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VASCULAR-INTERVENTIONAL

A new kaolin-based haemostatic bandage compared with manual compression for bleeding control after percutaneous coronary procedures

Daniela Trabattoni · Piero Montorsi · Franco Fabbiocchi · Alessandro Lualdi · Pamela Gatto · Antonio L. Bartorelli

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Abstract
Objective Bleeding and vascular access site complications are an important cause of morbidity after percutaneous femoral procedures. New haemostatic dressings have been developed to control heavy bleeding. To evaluate the efficacy of a new kaolin-based haemostatic bandage for femoral artery closure after diagnostic or interventional procedures compared with manual compression.
Methods The first pilot European trial using this haemostatic bandage was performed at the in Milan, Italy. Two-hundred patients (71% male, mean age 66±11 years) undergoing angiography or PCI via a femoral approach were randomised to the haemostatic bandage (n=100) or manual compression (n=100) following sheath removal. The mean active clotting time (ACT) at haemostasis was 146±24 s (range 98–198 s). Haemostasis was achieved in 5.4±1.5 min with the bandage vs 25±15 min after manual compression, $p<0.001$. No haemostasis failure occurred in either group. No differences in oozing, minor and major haematomas and pseudoaneurysms were observed. All patients ambulated at 4 h. Major bleeding, re-bleeding or haematoma did not occur after early (4 h after the procedure) ambulation following use of the bandage.
Conclusions The haemostatic bandage obtained prompt and significantly shorter haemostasis than controls. This novel haemostatic device allowed for early ambulation without clinical complications.

Keywords Kaolin · Haemostasis · Vascular closure devices

Introduction

Vascular closure begins with a proper arterial puncture. Vascular access site complications and bleeding may occur in approximately 5% to 10% of patients and represent the single major cause of morbidity following percutaneous femoral procedures [1]. Among major vascular complications pseudoaneurysm, haematoma, arteriovenous fistula and retroperitoneal haemorrhage are mainly due to technical issues and inadequate bleeding control and may lead to surgical repair in 1.5% of cases [1, 2].

Vascular closure devices (VCD) have been studied extensively to achieve haemostasis at the vascular access site, to decrease the hospital stay, patient discomfort, costs and the rate of complications. During the early use of these devices the risk of complications exceeded that of manual compression [3, 4]. More recently reported experiences have shown VCD to have reduced the rate of vascular complications although in the USA they are still used in only a few patients (34.6% in diagnostic procedures, 37.6% in PCIs), according to the American College of Cardiology 2009 NCDR registry [5]. Consequently no large randomised trials are yet available on VCDs compared with manual compression [6]. In a few cases the anatomical characteristics of the femoral artery (severe vascular calcifications, peripheral artery disease,

D. Trabattoni · P. Montorsi · F. Fabbiocchi · A. Lualdi · P. Gatto · A. L. Bartorelli
Department of Cardiovascular Sciences,
Centro Cardiologico Monzino, University of Milan,
Milan, Italy

D. Trabattoni (✉)
Centro Cardiologico Monzino, IRCCS,
Via Parea, 4,
20138 Milan, Italy
e-mail: daniela.trabattoni@ccfm.it

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vessel diameter <3 mm) and the site of the arterial sheath insertion (i.e. the femoral bifurcation, superficial femoral artery, collaterals – i.e. inferior epigastric artery) may translate into major predictors of VCD failures and bleeding and contraindicate a systematic VCD placement [7, 8].

In recent years, new haemostatic dressings have been developed to avoid collagen-based or suture-based haemostasis in specific vascular and patient settings and to control heavy bleeding [9, 10]. Previous in vivo animal haemorrhage models found a novel kaolin-based haemostatic gauze to be the most effective product among several new dressings. This device allowed the least amount of haemorrhage and the highest survival rate in animal tests [11]. After a preliminary clinical report regarding the safety and efficacy of femoral puncture site closure with QuikClot™ Interventional Hemostatic Bandage use in the catheterization laboratory [12], we now report the first European safety clinical study comparing standard manual compression to QCI, a novel kaolin-based haemostatic dressing.

The aim of our study was to assess the safety, efficacy and performance criteria of QCI compared with standard manual compression.

Materials and methods

Between January and March 2010, 200 patients undergoing coronary diagnostic (n=102) or interventional procedures (n=98) by the femoral approach at the Centro Cardiologico Monzino in Milan, Italy, were randomised in a 1:1 fashion to standard manual compression (M, n=100 patients) or to QuikClot™ use (QCI, n=100 patients) for achieving haemostasis. Patients with baseline INR >1.4 or who had had a previous arterial access at the same femoral site within 30 days were excluded. Only experienced personnel performed femoral artery access and closure with QCI or manual compression. The femoral arterial sheath was removed once the activated clotting time (ACT) was ≤180 s. Ambulation was allowed 4 h after haemostasis. Complete blood count were obtained at baseline and at 24 h in all cases.

Patients were evaluated at 15 min, 1 h, 4 h and 24 h after haemostasis achievement for vascular complications.

Study enrollment

If inclusion criteria were met, the patients were asked for written informed consent, as required by the institutional review board in accordance with the Declaration of Helsinky. The protocol was approved by the local Ethical Committee (approval number S131/609) and performed in compliance with good clinical practice.

Definitions

Major and minor bleeding were defined according to the Thrombolysis in Myocardial Infarction trial [13]. Major bleeding included ≥5 g/dl decrease in haemoglobin or >15% decrease in haematocrit; minor bleeding included gastrointestinal or genitourinary bleeding, bleeding with a decrease in haemoglobin ≥3 g/dl or >10% decrease in haematocrit or any absolute decrease in haemoglobin ≥4 g/dl or 12%, respectively. *Oozing* was any minimal bleeding of cutaneous or subcutaneous origin controlled with the application of light compression methods.

Time to haemostasis was defined as the time from the start of compression to the time at which no further compression was required to control bleeding at the arteriotomy site.

Statistical methods

Continuous data are expressed as mean value with standard deviation and compared using Student's *t-test.* Qualitative data are presented as frequencies and/or percentages and compared using the Chi-squared test or Fisher's exact test when cell values were <5.

All statistical analyses were performed using the software package SPSS version 17.0 (SPSS, Chicago, IL, USA).

Device description

QuikClot™ Interventional Hemostatic Bandage (QCI; Z-Medica, Wallingford, CT, USA) is a non-woven coated gauze impregnated with kaolin (Fig. 1). Each dressing is a multiple-ply 1.5 in.×1.5 in.×0.5 in. (381 mm×381 mm×

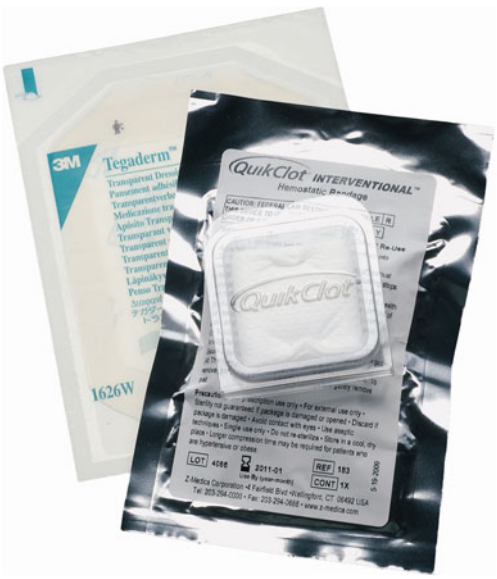

Fig. 1 QuikClot™ Interventional hemostatic bandage

127 mm) rayon/polyester construction. Kaolin is an aluminium silicate, a very potent coagulation initiator that acts as a surface activator. Its inert characteristics eliminate the possibility of skin allergies at the site of application. The gauze is stable after opening the external aluminium envelope. It is absorbent and has a good clotting ability. This advanced clotting gauze is a Food and Drug Administration (FDA)- and CE (European Community)-cleared device.

Technical specifications

The method for QCI use was as follows:

1) Apply a firm manual pressure on the femoral artery using the QCI above the entry site while removing the arterial sheath;
2) Maintain firm compression for 5 min;
3) Leave QCI over the access site and cover it with a non-compressive dressing;
4) Allow the patient to ambulate 4 h after haemostasis is achieved.

Results

This first European comparative study enrolled 200 patients undergoing invasive diagnostic angiography or PCI via a femoral approach. The introducer size was 6-Fr in 90% and 7-Fr in the remaining 10% of cases in which a larger sheath size was required for complex coronary lesion treatment. Haemostasis following arterial sheath removal was performed with QCI (n=100) or with standard manual compression (n=100) at a mean time of 91±112 min after the procedure. Patients were well matched regarding clinical characteristics and antiplatelet therapy as shown in Table 1. Time intervals are summarised in Table 2. Mean time to haemostasis was significantly shorter with QCI compared with standard manual compression (5.4±1.5 vs. 25±15 min, p<0.001). Indeed, in the QCI arm, PCI patients required a slightly longer total compression time (6.0±2.0 min) compared with diagnostic patients (5.3±1.7 min; p<0.001). Oozing similarly occurred in 12% of QCI and 10% of manual compression cases (p=0.41) and was completely resolved with prolonged manual compression (mean additional compression time of 3.8±2.0 min) in both groups. This occurrence was more frequently observed in patients treated with PCI, under double antiplatelet treatment and with a higher activated clotting time (ACT) value at the time of sheath removal compared with diagnostic-alone patients (171±42 vs 137±24 s, respectively), thus requiring adjunctive compression at the arterial access site (26% in PCIs vs 17% diagnostics, respectively; p=0.08).

Table 1 Patients demographics

	QuikClot™ (n=100)	Manual Compression (n=100)	P value
Male (%)	70	60	0.09
Mean age (years)	65.7±13	73.6±6.2	0.09
Weight (Kg)	73.9±12	71.2±15	0.53
Diabetes (%)	15	16	0.15
Renal Failure (%)	7	6	0.50
Hypertension (%)	45	42	0.38
LMW Heparin (%)	4	2	0.34
Aspirin + Clopidogrel (%)	29	26	0.37
Aspirin (%)	60	60	0.11
Aspirin + Warfarin (%)	7	3	0.16
None (%)	-	9	0.50

Table 2 Haemostasis effectiveness

	QuikClot™	Manual Compression	P value
ACT at haemostasis time (sec)	145.4±29.6	140.2±20.4	0.67
Time to haemostasis (min)	87±137.8	94±126	0.21
Mean haemostasis time	5.4± 1.5 min	26.2± 15 min	< 0.001
Cumulative Frequencies			
5 min	83%	10%	<0.001
6 min	91%	30%	<0.001
8 min	100%	38%	<0.001
Median time to ambulation (hours)	4	4	NA
Delay in ambulation beyond 4 h (%)	8	NA	NA

NA = Not applicable

Table 3 Vascular complications

	QuikClot™ (n=100)	Manual Compression (n=100)	P value
Major Bleeding (%)	1	1	0.50
Retroperitoneal (%)	1	1	0.50
Haematoma, > 5 cm (%)	1*	2	0.37
Pseudoaneurysm (%)	1*	1	0.50
Total (n=patients)	2	4	0.23

*same patient

Occurrence of bleeding and vascular complications is described in Table 3. Major bleeding, re-bleeding and haematoma did not occur after ambulation.

Discussion

The incidence of vascular complications comparing VCD with manual compression after percutaneous coronary interventions was assessed in a previous observational study by Dangas et al. [3]. The use of a VCD was associated with a significantly higher rate of haematomas (9.3% vs. 5.1%, $p<0.001$), a greater decrease in haematocrit (5.2% vs 2.5%, $p<0.001$) and an increased need for surgical repair (2.5% vs. 1.5%, $p=0.003$). According to initial studies in the late 1990s, vascular complications were twice as common compared with manual compression and frequency of surgical repair of arterial damage, formation of haematoma and a drop in haematocrit were noted to be higher among the VCD cases [13]. However, the experience in VCD use gained by interventionalists and improvements in device design also allowed better results with reduced or similar vascular complications between device use and manual compression in more recently reported data [4, 14]. It is however known that anatomical issues (the presence of collateral vascularisation, peripheral artery disease, severe vessel calcifications, small vessel size, puncture at the bifurcation site, previous multiple femoral artery sutures) may contraindicate VCD deployment. Therefore, when a coronary interventional procedure is performed in these subsets with a specific contraindication to VCD deployment and heparin, bivalirudin or glycoprotein IIb-IIIa inhibitors administered, standard manual or mechanical compression need to be applied for a longer time after the end of procedure in order to reduce the excess bleeding and bed-rest is therefore prolonged. Furthermore, according to the literature, groin haematoma is expected in 5% to 23% of patients after manual compression, pseudoaneurysm in 0.5% to 9%, and arteriovenous fistula in 0.2% to 2% [4]. Patients with advanced age and/or peripheral vascular disease were shown to have a higher risk of major complications, approaching 5–10% [15]. Our first preliminary clinical evaluation in the interventional cardiology field showed QCI to be an easy to use and effective device in achieving a short-term passive haemostasis together with a very low incidence of vascular complications [12]. Politi et al. [16] further evaluated the occurrence of 24-hour radial artery occlusion and the incidence of bleeding after 15 min of radial artery compression using the QuikClot Interventional pad after percutaneous interventions. The investigators demonstrated the superiority of QuikClot haemostasis in achieving bleeding control compared with standard manual compression and a 20% occurrence of active bleeding after compression in patients with high ACT levels at the time of sheath removal. The availability of this adjunctive alternative technique expedites the formation of a blood clot and a barrier to bleeding when combined with manual compression, allowing a shorter and painless haemostasis procedure as well as a safe, early ambulation time without major vascular complications. In the present study, major and minor bleeding associated with QCI or manual compression haemostasis were demonstrated to be similar. This preliminary comparative study confirmed that early haemostasis and ambulation may be possible even without a VCD, when adequate arterial compression is successfully achieved.

Conclusions

The kaolin-based QuikClot^{TM} Interventional Hemostatic Bandage (QCI) obtains prompt haemostasis and allows early, safe ambulation following coronary diagnostic and interventional procedures via a femoral approach. QCI is a useful adjunctive tool in assisting manual or mechanical compression. This device may contribute to making the haemostatic process easier and shorter than with standard manual compression and could lead to a complete avoidance of intra- or extravascular device deployment. Further multicentre, randomised clinical evaluations comparing the safety and efficacy of QCI vs. VCD in PCI cases are warranted and currently underway and their results will gather further scientific evidence on QCI use for bleeding control at vascular access sites.

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