Hemostasis success rates and local complications with collagen after femoral access for cardiac catheterization: Analysis of 6007 published patients

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Since the first clinical studies regarding sealing of arterial puncture sites with collagen with the use of the vascular hemostatic device (VHD) and the hemostatic puncture closing device (HPCD) in the early 1990s were performed, no analysis summarizing the published patients has been reported. Therefore we performed a Medline search of data as far back as 1990 and included abstracts presented at the major scientific meetings in the United States (American Heart Association, American College of Cardiology), Europe (European Society of Cardiology), and Germany (German Society of Cardiology). A total of 6007 patients were found to have been enrolled in studies with VHD (4448 patients) or with HPCD (1559 patients). Parameters analyzed in this review were hemostasis success rates and local complications. To assess the impact of the sealing devices on local complications, studies without control groups were excluded. The hemostasis success rates immediately after deployment seemed to be higher for HPCD, but at 2′ to 5′ after sheath removal, they were in the same range for VHD and HPCD. In controlled studies minor local complications occurred at a rate of 7.6% in the VHD group and in 6.7% of the HPCD group. Because the control group in the HPCD studies showed a considerably higher rate of minor complications than the VHD group (11.7% vs 5.7%), the reduction in minor complications was statistically significant for HPCD, whereas VHD did not reduce minor local complications. Major local complications were reported in 3.8% of the VHD group but in only 1.8% of the HPCD group. The increase of major local complications was statistically significant with VHD (control, 1.7%) but not with HPCD (control, 1.4%). Our analysis shows that some differences between collagen devices may exist, but neither device has been proven to reduce major local complications. (Am Heart J 1998;135:152-6.)

Since the first clinical study regarding sealing of arterial puncture sites with collagen with the use of the vascular hemostatic device (VHD) in 1991[1] and the hemostatic puncture closing device (HPCD) in 1992,[2] many controlled and uncontrolled studies have been reported. Because there has been no published overview summarizing and analyzing these results, it is the purpose of this article to review these data and to provide an analysis of the hemostasis success rates and of local complication rates for patients undergoing cardiac catheterizations.

Methods

Selection of reviewed literature and statistical analysis

Full articles dating as far back as 1990 were searched with the Medline service. In addition, abstracts were included if presented at one of the following scientific sessions and published in a supplement of a Medline-listed journal: Annual Meeting of the American Heart Association, American College of Cardiology, European Society of Cardiology, and German Society of Cardiology. Articles published in journals not listed in Medline and abstracts presented at other regional meetings were not accessible and therefore were not analyzed. After the data were carefully reviewed, the mean values provided for local complications were based on a weighted average, taking into account the number of patients enrolled in each individual study. Statistical analysis was performed with the chi-squared test. A p value <0.5 was considered significant.

Hemostasis success rate

The hemostasis success rate reveals the percentage of patients showing *complete* hemostasis at a specified point of time. The shorter the time interval defined was, the lower the success rate was. Thus in addition to sheath size and level of anticoagulation, when the results for hemostasis success rates are compared, possible differences of the time points at which the success rate was measured must be considered.

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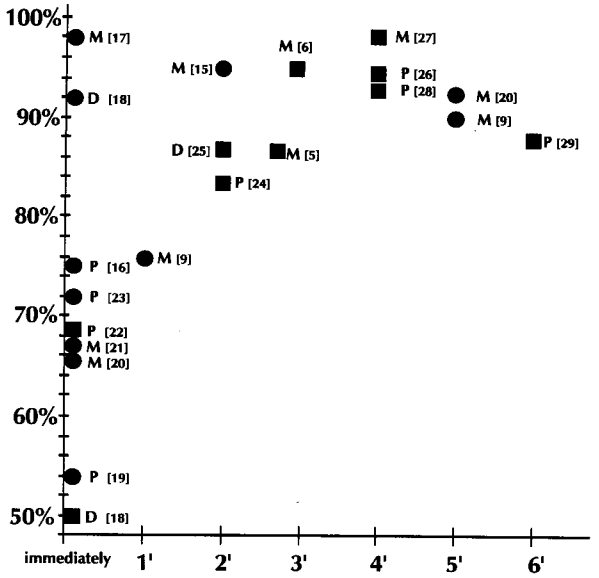
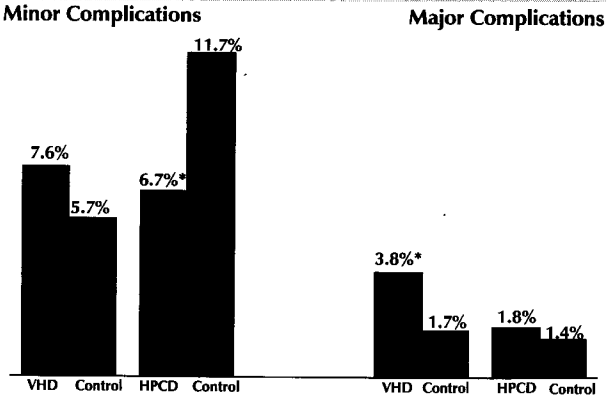
Figure 1



Hemostasis success rates at specified time intervals with VHD *(solid squares)* or HPCD *(solid circles)* in diagnostic patients *(D)*, patients who underwent percutaneous transluminal coronary angioplasty *(P)*, or mixed-patient groups *(M)*. Numbers in brackets represent reference numbers.

Figure 2



Rates on minor or major local complications with VHD or HPCD in controlled studies (*$p < 0.05$).

Classification of local vascular complications and its likelihood of bias

Local vascular complications are usually described as minor or major. These terms, however, are not generally defined and therefore are used in different ways; for example, a pseudoaneurysm was not always classified as a major complication but rather only if ultrasound-guided therapy did not help and vascular surgery was needed.[3,4] In addition, there is no generally accepted definition for the sizing of hematomas; some authors used a classification with two sizes (2 to 6 cm and >6 cm^3), whereas others specified three sizes such as mild (<2 cm), moderate (2 to 6 cm), and severe (>6 cm^4[4,5]). Others defined a small hematoma as <5 cm^6[6,7] or even <6 cm.[8] Therefore a small hematoma in one study may parallel a medium-sized hematoma in another study. Furthermore slight bleeding after device deployment was not even mentioned in some studies, whereas others reported any bleeding, even slight, as a minor complication.[9] Some authors did not consider a hematoma of <6 cm as a complication.[10] Most studies did not differentiate between a hematoma in its strict sense, defined as "palpable mass," and ecchymosis as subcutaneous blood without a palpable mass.[9] Obviously, the classification of bleeding strength and measurements of hematoma size may be a matter of substantial bias.

To rule out at least the problem of using various definitions, the terms "minor" and "major" local complications were used in this analysis according to the definitions applied in the U.S. multicenter trial.[3] The following complications were classified as major: thrombosis or loss of distal pulses, large pseudoaneurysm or arteriovenous fistula, and bleeding with need for transfusion or vascular surgery. Bleeding from puncture site not needing transfusion or vascular surgery and a small pseudoaneurysm treated medically were classified as minor complications. Therefore, for example, a bleeding complication classified as "major" by the investigators may have been reclassified in this analysis as "minor," if there was no need for transfusion, vascular surgery, or both.

Collagen devices

The vast majority of clinical experience has been gained with bovine collagen devices; the prototype was the VHD (VasoSeal, Datascope Corp., Montvale, N.J.), a pure collagen plug device, followed by the HPCD (Angio-Seal, originally developed by the Kensey Nash Corporation, Exton, Pa., now a trademark of Quinton Instrument Company, Bothell, Wash., within the United States, and of Sherwood Davis & Geck, St. Louis, Mo., outside the United States). The basis of VHD and HPCD is collagen. Purified bovine collagen has been used in vascular, abdominal, and dental surgical procedures since late 1960 as an adjunct to hemostasis when control of bleeding by ligature or other conventional methods has been insufficient.[11-13] The biodegradable collagen plug induces platelet activation and aggregation, releasing coagulation factors and resulting in the formation of fibrin and the subsequent generation of a thrombus.[14] The VHD consists of a purified collagen plug that induces the formation of a hemostatic cap directly over the arterial puncture site when inserted adjacent to the arterial wall. The method of its deployment is described in detail elsewhere.[3,5] In contrast, the HPCD provides a mechanical block of the arterial puncture

Table I. Disclosure of individual studies reporting local complications after using VHD or HPCD in diagnostic patients (*D*), patients who underwent percutaneous transluminal coronary angioplasty (*P*), or mixed-patient groups (*M*).

			Device group			Control group		
First author	**Reference**	**Patients investigated**	**No. of patients**	**Minor complications**	**Major complications**	**No. of patients**	**Minor complications**	**Major complications**
VHD								
Camenzind	26	P	62	4	6	62	0	4
Gwechenberger	10	M	33	5	0	29	4	1
Kiemenej	32	P	18	2	1	17	3	0
Legrand	30	P	120	10	3	120	4	0
Lehmkuhl	33	D	25	6	0	25	0	0
Nagtegaal	31	P	80	5	1	100	9	4
Sanborn	3	D	90	2	0	75	1	0
Sanborn	3	P	156	7	2	134	4	1
Schräder	27	M	50	0	0	50	6	0
Silber	24	P	74	4	1	76	3	0
Slaughter	4	P	51	4	0	50	0	0
v. Hoch	29	P	154	20	21	155	17	5
			913	69	35	893	51	15
HPCD								
Chevalier	21	M	52	4	0	48	11	0
Condon	34	D	31	1	0	18	1	0
de Swart	36	M	55	4	0	54	3	0
Kussmaul	9	D	168	9	6	152	17	4
Kussmaul	9	P	46	6	1	63	16	1
Murray	35	M	95	6	1	92	2	1
			447	30	8	427	50	6

site with an anchor from inside the artery, guiding and holding the collagen in the tract. Its technique of deployment has also been described elsewhere.[9,15]

Results

Reports on a total of 6007 patients were found to be published in controlled and uncontrolled studies with VHD (4448 patients) and HPCD (1559 patients).

Hemostasis success rates

The results of reports comprising diagnostic and therapeutic cardiac catheterizations and a mixture of both are depicted in Fig. 1. Immediately after deployment, the reported hemostasis success rates for HPCD seem to be higher than those reported for VHD, although some overlap is evident (Fig. 1). At 2' to 5' after sheath removal, the hemostasis success rates are in the same range for VHD and HPCD (Fig. 1). One group reported the hemostasis success rate for VHD to be 100% after 1 hour.[7] Only one study directly compared VHD with HPCD in diagnostic patients, finding a statistically significant difference.[18]

Local complications

Of the 4448 patients enrolled in VHD studies, only 1806 participated in a controlled protocol. In the HPCD studies only 874 of the 1559 published patients were enrolled according to a controlled protocol. The detailed results for minor and major local complications after the deployment of VHD or HPCD compared with those of their control groups are listed in Table I. Obviously, the number of patients who underwent percutaneous transluminal coronary angioplasty and who were investigated with VHD is much larger than that with HPCD; there is no study directly comparing VHD and HPCD in patients who have undergone percutaneous transluminal coronary angioplasty. The overall results from Table I are depicted in Fig. 2. Whereas VHD did not influence the rate of minor local complications, a statistically significant increase in major complications was seen with VHD (1.7% vs 3.8%). For HPCD the results were different. This device significantly reduced the minor local complication rate from 11.7% to 6.7% without affecting the rate of major complications (1.4% vs 1.8%).

One of the possible reasons for an increased risk of major complications with VHD is the inadvertent intraarterial placement; total or partial intraarterial insertions of VHD have been reported in the range from 0.3% to 2.0% with a mean value of 0.7%.[3,6,22,26,29,37-39] It is interesting that no intraarterial placement of the collagen with HPCD has been reported. Once either VDH or

HPCD has been successfully deployed and effective hemostasis achieved, no long-term complications have been reported. Reaccessing the vessels has never been a relevant problem.

Conclusions

The present data analysis revealed that VHD and HPCD show comparable success rates for hemostasis. However, some differences may exist regarding local complications. Neither device has been shown to reduce major local complications. Prospective trials directly comparing VHD and HPCD in patients who undergo percutaneous transluminal coronary angioplasty and addressing the cost-effectiveness of arterial closure devices are necessary.

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