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PURPOSE: To assess the relative efficacy of three compression adjuncts—D-Stat Dry (D-Stat), QR Powder (QR), and XS Powder (XS)—for reducing time to hemostasis in patients who underwent diagnostic and interventional percutaneous procedures.

MATERIALS AND METHODS: D-Stat, QR, or XS was applied in 176 percutaneous diagnostic arterial, therapeutic arterial, venous, and arteriovenous dialysis access (AVDA) procedures in 138 patients. The mean time to hemostasis and application-related complications were retrospectively assessed.

RESULTS: Mean time to hemostasis was significantly reduced in all applications of QR (3.1 minutes ± 1.1) and XS (3.7 minutes ± 1.1) relative to D-Stat (6.2 minutes ± 1.1, $P < .001$ vs both). For therapeutic arterial procedures, mean time to hemostasis for QR and XS was 3.6 minutes ± 1.1 and 4.8 minutes ± 1.1, respectively, and this was significantly less than that of D-Stat (10.0 minutes ± 1.2; $P < .001$ vs QR, $P < .01$ vs XS). Mean times to hemostasis for QR and XS were also shorter than that with D-Stat in diagnostic arterial and AVDA procedures ($P < .05$). For venous procedures, mean time to hemostasis for QR (1.9 minutes ± 1.2) was significantly shorter than that with both D-Stat (4.0 minutes ± 1.2, $P < .05$) and XS (3.7 minutes ± 1.2, $P < .05$). Minor immediate complications (hematoma <5 cm) occurred in 2.8% of applications. No access site infections were observed.

CONCLUSIONS: All three agents effectively reduced time to hemostasis with minimal associated complications. QR was found to be more effective than D-Stat in all four procedure types.

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ACHIEVEMENT of vascular access site hemostasis after diagnostic and interventional percutaneous procedures is of paramount importance. Access site complications include hemorrhage, thrombosis, hematoma, pseudoaneurysm, and infection (1–4). Manual compression, originally described by Seldinger in 1953 (5), remains the gold standard for vascular access closure. This typically requires sustained manual pressure over the access site for 15–25 minutes followed by 6–8 hours of bed rest (6). Although a proven method, manual compression is time-consuming, requires prolonged patient immobilization, and can cause substantial patient discomfort (7,8). Furthermore, the increased use of periprocedural anticoagulation and antiplatelet therapies and advances in endovascular techniques that require larger-diameter sheaths have increased access-related complication rates to as high as 11% (9,10). These factors have spurred the development of myriad alternative strategies to effectively achieve access site hemostasis while minimizing complications.

The past decade has witnessed the introduction of a plethora of vascular closure devices designed to replace traditional manual compression for arteriotomy closure. These devices can be categorized into those that perform closure by means of suture (Perclose, Abbott Vascular Devices, Redwood City, Calif; X-Site, Datascope, Montvale, NJ) (11), clip (Starclose; Abbott Vascular Devices) (12), staple (EVS, Medtronic, Santa Rosa, Calif; X-Press, X-SITE Medical, Blue Bell, Pa; Surestitch, Sutura, Fountain Valley, Calif) (13), and deposition of collagen and/or thrombin plugs

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(Angio-Seal, St Jude Medical, Minnetonka, Minn; Vasoseal, Datascope; Duett, Vascular Solutions, Minneapolis, Minn) (14,15). In aggregate, these devices have generally demonstrated high technical success rates, effective arterial puncture closure, reduced times to hemostasis, and earlier patient ambulation and discharge (7,16,17). Although each has their distinct disadvantages and advantages, widespread use of this class of devices has been hindered by economic considerations ($150–$250 per application) and the emergence of device-specific complications (8,18–20). Many of these devices deposit a foreign body that can serve as a nidus for infection (20); furthermore, collagen and/or thrombin plug devices can potentially embolize distally or cause local thrombosis (7,21). Because of this embolization risk, peripheral vascular disease is a relative contraindication for the use of many of these devices (7). Moreover, after device-mediated closure, repeat access of the puncture site is often precluded for extended periods of time.

More recently, a new class of products have been developed that are noninvasive, topically applied, and remain extraluminal without leaving any foreign material behind (22). These are hemostatic pads, patches, and powders that potentiate clot formation through pharmacologic and/or chemical mechanisms and are designed to augment and not replace conventional compression. All require compression, but at substantially decreased times, and most require contact with blood for activation. Such products include the SyvekPatch (Marine Polymer Technologies, Danvers, Mass) (23,24), Clo-Sur PAD (Scion Cardio-Vascular, Miami, Fla) (25–27), and ChitoSeal (Abbott Vascular Devices) (28). D-Stat Dry (D-Stat) (Vascular Solutions), Quick Relief Powder (QR) (Biolife, Sarasota, Fla), and Extra-Strength Powder (XS) (Biolife) are newer products within this class that are now being used as manual compression adjuncts for closure of vascular access sites. D-Stat is a dry pad coated with lyophilized bovine thrombin, which stimulates the conversion of fibrinogen to fibrin, promotes platelet aggregation, and activates clotting factors VIII, V, and XIII (27,29,30). Its indication was expanded by the U.S. Food and Drug Administration in October 2006 for topical application as a manual compression adjunct to control surface bleeding from vascular access sites in patients undergoing diagnostic endovascular procedures with 4–6-F sheaths (31). QR (potassium iron salt and hydrophilic polymer), classified by the Food and Drug Administration as a Class I Exempt wound dressing, is a powder that creates a physical seal through iron-mediated agglomeration of serum proteins and a hydrophilic polymer that rapidly dehydrates blood (32). XS is the more concentrated form of QR. QR is readily available to the public and marketed for the management of superficial wounds and epistaxis.

The optimal method for access site management remains controversial. In this study, we retrospectively evaluated our experiences with D-Stat, QR, and XS for achieving hemostasis in percutaneous vascular procedures. To assess their efficacy in a wide range of interventional settings, applications in diagnostic arterial, therapeutic arterial, venous, and arteriovenous dialysis access (AVDA) procedures were reviewed.

MATERIALS AND METHODS

Study Design

We performed a single-institution retrospective review over a 9-month period of patients in whom adjuncts for manual compression were applied after undergoing vascular interventional radiology procedures. Analyses were based on the type of hemostasis adjunct applied (D-Stat, QR, or XS) and performed on a per-application-site basis. In a subcohort analysis, we separately analyzed treatment arms according to the vascular access procedure type (diagnostic arterial, therapeutic arterial, venous, or AVDA). Only treatment applications in which complete data were available were included in this analysis. This study was approved by the institutional review board.

Access Site Management Technique

For all patients, manual compression was initially applied in standard fashion over the vascular access site proximally in arterial and AVDA applications and peripherally in venous applications to obtain initial vascular control. The hemostatic agent was then applied over the skin entry access site and held with firm, nonocclusive pressure such that no bleeding around the hemostatic agent or hematoma development was observed. For QR and XS applications, a small amount of blood was allowed to seep through the access site tract to the skin before application to activate the hemostatic agent. For D-Stat applications, the hemostatic adjunct was applied directly over the skin entry site without an activation step.

For arterial and AVDA procedures, pressure was maintained both upstream and directly over the access site with the hemostatic compression adjunct in place for 3 minutes. At this time, compression was slowly released and the access site was observed for bleeding or hematoma development. If either was observed, the agent was re-applied and the procedure repeated in similar fashion at 1-minute intervals henceforth. In venous procedures, the access site was observed for bleeding after the 1st minute of application and repeated every minute as needed. Once hemostasis was obtained, patients were observed in standard fashion for six hours for diagnostic and therapeutic arterial procedures and two hours for AVDA and venous access procedures. The overlying dressing and hemostatic adjunct were removed after postprocedural observation.

Study Endpoints

The primary study endpoint was time to hemostasis, which was defined as the time (in minutes) from the initial application of the hemostatic agent to the time in which manual compression was released and absence of bleeding from the skin entry site or hematoma development and/or expansion was observed for a period of at least 5 minutes. Secondary endpoints included major and minor complications immediately after the procedure (defined as 6 hours for diagnostic and therapeutic arterial procedures and 2 hours for AVDA and venous procedures) and up to two weeks post procedure. Major and minor complications were defined according to the SIR reporting standards (33).

For all applications, the time to hemostasis; type of interventional procedure performed; outer diameter (in French) of the sheath or catheter used;

Table 1
Baseline Patient Characteristics

Parameter	D-Stat (n = 41)	Group QR (n = 59)	XS (n =76)	P Value*
Age (y)	55.5 (14)	58.7 (32)	57.2 (20)	.8595
Male sex	24 (58)	31 (53)	39 (51)	.7844
Race				
White	9 (27.3)	22 (47.8)	32 (56.1)	.3270
African American	5 (15.2)	5 (10.9)	6 (10.5)	.3270
Hispanic	16 (48.5)	14 (30.4)	15 (26.3)	.3270
Asian	2 (6.1)	2 (4.4)	2 (3.5)	.3270
Unknown	1 (3.0)	3 (6.5)	2 (3.5)	.3270
Blood pressure				
Systolic (mm Hg)	126 (27)	129.5 (40)	125 (35)	.8584
Diastolic (mm Hg)	69 (25)	64.5 (23)	60 (25)	.5917
Coagulation values				
International normalized ratio	1.1 (0.1)	1.1 (0.2)	1.1 (0.1)	.4863
Prothrombin time (sec)	10.6 (1.5)	10.3 (1.6)	10.3 (0.9)	.6117
Partial thromboplastin time (sec)	28.2 (3.9)	30.6 (7.3)	27.8 (4)	.0190
Platelet count ($\times 10^9$/L)	218.5 (152.5)	241 (190)	181 (115)	.0633
Comorbidities†				
Diabetes	12 (22.6)	21 (20.8)	35 (28.9)	.1597
Hypertension	16 (30.2)	33 (32.7)	44 (36.4)	.1597
End-stage renal disease	13 (24.5)	20 (19.8)	23 (19.0)	.1597
End-stage liver disease	3 (5.7)	6 (5.9)	7 (5.8)	.1597
Active malignancy	5 (9.4)	17 (16.8)	4 (3.3)	.1597
Peripheral vascular disease	4 (7.6)	4 (4.0)	8 (6.6)	.1597

Note.—Continuous data are presented as the median; numbers in parentheses are the interquartile range. Categorical data are presented as number of patients; numbers in parentheses are percentages.
* Differences between groups for continuous nonparametric data were tested with the Kruskal-Wallis test and analysis of variance for continuous parametric data. Categorical data were tested with the Pearson χ^2 test and Fischer exact test, where appropriate.
† Some patients had more than one comorbidity.

prothrombin time; partial thromboplastin time; international normalized ratio; platelet count; blood pressure at application; periprocedural use of anticoagulation, antiplatelet, or thrombolytic agents; and presence and type of adverse event observed immediately after the procedure and at 2-week follow-up were documented.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics between groups. Differences in patient characteristics for continuous data were investigated by using a two-tailed Wilcoxon-Mann-Whitney test and Kruskal-Wallis test with post-hoc testing with one-way analysis of variance on the ranks of the observations with Tukey-Kramer correction for multiple comparisons. The Pearson χ^2 or Fisher exact test was used for categorical data. Normal distribution was determined with QQ plots and the Kolmogorov-Smirnov test. The distribution of our primary outcome measure, time to hemostasis, was skewed to the right. Log transformation of this outcome measure normalized this distribution. Analysis of covariance (ANCOVA) was used to compute a covariate-adjusted mean time to hemostasis because patient characteristics between groups were different. Tukey-Kramer adjustment of P values was used for post-hoc comparisons. Analyses were performed with software (Excel 2003; Microsoft, Redmond, Wash) and a statistical package (SAS 9.1; SAS, Cary, NC). A P value of less than .05 was considered statistically significant.

RESULTS

Patient Population

From February 2006 to December 2006, 176 applications of D-Stat, QR, and XS in 138 patients were retrospectively reviewed. Baseline patient characteristics, laboratory data, and comorbidities are summarized in **Table 1**. For patients who received D-Stat, QR, or XS, median ages were 56, 58, and 57 years, respectively, with a slight majority among all three groups being male. Partial thromboplastin time was significantly different between groups (P = .019), with post-hoc comparisons showing a difference in partial thromboplastin time between QR and XS groups (P = .0151). The platelet count trended toward being significantly different (P = .063). No significant differences in comorbidities were revealed by means of Pearson χ^2 analysis.

Type of Interventional Procedure Performed

Among the hemostatic adjuncts applied, Pearson χ^2 analysis revealed no significant difference in the distribution of interventional procedure performed (**Table 2**). The median outer diameters of the sheath or catheter

used in these procedures were similar among the three groups.

Periprocedural Anticoagulation, Antiplatelet, and/or Thrombolytic Therapies

Most patients did not receive anticoagulation, antiplatelet, or thrombolytic therapies the day of the interventional procedure (**Table 2**). Five patients received tissue-type plasminogen activator. Results of the Fisher exact test showed no statistically significant difference in periprocedural use of these therapies among the three groups.

Mean Time to Hemostasis

Hemostasis was achieved in all applications of D-Stat, QR, and XS. There were no substantial technical difficulties in applying these agents and no instances of repeat bleeding after removal. As detailed in **Table 3**, the mean time to hemostasis (±standard error) was significantly shorter in those who received QR (3.44 minutes ± 1.07) or XS (3.76 minutes ± 1.06) than in those who received D-Stat (5.69 minutes ± 1.08, $P < .001$ for both comparisons). The times to hemostasis for QR and XS were not significantly different ($P = .5536$).

Because of differences in patient characteristics among the treatment groups, ANCOVA was used to compute a covariate-adjusted mean time to hemostasis to account for these differences (**Table 3**). After controlling for partial thromboplastin time, platelet count, number of product applications, sheath or catheter outer diameter, periprocedural anticoagulation, and type of interventional procedure performed, the covariate-adjusted mean time to hemostasis remained significantly shorter for the QR (3.05 minutes ± 1.06) and XS (3.74 minutes ± 1.06) treatment groups than for the D-Stat group (6.20 minutes ± 1.07; $P < .001$ for both comparisons). Furthermore, this covariate-adjusted analysis uncovered a statistically significant shorter mean time to hemostasis for the QR group relative to the XS group ($P = .0293$).

Table 2
Type of Procedure Performed, Sheath Size, and Use of Periprocedural Anticoagulation, Antiplatelet, or Thrombolytic Therapies According to Patient

Parameter	D-Stat ($n = 41$)	Group QR ($n = 59$)	XS ($n = 76$)	P Value
Procedure type				
Arterial, diagnostic	10 (24)	15 (25)	26 (34)	.9063
Arterial, therapeutic	9 (22)	14 (24)	14 (18)	.9063
AVDA	12 (29)	16 (27)	21 (28)	.9063
Venous	10 (24)	14 (24)	15 (20)	.9063
Sheath/catheter outer diameter (F)	8 (4)	7 (3)	7 (4)	.4632
Therapies affecting hemostasis				
None	34 (83)	48 (81)	47 (62)	.0905
Heparin	4 (9.8)	5 (8.5)	19 (25)	.0905
Warfarin	2 (4.9)	1 (1.7)	1 (1.3)	.0905
Aspirin	0 (0)	1 (1.7)	2 (2.6)	.0905
Clopidogrel	0 (0)	1 (1.7)	4 (5.2)	.0905
Tissue-type plasminogen activator	1 (2.4)	3 (5.1)	3 (4.0)	.0905

Note.—Continuous data are presented as median; numbers in parentheses are the interquartile range. Categorical data are given as numbers of patients; numbers in parentheses are percentages.

Table 3
Mean Time to Hemostasis (in minutes) According to Treatment and Procedure Type

Parameter	Unadjusted	Adjusted*
Treatment type		
D-Stat	5.69 ± 1.08	6.20 ± 1.07
QR	3.44 ± 1.07†	3.05 ± 1.06†
XS	3.76 ± 1.06†	3.74 ± 1.06†‡
Procedure type		
Arterial, diagnostic	4.43 ± 1.07§	4.78 ± 1.07§
Arterial, therapeutic	5.20 ± 1.08§	5.35 ± 1.07§
AVDA	4.49 ± 1.07§	4.02 ± 1.08§
Venous	2.98 ± 1.08	2.85 ± 1.10

Note.—Data are given as means ± standard errors.
* Based on ANCOVA of log time to hemostasis, adjusting for platelet number, partial thromboplastin time, number of applications, outer diameter of the sheath or catheter, anticoagulation status, and procedure type. ANCOVA results are presented as actual time.
† $P < .05$ versus D-Stat.
‡ $P < .05$ versus QR.
§ $P < .05$ versus venous procedures.

Effect of Time to Hemostasis according to Procedure Type

Among all applications, regardless of hemostatic agent applied, the unadjusted mean time to hemostasis was significantly shorter among the venous procedures (2.98 minutes ± 1.08) relative to arterial diagnostic (4.43 minutes ± 1.07, $P = .0012$), arterial therapeutic (5.20 minutes ± 1.08, $P < .001$), and AVDA (4.49 minutes ± 1.07, $P = .007$) procedures (**Table 3**). The unadjusted mean times to hemostasis among these latter three procedure types were not significantly different. ANCOVA controlling for the same variables described earlier did not alter these relationships.

Given these findings, comparisons between the three hemostatic adjuncts were performed for each procedure type (**Table 4**). For arterial diagnostic, arterial therapeutic, and AVDA procedures, the mean times to hemostasis for both QR and XS were significantly shorter than that for D-Stat. For example, among applications for therapeutic arterial procedures, the mean times

Table 4
Mean Time to Hemostasis According to Procedure Type for Each Treatment Group

	D-Stat		QR		XS	
Parameter	No. of Procedures	Time to Hemostasis (min)*	No. of Procedures	Time to Hemostasis (min)	No. of Procedures	Time to Hemostasis (min)*
Arterial, diagnostic	10	7.91 ± 1.08	15	3.36 ± 1.07†	26	3.85 ± 1.05†
Arterial, therapeutic	9	9.99 ± 1.18	14	3.56 ± 1.14†	14	4.78 ± 1.14†
AVDA	12	7.26 ± 1.13	16	3.41 ± 1.11†	23	3.87 ± 1.09†
Venous	10	3.96 ± 1.16	14	1.93 ± 1.16†	15	3.74 ± 1.16‡

* Data are given as means ± standard errors.
† $P < .05$ versus D-Stat.
‡ $P < .05$ versus QR.

Table 5
Mean Time to Hemostasis: Effect of Periprocedural Anticoagulation, Antiplatelet, and Thrombolytic Therapies per Application

	D-Stat		QR		XS	
Type of Therapy	No. of Procedures	Time to Hemostasis (min)*	No. of Procedures	Time to Hemostasis (min)	No. of Procedures	Time to Hemostasis (min)*
None	34	5.55 ± 1.07	49	3.64 ± 1.06	48	4.01 ± 1.06
Anticoagulation	5	4.47 ± 1.24	3	2.59 ± 1.19	22	3.43 ± 1.10
Antiplatelet	0	NA	1	3.51 ± 1.51	5	4.20 ± 1.13
Anticoagulation and antiplatelet	1	9.16 ± 1.52	3	2.84 ± 1.53	0	NA
Thrombolytic	1	33.32 ± 1.54†‡	3	3.79 ± 1.27	3	3.12 ± 1.21

* Data are given as means ± standard errors. NA = not applicable.
† $P < .05$ versus no therapy.
‡ $P < .05$ versus anticoagulation.

to hemostasis for QR and XS groups were 3.56 minutes ± 1.14 and 4.78 minutes ± 1.14, respectively. Both were significantly shorter, less than half, than that of the D-Stat group (9.99 minutes ± 1.18; $P = .0002$ vs QR, $P = .0055$ vs XS). The mean times to hemostasis were not significantly different between QR and XS groups for all three procedure types.

For venous procedures, however, the mean time to hemostasis for QR (1.93 minutes ± 1.16) was significantly shorter than that for both D-Stat (3.96 minutes ± 1.16, $P = .0151$) and XS (3.74 minutes ± 1.16, $P = .0269$), whereas the mean times to hemostasis for D-Stat and XS were relatively similar.

Although not formally evaluated, a number of interventional procedures such as AVDA and transarterial chemoembolization of hepatic lesions required repeat access of vascular access sites that were previously managed with D-Stat, QR, or XS in less than 6 months. No difficulties in repeat access or associated complications were observed.

Effect of Periprocedural Anticoagulation, Antiplatelet, and Thrombolytic Therapy on Time to Hemostasis

Within each hemostatic adjunct group, mean times to hemostasis were compared among patients receiving periprocedural anticoagulation, antiplatelet therapy, anticoagulation and antiplatelet therapies concomitantly, thrombolytics, or none of the above (**Table 5**). These therapies did not significantly alter the mean time to hemostasis for the QR and XS treatment groups. Within the D-Stat group, the time to hemostasis was significantly increased in the one patient who received thrombolytic therapy (33.32 minutes ± 1.54) relative to applications without hemostasis-altering treatments (5.55 minutes ± 1.24, $P = .0019$).

Complications

Five procedures (2.8%) had minor complications, consisting of hematomas smaller than 5 cm, during the immediate postprocedural observation period. One complication occurred with D-Stat and two each occurred with QR and XS. The difference between the groups was not statistically significant. Two weeks after the procedure, there were no related complications for all three groups. No major complications or access site infections were observed.

DISCUSSION

With the global market for vascular closure devices alone approximating $500 million in 2005 and expected to exceed $750 million by 2008 (34), the need and enthusiasm for percutaneous vascular access closure alternatives superior to traditional manual compression is evident. Despite this, vascular closure devices are clearly not without risks of complications and technical failure. Larger prospective randomized case series have reported major complication rates of 0.5%–13% (7,35). The deposition of a foreign body leading to infectious and occlusive complications is a design flaw inherent to most of these devices. More recently, hemostatic compression adjuncts, which are applied topically and remain extravascular, have received considerable attention and use despite a relative dearth of clinical data. In the form of pads, patches, and powders, hemostatic compression adjuncts augment manual compression by means of pharmacologic and/or chemical acceleration of physiologic coagulation and clot formation (22). In this study, we retrospectively evaluated the relative efficacy of D-Stat, QR, and XS in achieving access site hemostasis in patients who underwent percutaneous vascular procedures. To assess their applicability in various settings, these agents were applied in not only diagnostic and therapeutic arterial procedures but also in venous and AVDA interventions. The use of vascular closure devices in venous access site management has been reported previously (36).

Although manual compression was not used as a formal control in this study, it is well known that the time to hemostasis with this standard method in arterial punctures generally ranges from 10 to 25 minutes. As detailed in **Table 4**, the mean time to hemostasis for D-Stat, QR, and XS were all relatively less than historically accepted parameters for manual compression for therapeutic arterial interventions (9.99, 3.56, and 4.78 minutes, respectively), for diagnostic arterial procedures (7.91, 3.36, and 3.85 minutes, respectively), and in all applications in aggregate (covariate adjusted, 6.20, 3.05, and 3.74 minutes, respectively). In a comprehensive review of large case series ($N > 100$) evaluating specific vascular closure devices, the mean time to hemostasis for arterial and diagnostic arterial procedures ranged from 1 to 20 minutes and averaged 4.4 and 13.4 minutes for Angio-Seal and Perclose, respectively (7). Although direct comparisons with vascular closure devices cannot be made, comparable hemostatic efficacy is suggested.

To illustrate the broad applicability of these agents, their use in AVDA and venous procedures was also reviewed. The mean time to hemostasis for D-Stat, QR, and XS were, respectively, 7.26, 3.41, and 3.87 minutes in AVDA procedures and 3.96, 1.93, and 3.74 minutes for venous interventions. This is of particular interest given that no ideal means of vascular hemostasis exists for AVDA procedures, with existing mechanical closure devices generally being contraindicated.

In the lone published prospective randomized trial of D-Stat (29), the mean times to hemostasis for D-Stat and manual compression were 7.8 and 13.0 minutes, respectively, in patients who underwent diagnostic arterial procedures. Time to ambulation was also reduced, and there were no differences in complications. In the present study, mean time to hemostasis for D-Stat in patients who underwent diagnostic arterial procedures was comparable (7.91 minutes). We are not aware of any other reports assessing the efficacy of QR or XS in controlling access site bleeding.

As expected, the covariate-adjusted mean time to hemostasis for therapeutic arterial procedures, regardless of hemostatic agent used, was significantly longer than that for venous procedures (5.35 minutes ± 1.07 vs 2.85 minutes ± 1.10). Likely due to the already decreased hemostasis times with use of these adjuncts, the mean time for therapeutic arterial procedures was increased, but not significantly, compared with that of diagnostic arterial (4.78 minutes ± 1.07) and AVDA (4.02 minutes ± 1.08) procedures.

After adjusting for differences in patient characteristics, comparisons between the thrombin-based D-Stat and the iron- and dessicant-based QR and XS in all procedure settings yielded significantly decreased hemostasis times for QR (3.05 minutes ± 1.06) and XS (3.74 minutes ± 1.06) relative to D-Stat (6.20 minutes ± 1.07). The hemostatic superiority of QR and XS continued with unadjusted subcohort analyses stratified according to procedure type for therapeutic arterial, diagnostic arterial, and AVDA procedures but not for venous procedures. For therapeutic arterial procedures, mean hemostasis times were 9.99 minutes ± 1.18 with D-Stat and 3.56 minutes ± 1.14 and 4.78 minutes ± 1.14 with QR ($P < .001$) and XS, ($P < .01$). In venous procedures, mean time to hemostasis with QR, but not XS, was significantly shorter than that with D-Stat.

These data suggest that both QR and XS are more efficacious than D-Stat in reducing time to hemostasis. The hemostatic efficacy of D-Stat is primarily mediated through the action of thrombin. Although D-Stat provides a physical barrier to bleeding in the form of a pad, QR creates a sealant through rapid desiccation of blood and iron-mediated agglomeration of serum proteins (32). Unlike D-Stat, QR should theoretically not accelerate physiologic coagulation and thus should yield longer hemostasis times. Aside from the publicly available patent for QR, however, there are no other published data about its mechanism and it is possible that its active ingredients may directly promote coagulation. Further studies are certainly warranted.

It is interesting that for venous procedures, mean hemostasis time for QR (1.93 minutes) was significantly shorter than that with both XS (3.74 minutes, $P = .0269$) and D-Stat (3.96 minutes, $P = .0151$). Furthermore, for all applications, adjustment of inherent differences in patient characteristics revealed a significantly longer mean time to hemostasis with XS (3.74 minutes) compared with QR (3.05 minutes, $P = .0293$). XS is reportedly the more concentrated form of QR, so this weak suggestion that XS may not be as efficacious as QR was unexpected. However, it is unclear whether there are other differences in product compositions. These results may also imply that the relationship between concentration and efficacy may not be linear and that there is an optimal concentration for obtaining access site hemostasis. Nevertheless, further investigation into the differences between QR and XS in both product composition and efficacy is needed.

The presence of anticoagulation, antiplatelet, and/or thrombolytic agents did not significantly increase the time to hemostasis in patients who received QR or XS. Although this suggests that the efficacy of QR and XS is resilient to the periprocedural use of these agents, these results are limited due to low sample sizes. However, 22 patients treated with XS received anticoagulation, and the mean times to hemostasis for these patients were not significantly altered. In the D-Stat group, anticoagulation did not have a significant effect on hemostasis time, but no patients received antiplatelet therapy alone and only one patient received tissue-type plasminogen activator, in whom the time to hemostasis was 33.32 minutes. Thus, no conclusions can be drawn with regard to whether tissue-type plasminogen activator or antiplatelet therapy has an effect on the hemostatic efficacy of D-Stat.

Likely due to the noninvasive nature of these topically applied compression adjuncts, the minor complication rate immediately after the procedure was minimal (2.8%), and there were no major complications or complications at 2-week follow-up. Five hematomas (<5 cm) developed during the immediate postprocedural observation period. In the QR and XS groups, a few patients reported feeling mild heat, none to the point of causing discomfort, and there were no superficial burns. Because these products remain extravascular and are sloughed off after hemostasis is achieved, there were no reports of access site infectious or occlusive complications. Peripheral vascular disease was documented in eight patients.

In the present study, we retrospectively demonstrated an overall efficacy of D-Stat, QR, and XS for achieving reduced time to hemostasis in diagnostic arterial, therapeutic arterial, venous, and AVDA procedures. In a systemic review and meta-analysis of 33 trials of vascular closure devices, Koreny et al (8) found only marginal evidence for improved hemostatic efficacy as well as a possible increased risk for hematoma and pseudoaneurysm formation. The less than ideal risk and cost benefit ratios of vascular closure devices have hindered their widespread acceptance. Noninvasive compression adjuncts may provide a reasonable alternative that is broadly applicable, easier to use, cheaper, and safer given that they are topically applied and remain extravascular. It is important to note, however, that this class of agents encompasses a wide spectrum of underlying mechanisms and, thus, in turn, efficacies. Herein, we showed that QR is superior to D-Stat in reducing time to hemostasis although the underlying reason for this is unknown. Further investigation into the mechanisms of these agents is warranted, and, more specifically, additional information with regard to QR and XS is needed from the manufacturer. Whether the efficacy of these three agents is robust to the presence of anticoagulation, antiplatelet, and thrombolytic therapies also requires further elucidation. Moreover, it is unclear what effect these agents may have on time to ambulation as this was not assessed here. Given that this was a retrospective analysis of a single institution's early experience with this novel class of agents, this study has a number of inherent limitations, and the conclusions of this investigation should be viewed within this context. Larger sample size prospective randomized clinical trials comparing D-Stat, QR, or XS to manual compression or even vascular closure devices are necessary before their widespread use in the interventional setting can be recommended.

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