QuikClot® Interventional™ Hemostatic Bandage (QCI): A Novel Hemostatic Agent for Vascular Access

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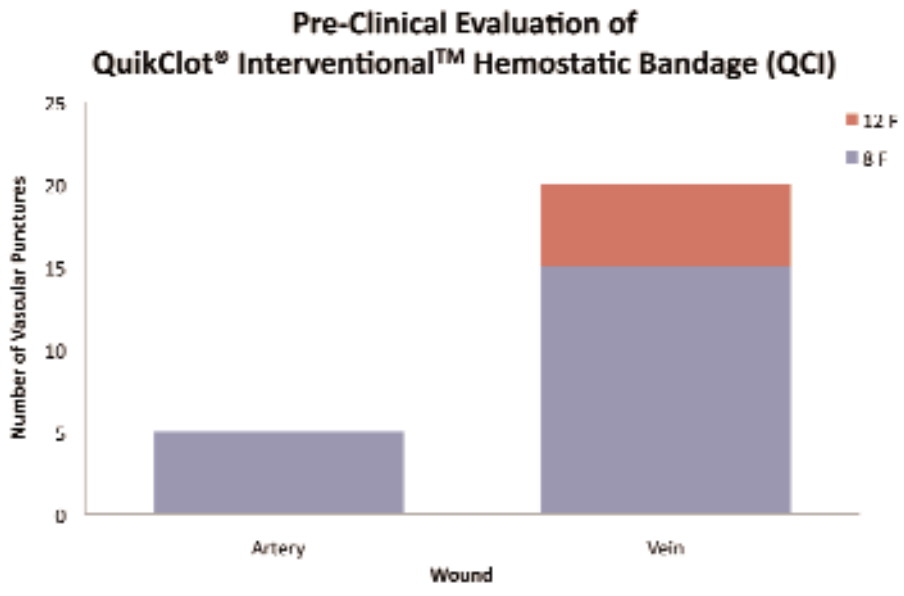

Figure 1. Arterial and venous vascular access in swine models

More than 1,000,000 percutaneous coronary intervention (PCI) procedures are performed in the U.S. every year and many more are performed annually worldwide.[1] Even though hemostasis at the vascular access site has conventionally been achieved by manual compression followed by a period of recumbency, new devices have significantly increased the methods available to achieve hemostasis at the entry site.[2] A number of complications are associated with percutaneous femoral access, including hemorrhage, thrombosis, embolization, and infection.[3] Moreover, vascular complications occur in up to 7% of patients after PCI, including the development of arteriovenous fistulas, pseudoaneurysms, or large hematomas,[4] and can require surgical repair and/or blood transfusions. Also, vascular complications at the femoral artery puncture site have been reported in 2.6-16.8% of patients after percutaneous transluminal coronary angioplasty (PTCA) or coronary stenting. Thus, there is a need for better and more effective methods[5] to achieve hemostasis. For more than 50 years, manual compression has remained the gold standard for access site management; nevertheless, the development of interventional cardiovascular procedures has called for larger sheaths and anticoagulation.[2] These new procedures led to a rising interest in the development of vascular closure devices (VCDs) to better manage bleeding at the access site. There are three main categories of VCDs: collagen-based, suture-based, and external methods such as pads, staples and clips. VCDs have been demonstrated to reduce time to hemostasis, facilitate ambulation, and potentially decrease length of stay. The choice of a device usually depends on the availability of that particular device, operator preference, anticipation of repeat arterial access, size of the arteriotomy, and the cost associated with the device. This study introduces a novel kaolin-based hemostatic device, the QuikClot® Interventional™ hemostatic bandage (QCI) (Z-Medica Corporation, Wallingford, CT), which is designed to control bleeding at the vascular access site.

Methods

Device description. The QuikClot Interventional hemostatic bandage (QCI) consists of a non-woven rayon and polyester gauze pad impregnated with kaolin, an inert mineral that does not contain animal or human proteins. Contact between kaolin and blood initiates the clotting process by activating Factor XII.[6,7] Factor XI and prekallikrein are then changed to their activated forms. QCI is FDA-cleared as an adjunct to manual compression and is indicated for the local management and control of surface bleeding from vascular access sites, percutaneous catheters, or tubes utilizing introducer sheaths up to 12 F.

QCI is intuitive to use and does not contain human or animal protein, carrying virtually no risk of transmitting infection. It is safe and effective in controlling bleeding and could represent significant cost savings, given its reasonable price.

Pre-clinical Swine Model. Yorkshire swine were obtained from Parsons Farms in Hadley, Mass. Experiments were conducted at the University of Massachusetts Animal Laboratory. The institutional laboratory animal review board for the care and use of animals at the University of Massachusetts approved this study. All research was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals. The study adhered to the principles stated in the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996 edition).

Protocol. Under general anesthesia, the animals were prepped and draped, consistent with standard protocol. The femoral artery, femoral vein, carotid artery, and jugular vein were accessed percutaneously using the Seldinger technique. Tissue dilators and introducer sheaths were used to produce wound tracts of 8 to 12 F in size. Each animal and each vessel was used for more than one access. Once the dilator and the introducer were placed within the vessels, they were removed and the QCI pad was subsequently placed over the bleeding site at the groin. Manual compression was held for 2 minutes and then a 10 cm x 12 cm 3M® Tegaderm™ Transparent Dressing was applied over the pad for an additional 3 minutes. At 5 minutes, the Tegaderm and pad were both removed and the site was evaluated for bleeding and/or hematoma formation. Video recordings and photographs were taken throughout the study to accurately depict the observations and measurements recorded throughout the procedure. All animals had their vital signs recorded during the procedure with particular attention to blood pressure measurement. Animals were euthanized at the end of the procedure.

Human clinical data. Z-Medica Corporation, the manufacturer of QCI, has collected considerable clinical data on the use of this device as part of a post-market surveillance effort in fifteen institutions throughout the United States. Physicians and other health care providers were required to fill out a Use Report Form describing their overall clinical experience and outcome following each use. Data regarding 243 documented human uses are hereby reported.

Results

A total of 25 vascular access procedures in a swine model are reported. Wound type and vascular access characteristics are summarized in Figure 1. Blood pressure and bleeding status were recorded at 5 minutes after QuikClot Interventional hemostatic bandage (QCI) was placed over the wound. On average, animals were normo-tensive throughout the procedures (Table 1).

QCI successfully controlled surface bleeding within 5 minutes in all cases

Table 1. Vascular Access in Swine Models

Total number of vascular access procedures	25
Arterial (carotid & femoral)	5
Venous (femoral & jugular)	20
Blood pressure during procedure	101 ± 17.0 Systolic; 33 ± 8.1 Diastolic

Table 2. Outcome of Various Tissue Dilator Access in Swine Models

Type of Access	Tissue Dilator Size	Percentage of bleeding controlled at 5 minutes
Arterial	8 F	100%
Venous	8 F	100%
Arterial/Venous	12 F	100%

Table 3. Human Clinical Outcomes From Use Report Forms

Type of Access	No. of Procedures	Success	Failure
Arterial	238	231	7
Venous	5	5	0
Total	***243***	***236***	***7***

using 8 and 12 F tissue dilators at the vascular access site. No hematoma formation was observed (Table 2).

QCI was used as an adjunct to manual compression in a total of 243 human clinical procedures, some in the presence of anti-coagulation, in fifteen different institutions throughout the United States. The size of tissue dilators used ranged from 4 to 8 F. Two hundred thirty-eight (238) of the 243 procedures performed were arterial procedures and the remaining 5 procedures were venous, as shown in Table 3.

QCI successfully controlled bleeding in 97.12 percent of the clinical procedures, even in the presence of anti-coagulation. Physicians and health care providers who filled out the evaluations stated that they were highly satisfied with the product and would use it again (Figure 2).

Discussion

Hemostasis following percutaneous arterial procedures is the final, but not the least important, stage of a complicated procedure. Vascular access closure devices can decrease the time to hemostasis and ambulation; more rapid hemostasis may result in cost savings by allowing earlier patient discharge. However, some of the closure devices currently on the market come at a significant cost, given their level of sophistication and complexity, and therefore are not frequently employed. In addition, some of these available devices are quite complicated to use, require a considerable amount of training before they can be used routinely, and contain many significant restrictions anatomically and of other nature for their use. Vascular access closure devices that act at the arteriotomy level carry the risk of significant complications, including device embolization and entrapment,[8] arterial stenosis/thrombosis, perforation, and infection, which can result in neurologic injury, limb loss, and even death. Furthermore, the release of foreign material at the vessel site and within the soft tissue can cause sizeable scarring, which could make a subsequent intervention at the same level more difficult. In summary, high cost,[9] device complexity, and complication rates have kept vascular access closure devices from replacing manual compression as the standard for access management. Thus, it is no surprise that manual compression still remains not only a fundamental component for sheath management in achieving hemostasis, but also continues to be the most commonly used closure technique, utilized in 70 percent and 90 percent of cases in the U.S. and in the rest of the world, respectively.[10] The QuikClot Interventional hemostatic bandage (QCI) contains kaolin as its main ingredient. Kaolin is an inert mineral known to promote clotting via a direct interaction with Factor XII, the first protein of the intrinsic pathway of the coagulation cascade. Kaolin causes an electrostatic re-arrangement of Factor XII in space, making it more susceptible to become activated in a process overall defined as "contact activation."[6,11] Kaolin improves clotting time by about 7-fold *in vitro* and has been tested extensively in stringent models of lethal vascular injury *in vivo*. In fact, QCI is directly derived from Combat Gauze™, which is currently the main hemostatic agent of choice for all branches of the U.S. military. The present study indicates that QCI is very effective in controlling bleeding following vascular access in both experimental animals and for routine clinical use. In combination with brief manual compression, QCI is successful in arresting hemorrhage in almost all instances following arterial and venous interventions for both diagnostic and interventional purposes, with no complications, even when larger-size catheters were used. QCI is intuitive to use and does not contain human or animal protein, carrying virtually no risk of transmitting infection. It is safe and effective in controlling bleeding and could represent significant cost savings, given its reasonable price. Randomized, prospective clinical trials are currently underway to confirm these preliminary results. n

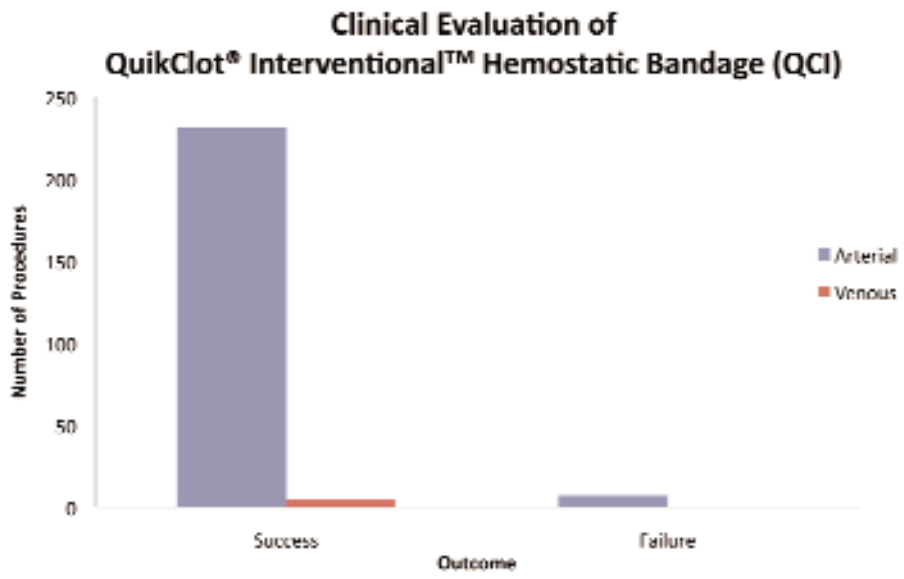

Figure 2. Human clinical outcome

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References

1. Smith SC Jr, Dove JT, Jacobs AK, et al. ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines)–executive summary. *Circulation* 2001;103:3019-3041.
2. Tu TM, Tremmel JA. Management of femoral arterial access: to close or hold pressure? *Endovascular Today* 2007; 38-42.
3. Wagner SC, Gonsalves CF, Eschelman DJ, et al. Complications of a percutaneous suture-mediated closure device versus manual compression for arteriotomy closure: a case-controlled study. *J Vasc Interv Radiol* 2003;14:735-741.
4. Resnic FS, Blake, GJ, Ohno-Machado L, et al. Vascular closure devices and the risk of vascular complications after percutaneous coronary intervention in patients receiving glycoprotein IIb-IIIa inhibitors. *Am J Cardiol* 2001;88:493-496.
5. Tron C, Koning R, Eltchaninoff H, et al. A randomized comparison of a percutaneous suture device versus manual compression for femoral artery hemostasis after PTCA. *J Interven Cardiol* 2003;16:217-221.
6. Griffin JH, Cochrane CG. Mechanisms for the involvement of high molecular weight kininogen in surface-dependent reactions of Hageman factor. Proceedings of the National Academy of Sciences of the United States of America 1976;73:2554-2558.
7. Kirby EP, McDevitt PJ. The binding of bovine factor XII to kaolin. *J Blood* 1983;61:652-659.
8. Sotomonte JC. Hematoma, bleeding, and infection. In: Marchena ED, Ferreira AC, editors. *Interventional cardiology secrets*. Philadelphia (PA): Hanley & Belfus: An Imprint of Elsevier; 2003, 228-233.
9. Resnic FS, Arora N, Matheny M, Reynolds MR. A cost-minimization analysis of the angio-seal vascular closure device following percutaneous coronary intervention. *Am J Cardiol* 2007;99:766-770.
10. Turi ZG. Vascular closure devices. In: Heuser RR, Henry M, editors. *Textbook of Peripheral Vascular Interventions. 2nd ed*. London (UK): Informa UK Ltd. 2008, 168-178.
11. Griffin JH. Role of surface in surface-dependent activation of Hageman factor (blood coagulation factor XII); Proceedings of the National Academy of Sciences of the United States of America 1978;75:1998-2002.