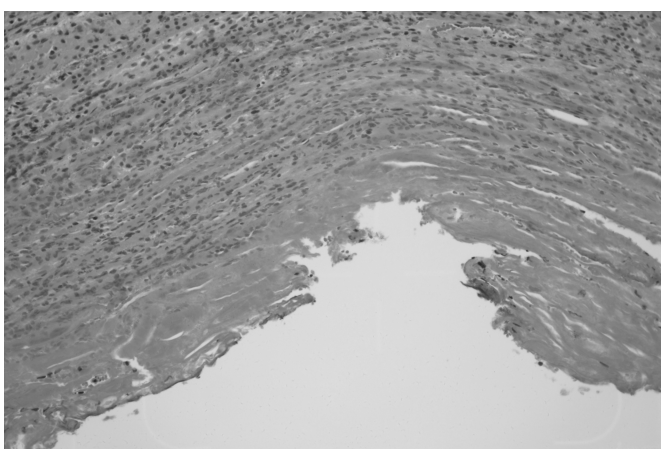

**Figure 3.** Hematoxylin and Eosin staining showing no evidence of residual microporous polysaccharide hemospheres at the resection zone one week after laparoscopic partial nephrectomy (magnification 400x).

## DISCUSSION

Effective parenchymal hemostasis remains an ongoing technical concern with LPN.[1–9] Although LPN techniques that duplicate open nephron-sparing surgery have been

reported, the need for intracorporeal suturing represents a limitation.[1] Various alternative surgical techniques, devices, and topical hemostatic agents have been proposed, yet none have emerged as the optimal treatment for LPN.[2–9] On-going concerns regarding topical hemostatic agents have centered around ease of use, preparation time, the potential for viral transmission, biological inertness, and cost.

MPH has successfully been applied in a clinical setting for Mohs microsurgery.[11] However, its efficacy has not yet been proven in a minimally invasive setting. Advantages of MPH include single-step application with no premixing, no risk of viral transmission, low cost, and its flexibility in delivery (either as a powder, a spray, or molded into a solid form). However, as emphasized by Tan et al,[11] MPH must be applied accurately and evenly to the bleeding area, and time is needed for the blood clot to form.

Encouraging results were observed with MPH during LPN in this pilot evaluation. Using the custom laparoscopic applicator, MPH was easily applied onto the resected kidney surface. Although we used a 12-mm trocar for delivery of MPH, subsequent applicators can be used through 5-mm through 12-mm trocars. Intraabdominal pressure generated by the 15mm Hg of the pneumoperitoneum was sufficient to sustain contact between MPH and the resected renal tissue, and direct pressure of the applicator on the resection zone was not required. In two thirds of the partially resected kidneys, almost immediate hemostasis was achieved and maintained following reperfusion after one application.

MPH appeared to work best when applied to a dry field and then exposed to blood. Due to the unique molecular properties of MPH, it is important that the vessels are unclamped after its application because the presence of blood is required to activate the MPH and promote subsequent clotting. In one case during the study, an additional 2-gram MPH application was needed to stop bleeding in the central portion of the renal parenchyma. For this secondary application, it was necessary to first remove the residual MPH with saline so that the new MPH powder would come in contact with fresh blood. The cause of the bleeding was unknown, because the technical aspects of this experiment were no different than those of the other experiments in the protocol. During 3 other LPN procedures in the study, minor oozing continued after the initial MPH application. These instances could possibly be explained by insufficient or inappropriate wound coverage with MPH using the laparoscopic applicator. In all of these cases of minimal on-going bleeding, adding more MPH powder to the wound easily resulted in complete hemostasis.

While MPH did provide excellent parenchymal hemostasis, additional study is needed to determine whether MPH can seal collecting system violations. In 2 of 6 chronic treatment kidneys, an asymptomatic small urinoma less than 2cm in diameter was noted at necropsy. Clinically, because many small renal tumors treated laparoscopically are exophytic and because one may expect the collecting system to be away from the resection site, the issue of collecting system sealing with MPH may be of lesser significance.

A number of limitations are associated with our study. Because it was designed only for feasibility, the current study lacked a control arm. Thus, any comparisons with open techniques should be made with caution. The method of measuring the blood loss was somewhat imprecise because not all blood loss could be reliably collected via the suction irrigator. In fact, in all but one case, the bleeding was controlled so rapidly with MPH that we could not quantify the blood loss with our suction device. Lastly, one could argue that the percentage of excised kidney tissue was small. However, for exophytic tumors that we believe are amenable to LPN, a small percentage of normal renal parenchyma is typically resected, and our study was purposefully designed to answer the issue of MPH efficacy in this specific clinical situation. Additional experimentation is required to evaluate how deep the renal parenchyma can be cut before uncontrollable bleeding occurs.

## CONCLUSION

In the experimental porcine model, this initial study suggests that MPH provides effective parenchymal hemostasis during laparoscopic resection of an exophytic kidney lesion.

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