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Research Article

# Novel Intravascular Catheter Securement Cyanoacrylate Achieves Hemostasis against Moderate to Severe Bleeding in Porcine Liver Model

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**Abstract**

**Background:** Bleeding at the site of intravascular catheter insertion often causes a need for same-day dressing changes, and in some cases, premature catheter removal prior to the completion of necessary intravenous therapy. Furthermore, bleeding has the potential to cause patient dissatisfaction, increase hospital stays, and increase overall costs associated with intravascular catheterization. Therefore, it is essential to find a solution that can not only secure the intravascular catheter but also protect the insertion site from potential unwanted bleeding.

**Objective:** This study is aimed to demonstrate the potential hemostatic effect a catheter securement cyanoacrylate has to severe bleeding at an incision site.

**Method:** An innovative testing model was used to compare the catheter securement cyanoacrylate to a known hemostatic agent when treating incisions in a porcine liver. The incisions created were 20mm in length, 15mm in depth, and consistently produced severe blood flow at time zero. The incisions were monitored; blood flow was scored after 1, 3, 6, and 9 minutes post application of either the catheter securement cyanoacrylate treatment, known hemostatic agent treatment, or no treatment (negative control).

**Results:** The catheter securement cyanoacrylate proved significantly more effective than the known hemostatic agent, decreasing severe blood flow by 92% within one minute and by 100% within three minutes.

**Conclusion:** The catheter securement cyanoacrylate provided substantial hemostasis in the presence of severe bleeding at an incision. This suggests that the cyanoacrylate has the potential to provide hemostasis at the site of intravascular catheterization in a clinical setting.

**Keywords:** Blood; Catheters; Cyanoacrylates; Hemostasis; Liver

## Abbreviations

CSC: Catheter Securement Cyanoacrylate; KHA: Known Hemostatic Agent; IFU: Instructions For Use; NC: Negative Control

## Introduction

Intravascular catheterization is one of the most common medical procedures performed in hospitals worldwide. During this process, unwanted bleeding at the insertion site can create a precarious situation for clinicians and patients. Bleeding may require frequent dressing changes or a need for gauze compressions at the site of insertion, and increase the potential for more serious complications such as the development of hematomas, a leakage of blood from the vessel into the surrounding soft tissue [1]. The anatomical location of the insertion site can play a role in the severity of bleeding following intravascular catheter insertion according to Galloway [2]. The prevention of venous bleeding is an issue that deserves more attention, especially in patients that are at a higher risk for bleeding [3]. Gabriel J. reported that when a Central Venous Access Device (CVAD) is placed, an initial amount of slight oozing of blood usually occurs that will often lead to a dressing change within 24 hours of initial placement [4].

Furthermore, it has been previously reported by Scoppettuolo et al. that bleeding complications with PICCs and Large-Bore Dialysis catheters can occur within one hour of placement in up to 40% and 50% of catheter placements, respectively [5]. Up to 1.6% of Central Venous Catheters (CVC) are reported to have bleeding complications that require intervention according to Kander et al. [6].

To promote less frequent dressing changes, less time spent on compressions, and less risk of serious bleeding complications it is imperative to find a solution that can not only secure the intravascular catheter tubing and hub but also provide hemostasis at the site of insertion. Tissue adhesive has been discussed as an option to provide securement and hemostasis, thereby preventing or lessening the occurrence of bleeding at the insertion site and subsequently reducing premature intravascular catheter removal, increasing patient comfort. The use of cyanoacrylate-based tissue adhesive, such as the first and only FDA approved product, SecurePort IV®, to secure the insertion




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site has previously been reported to be effective for securing both central and peripheral venous catheters [7,8].

The number of studies to evaluate hemostasis against severe bleeding in a liver model has been very limited. Studies published by Slezak et al. MacDonald MH et al, and Hutchinson RW et al, evaluate liver hemostasis models utilizing punch biopsy techniques [9-11]. These models do not sufficiently correlate with the requirements for establishing hemostatic methods for intravascular catheterization, as the punch biopsy model does not have the capability to evaluate severe bleeding from the deep vascular parenchyma of the liver. For that reason, there is a need for further investigation into incision models that represent severe bleeding beyond surface wounds.

Studies evaluating hemostasis are commonly conducted on known hemostatic agents such as gauze, absorbable powders, gelatin matrix, or thrombin, while the novel study within evaluates a cyanoacrylate based product. In addition to SecurePort IV®, Adhezion Biomedical is currently developing a next generation catheter securement product. Due to the inclusion of a novel polymerization accelerator in this advanced adhesive formula, this product has been proven to be able to provide a significantly faster catheter securement. Therefore, it was predicted that the product would be able to have more effective hemostatic properties. The purpose of the study described is to evaluate the effectiveness of hemostasis using the novel catheter securement cyanoacrylate. To the authors' knowledge, this study is the first to present an evaluation of cyanoacrylate's ability to provide hemostasis in the presence of severe bleeding in a liver model utilizing deep parenchymal incisions.

## Materials and Methods

An *in vivo* model consisting of two female Yorkshire cross pigs with an average weight of 43.5kg was used. Incisions were made into the liver to produce moderate to severe blood flow to measure the hemostatic effect of the novel Catheter Securement Cyanoacrylate (CSC) compared to a negative control and a Known Hemostatic Agent (KHA). The study was conducted in two phases with the first phase determining the size of incision optimal for moderate to severe bleeding and the second phase measuring test article effectiveness in the porcine liver model. Phase 2 sites were scored by two observers - the surgeon and a veterinarian - to control bias.

A grading system was used to determine the bleeding score of the incisions based upon the amount of blood flow from the incisions: 0 = No Bleeding Observed; 1= Minimal, oozing from the incision Site; 2 = Mild, pooling blood around incision site; 3= Moderate, steady flow of blood from incision site; 4 = Severe, fast flowing blood from the incision site (not life-threatening); 5 = Life Threatening, blood flow is so severe from arterial involvement that a typical hemostatic agent could not be applied to achieve hemostasis.

### Phase 1 – Determination of defect size

For Phase 1, a target of five incisions were created to determine an incision size that consistently resulted in a pretreatment bleeding score of 3 (moderate). Next, a target of five incisions were created to determine an incision size that consistently resulted in a pretreatment bleeding score of 4 (severe).

The dimension of the incision size that produced a bleeding score of 4 was utilized to confirm consistency of the method and assess response to treatments. Ten incisions were created to achieve a bleeding score of 4, treated with the CSC, and then re-scored. If complete hemostasis was achieved (a score of 0 on or before the twelve minute scoring interval), ten additional incisions were created to achieve a bleeding score of 4, treated with the KHA, and then re-scored. If the CSC did not achieve hemostasis, the CSC was then used to treat incisions that produced a bleeding score of 3. Following the assessments of Phase 1, an incision size that provided the most consistency in bleeding and response to treatment was determined to be used in phase two of the study.

### Phase 2- Assessment of test article effectiveness

Phase 2 of the study assessed three treatments applied to incisions which produced moderate (score = 3) to severe (score = 4) bleeding, with 14 sites for each treatment (CSC, KHA comparative control, and the negative control). Two scores were recorded per incision at each time point, one by the veterinarian and one by the surgeon. A time zero "pretreatment" score was recorded once an incision was made, then the sites were scored at each of the following time points: 1, 3, 6, and 9 minutes post application of treatment. For the CSC, up to 5 drops of adhesive were used to provide enough volume to cover the length of the incision while the KHA was applied per its standard Instructions For Use (IFU).

Negative control sites received no treatment.

## Results and Discussion

During phase 1 of the study, the optimal incision length which consistently produced moderate to severe blood flow in the porcine liver model was determined to be a depth of 15mm and a length of 20mm. This incision size was used for all further incisions in phase 2. On average, the blood flow of the incisions prior to any treatment was between 3 (moderate) and 4 (severe). Within one minute following application of treatment to the incision site, the average blood flow was scored as 0.3, 1.9, and 2.2 for the CSC, KHA, and negative control, respectively. (Table 1) demonstrates the comprehensive results for all 42 incisions at all time points; the scores provided by the veterinarian and by the surgeon were the same for all sites.

As indicated by the scores, the CSC was able to decrease bleeding on average by 92% after 1 minute following application, while the KHA was only able to reduce bleeding by 43.5%. By 3 minutes following application, the CSC was 100% effective in stopping blood flow from incisions with bleeding scores of both 3 and 4. The CSC was proven to be more effective hemostatic agent than the KHA and the NC for all time periods post treatment application. Figure 1 graphically represents the drop in blood flow after 1 minute of applying the CSC treatment in comparison to the effectiveness of the KHA and the NC. Figures 2 and 3 contain representative images of incision sites treated with the CSC and KHA and the NC, respectively.

One of the challenges of this model was that the blood flow from the incision decreased over time due to the porcine body's natural clotting mechanisms, which resulted in a reduction in bleeding scores over the course of the nine minute testing period for the negative control (no treatment) sites. However, emphasis is placed on the first scores noted at the 1 minute time point, demonstrating the dramatic effectiveness of the CSC in comparison to the untreated

**Table 1:** Blood Flow Scores.

| Test # | Test Article | | | | | KHA | | | | | Negative Control | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Time 0 | 1 Min | 3 Mins | 6 Mins | 9 Mins | Time 0 | 1 Mins | 3 Mins | 6 Mins | 9 Mins | Time 0 | 1 Mins | 3 Mins | 6 Mins | 9 Mins |
| 1 | 3 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 4 | 3 | 3 | 3 | 2 |
| 2 | 3 | 0 | 0 | 0 | 0 | 3 | 2 | 2 | 2 | 0 | 3 | 3 | 3 | 1 | 1 |
| 3 | 4 | 0 | 0 | 0 | 0 | 3 | 2 | 2 | 1 | 0 | 4 | 3 | 2 | 2 | 2 |
| 4 | 4 | 0 | 0 | 0 | 0 | 4 | 3 | 3 | 2 | 1 | 3 | 2 | 2 | 2 | 2 |
| 5 | 3 | 1 | 0 | 0 | 0 | 4 | 3 | 2 | 1 | 0 | 3 | 2 | 2 | 1 | 0 |
| 6 | 4 | 0 | 0 | 0 | 0 | 3 | 3 | 2 | 1 | 0 | 4 | 1 | 1 | 1 | 0 |
| 7 | 3 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 1 |
| 8 | 4 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 3 | 3 | 3 | 3 | 3 |
| 9 | 3 | 0 | 0 | 0 | 0 | 3 | 2 | 2 | 2 | 0 | 4 | 4 | 4 | 1 | 0 |
| 10 | 4 | 0 | 0 | 0 | 0 | 3 | 2 | 2 | 1 | 1 | 4 | 4 | 3 | 3 | 2 |
| 11 | 4 | 0 | 0 | 0 | 0 | 4 | 3 | 3 | 3 | 1 | 3 | 2 | 2 | 2 | 2 |
| 12 | 3 | 1 | 0 | 0 | 0 | 3 | 3 | 1 | 0 | 0 | 3 | 2 | 2 | 1 | 0 |
| 13 | 4 | 0 | 0 | 0 | 0 | 3 | 3 | 1 | 1 | 0 | 4 | 0 | 0 | 1 | 0 |
| 14 | 4 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 4 | 1 | 1 | 0 | 0 |
| Mean | 3.6 | 0.3 | 0.0 | 0.0 | 0.0 | 3.3 | 1.9 | 1.4 | 1.0 | 0.2 | 3.5 | 2.2 | 2.0 | 1.5 | 1.1 |
| SD | 0.5 | 0.6 | 0.0 | 0.0 | 0.0 | 0.5 | 1.3 | 1.1 | 1.0 | 0.4 | 0.5 | 1.2 | 1.0 | 1.0 | 1.1 |

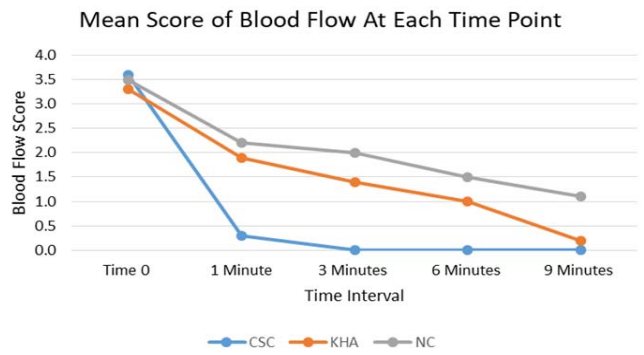


**Figure 1:** Mean Hemostasis Score for Each Treatment from Pretreatment to 9 Minutes Post Treatment.

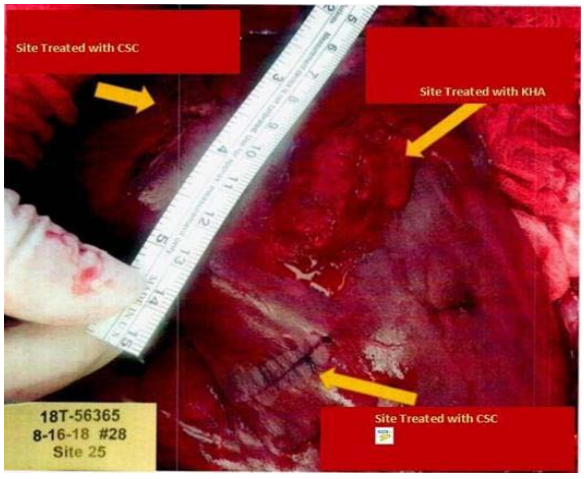


**Figure 2:** Representative Image of Liver Model with CSC and KHA Treatment Sites.


**Figure 3:** Representative Image of Liver Model with NC Treatment Sites.

negative control sites. This difference indicates that hemostasis was a direct result of the CSC treatment and not a factor of natural clotting capabilities of the porcine.

As seen in Figures 2 and 3, the amount of blood loss in the negative control is significant when compared to the incision sites that have been treated with the CSC. This result demonstrates how effective only five small drops of a catheter securement cyanoacrylate can be against severe blood flow. Compared to the KHA, the novel CSC exhibited rapid hemostasis, which may be due to the fast curing properties of the advanced formulation because of the addition of the polymerization accelerator. As a result, it is predicted that hemostasis will be improved using the novel CSC, compared to utilizing conventional cyanoacrylate-based products. Securing and sealing the insertion site with an FDA approved catheter securement

cyanoacrylate has the potential to provide significant clinical benefits. The clinical use of cyanoacrylate at the insertion site has been limitedly studied, and as reported by Scoppettuolo et al. no bleeding occurred at the insertion site in a total of 65 patients (45 with PICCs, 11 Dialysis Catheters, and 9 CVCs) treated with the use of cyanoacrylate [5]. Given the significant reduction in blood flow as a direct result of the application of five drops of cyanoacrylate demonstrated in this study model, the use of cyanoacrylate may have the potential to provide not only securement but also hemostasis at the site of intravascular insertion.

## Conclusion

The data produced by this original porcine liver model demonstrated the effectiveness of the CSC as a hemostatic agent against moderate to severe bleeding within the first minute of application, and the ability to maintain a hemostatic seal throughout the remainder of the study. The CSC also showed a statistically significant superior effect compared to the KHA and negative control treatments. These findings suggest that the clinical use of the FDA-approved CSC to secure intravascular catheters can be considerably enhanced by the ability the CSC has in creating a hemostatic seal against substantial amounts of blood flow.

### References

1. Kagel E, Rayan G. Intravenous Catheter Complications in the Hand and Forearm. The Journal of Trauma Injury, Infection, and Critical Care. 2004; 56: 123-127.

2. Galloway M. Insertion and Placement of Central Catheters in the Oncology Patient. Seminars in Oncology Nursing. 2010; 26: 102-112.

3. Kumar A, et al. Purse-String Suture & Anticoagulant: Bleeding Prevention from Insertion Site of Dialysis or CVCs. Trends in Anaesthesia and Critical Care. 2018; 22: 41-42.

4. Gabriel J. Vascualr Access Devices: Securement and Dressings. Nursing Standard 2010; 24: 41-46.

5. Scoppettuolo G, Annetta MG, Marano C, Tanzarella E, Pittiruti M. Cyanoacrylate Glue Prevents Early Bleeding of the Exit Site after CVC or PICC placement. Criticle Care. 2013; 17: 174.

6. Kander T, Frigyesi A, Kjeldsen-Kragh J, Karlsson H, Rolander F, Schött U. Bleeding Complications After Central Line Insertions and the Relevance of Pre-Procedure Coagulation Tests and Institutional Transfusion Policy. The ACTA Anaesthesiologica Scandinavica Foundation. 2013; 57: 573-579.

7. Ozkula U, Ozhasenekler A. Tissue Adhesives to Secure Peripheral Intravenous Catheters: A randomized Controlled Trial in Pateints over 65 Years. Turkish Journal of Emergency Medicine. 2019; 19: 12-15.

8. Guido A, Zhang S, Yang C, Pook L. An Innovative Cyanoacrylate Device Developed to Improve the Current Standard of Care for Intravascular Catheter Securement. The Journal of Vascular Access. 2019.

9. Slezak P, Keibl C, Redl H, Labahn D, Gulle H. An Efficacy Comparison of Two Hemostatic Agents in a Porcine Liver Bleeding Model: Gelatin/Thrombin Flowable Matrix versus Collagen/Thrombin Powder. Journal of Investigative Surgery. 2019.

10. MacDonald MH, Wang AY, Clymer JW, Hutchinson RW, Kocharian R. An *in vivo* comparison of the efficacy of hemostatic powders, using two porcine bleeding models. Medical Devices. 2017; 10: 273-279.

11. Hutchinson RW, Werrlein S, Johns DB, Zhang G, Clymer JW, Kocharian R. An *In Vivo* Comparison of Hemostatic Gelatin Matrix Products in a Porcine Spleen Biopsy-punch Model. Surgical Technology International. 2015; 27: 53-57.