ORIGINAL CONTRIBUTION

Intraprocedural Outcomes Following Distal Lower Extremity Embolization in Patients Undergoing Peripheral Percutaneous Interventions

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Abstract

Distal embolization (DE) commonly occurs during peripheral percutaneous interventions (PPI). It is unknown how "significant" distal embolization requiring further pharmacologic and/or mechanical therapy affects intraprocedural variables, including procedure length, contrast use, and radiation exposure. Eighteen patients who experienced "significant" DE were compared to 38 patients who underwent PPI and experienced no DE requiring further therapy. Demographic and clinical variables were well matched. Partial correlation analysis was conducted with multiple procedural variables as controls. The following procedural variables correlated positively with "significant" distal embolization: more contrast use (P = 0.001) and longer procedural (P = 0.003) and fluoroscopy times (P = 0.001). We conclude that DE adversely prolongs the procedural time of a PPI and requires the use of more contrast and fluoroscopy.

Introduction

Distal embolization (DE) has been documented during the treatment of all vascular beds, including the coronaries,[1] vein grafts[2,3] carotids,[4,5] renals,[6,7] and in the lower extremities.[8,9] DE in the lower extremities has been reported in patients with totally or subtotally occluded vessels, in moderately or severely calcified, long and irregular lesions, or in the presence of intravascular filling defect. Furthermore, patients undergoing rheolytic thrombectomy with or without thrombolysis and those treated with SilverHawk atherectomy (*ev3, Plymouth, Minnesota*) have been shown to experience significant lower extremity DE.[9–14] In the recently completed PROTECT registry (Preventing lower extremity distal embolization using embolic filter protection),[9] significant atheroembolization was seen in 45% of all patients treated with peripheral percutaneous interventions (PPI) captured in a distal embolic filter.

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It is unclear how macroembolization leading to distal vessel occlusion or slow flow, and requiring further pharmacologic and/or mechanical therapy, influences intraprocedural and clinical outcomes. In this study we assess the impact of DE on procedural time, contrast utilization, and fluoroscopic use. Hospital length and overall major adverse events (MAE) are also reported.

Methods

In-hospital demographics, clinical and procedural variables were prospectively collected on 677 patients undergoing PPI at 2 medical centers using web-based, electronic case report forms. Data from patients who have experienced distal embolization requiring further pharmacologic and/or mechanical therapy ("significant DE") were retrospectively reviewed from this main registry. Eighteen patients (2.6%) were identified and compared to 38 control patients with no significant DE. These control patients were previously enrolled in the PROTECT registry designed to assess the frequency of DE during PPI and the feasibility of embolic filter protection in capturing it.[9] These patients were specifically selected because they were thoroughly evaluated using digital subtraction angiography for the presence or absence of DE as part of their enrollment in PROTECT and had similar demographic, clinical, and procedural variables collected.

Patients were divided into 2 groups:

a. Those who have experienced lower extremity DE that required further treatment as per operator judgment ("significant DE") (group 1, n = 18)
b. Control patients that did not experience DE (group 2, n = 38).

The primary endpoints of the study were:

1. Contrast use (cc);
2. Total fluoroscopy time (minutes);
3. Length of procedure (minutes) defined from the start of sheath insertion in the groin to end of procedure as declared by the physician in the lab;
4. Hospital stay counted in days with each day defined as an overnight stay.

Furthermore, the combined rate of clinical MAE of death, unplanned amputation, unplanned urgent revascularization, acute renal failure, and blood loss requiring transfusions are also reported.

Table 1. Demographic and clinical variables between patients with DE versus no DE.

	DE—No (n = 38)	DE—Yes (n = 18)	*P* value
Demographic variables			
Age (years)	71.34 ± 11.58	69.4 ± 11.07	NS
BMI	27.81 ± 5.97	28.01 ± 4.06	NS
Male (%)	57.9	47.4	NS
Smoker (%)			
Never	44.1	42.9	NS
Past	29.4	35.7	
Current	26.5	21.4	
Clinical Variables			
Rutherford Class (%)			NS
II	5.6	0	
III	72.2	61.1	
IV	5.6	11.1	
V	16.7	27.8	
Prior peripheral angioplasty (%)	63.9	64.3	NS
Prior carotid endarterectomy (%)	5.6	14.3	NS
Prior Amputation (%)	8.3	0	NS
Premature CAD (%)	55.9	21.4	0.054
Family history of premature CAD (%)	11.8	21.4	NS
History of renal insufficiency (%)	26.5	28.6	NS
Hisotry of CVD (%)	11.8	21.4	NS
Hypertension (%)	73.5	78.6	NS
Hypercholesterolemia (%)	82.4	85.7	NS
Diabetic (%)	47.1	64.3	NS

DE = distal embolization; BMI = body mass index;
CAD = coronary artery disease; CVD=cerebrovascular disease.

Data were audited by an independent clinical research monitor. Statistical analysis was performed by an experienced biostatistician. Since this was a pilot exploratory study, no predefined statistical assumptions were made. Descriptive analysis was performed on all variables. Univariate analysis between the 2 groups was performed. Continuous variables were compared using t-testing and dichotomous variables using chi-square (or Fisher exact) testing. The relationship between the endpoints of contrast use, hospital days, fluoroscopy time, and procedure length and DE was assessed using partial correlation analysis. Partial correlation analysis was performed to allow for the control of alternative antecedent variables that might affect the dependent endpoints in this study. The Partial correlation analysis was conducted with the following control variables: lesion diameter, TASC-D lesions, *de novo* lesions, total occlusions, below knee, thrombus in vessel, number of successfully treated vessels, device (PTA and PTA with stent versus SilverHawk and Excimer [*Spectranetics, Colorado Springs, Colorado*] laser), gender, and age.

Results

Demographic and clinical variables are presented in Table 1 and appear to be well matched for age, gender, smoking, Rutherford-Baker class, and comorbidities between the 2 groups. Table 2 illustrates, however, significant differences between the 2 groups in the procedural and angiographic variables. Patients with clinically significant DE had more total occlusions (60.9% vs 25.5%, $P = 0.001$), TASC-D lesions (54.5% vs 22.2%, $P = 0.001$), intraluminal thrombus (42.2% vs 5.6%, $P = 0.001$), and below the knee lesions (45.5% vs 5.6%, $P = 0.001$). Also, Gp IIb/IIIa inhibitors were more often used, generally as a bail-out therapy in the group that had significant DE (50% vs 2.9%, $P = 0.001$). Patients who experienced significant DE had fewer vessels treated successfully and a reduced TIMI-flow pre- and postprocedure compared to the group with no significant DE.

Using partial correlation analysis to control for these significant procedural differences between the two groups, a higher contrast use ($P = 0.001$), and longer procedure ($P = 0.003$), and fluoroscopy times ($P = 0.001$) but not hospital stay did independently correlate with significant DE.

MAE did not occur in patients with no significant DE. Also, in patients with significant DE, there was no amputation or death. One patient with DE, however, experienced a wire perforation in the posterior tibialis artery and bivalirudin was stopped. He subsequently had an acute closure of a treated peroneal vessel. Another patient experienced an acute closure of the common femoral artery at the site of a closure device placement which was not related to DE.

Table 2. Procedural variables between patients with DE versus no DE.

	DE—No (n = 38)	DE—Yes (n = 18)	*P* value
Procedural Variables			
Run off vessels-right	1.79 ± 1.08	1.92 ± 0.95	NS
Run off vessels-left	1.63 ± 1.10	1.67 ± 1.11	NS
Vessels treated	2.11 ± 1.18	2.61 ± 1.46	NS
Pre treatment stenosis (%)	86.61 ± 14.55	91.84 ± 13.97	0.073
Post treatment stenosis (%)	7.59 ± 9.4	11.33 ± 12.63	0.095
lesion length (mm)	117.87 ± 94.55	137.39 ± 127.20	NS
Lesion diameter (mm)	5.26 ± 0.73	4.58 ± 1.55	0.01
Presence of calcium in vessels (%)			NS
None	18.5	15.9	
Little	37	47.7	
Medium	33.3	20.5	
Severe	11.1	15.9	
Lesion across joint (%)	20.4	22.7	NS
Acuity of total occlusions (%)*			NS
Acute/subacute	14.3	42.9	
Chronic	85.7	57.1	
Intraprocedural base anticoagulant (%)			NS
Heparin	8.8	5.6	
Bivalirudin	91.2	94.4	
Devices used (%)			
PTA	20	30.6	NS
PTA/Stent	58.2	55.1	NS
SilverHawk atherectomy (ev3)	21.8	14.3	NS
Excimer laser (Spectranetics)	7.3	26.5	0.015
TASC lesions (%)**			0.001
TASC A-C	77.8	45.5	
TASC D	22.2	54.5	
Total occlusions (%)**			0.001
No	74.5	39.1	
Yes	25.5	60.9	
Below-knee treatment (%)	5.6	45.5	0.001
Thrombus in vessel (%)	5.6	42.2	0.001
GpIIb/IIIa inhibitors use (%)			0.001
Eptifibatide/Abciximab	2.9	50	
None	97.1	50	
Mean number of vessels successfully treated	2.08 ± 1.17	1.11 ± 0.47	0.001
Pre-TIMI flow	2.13 ± 1.24	1.25 ± 1.33	0.001
Post-TIMI flow	2.98 ± 0.14	2.77 ± 0.42	0.003

** patient number is denominator, ** vessel number is denominator*

Discussion

Although lower extremity DE occurs at a very high rate during PPI,[6–11] "significant" DE requiring additional treatment appears to be in the 2.5% range, as seen in our registry. In this study, we defined "significant" DE as embolization requiring further intraprocedural treatment by the operator. This definition has its limitations because of the differences in threshold that operators might have in treating lower extremity DE. A standardized algorithm to when DE should be treated during PPI is currently not available. Furthermore, DE could go unnoticed by the operator if not critically examined for by digital subtraction angiography. Therefore, an underestimation of the actual rate of DE could have occurred in our study.

In this study, "significant" DE in the lower extremity appears to correlate with more radiation exposure to patients and operator, longer procedure times, and a higher contrast use. This finding was not surprising, as mechanical means[15] used to treat DE are time consuming and therefore are expected to prolong procedure and fluoroscopy times and lead to more contrast use, which have significant implications to operators and patients. It is not clear, however, whether these intraprocedural differences may have also been partly the result of more complex angiographic disease seen in the group with significant DE despite our attempt to adjust for these differences statistically. Our data need to be confirmed in a large multicenter cohort of patients undergoing PPI in order to capture a larger number of patients that experience "significant" DE.

In this study, hospital stay does not seem to be statistically affected by DE. Also, the complications that have occurred in the group of patients with DE were likely operator related (wire perforation) and closure device-related, but the small number of patients precludes a definite conclusion. The long-term outcomes of untreated DE are unknown, and long-term longitudinal studies are also needed to determine its consequences.

Table 3. Endpoints by distal embolization partial correlations.

	DE—No (n = 38)	DE—Yes (n = 18)	Partial r	*P*
Contrast use (cc)	246.46 ± 119.13	316.11 ± 162.88	0.49	0.001
Hospital stay (days)	1.03 ± 0.16	1.26 ± 0.75	0.28	NS
Fluoroscopy time (minutes)	21.58 ± 10.44	38.71 ± 20.72	0.52	0.001
Procedure length (minutes)	70.16 ± 27.00	120.94 ± 74.61	0.43	0.003

DE = distal embolization

In our lab, we have adopted the off-label use of embolic filter protection in patients that appear at high risk of DE, particularly in thrombotic lesions, long occlusions, and TASC D lesions undergoing a combined pharmacologic and/or mechanical treatment[12] and in the setting of SilverHawk atherectomy where the rate of DE appears to be high.[9] The cost-effectiveness of this approach is unknown and can best be answered from large randomized studies in high-risk patients with and without embolic filter use.

We conclude that DE judged by the operator as "significant" requiring further treatment is relatively small (approximately 2.5%), but might lead to a higher contrast and fluoroscopy use and longer procedure times. The overall short- and long-term clinical impact of these "significant" DE is unclear and needs to be further defined in a large cohort of patients undergoing PPI, where a larger number of patients with "significant" DE can be captured.

References

1. Limbruno U, De Carlo M, Pistolesi S, et al. Distal embolization during primary angioplasty: Histopathologic features and predictability. *Am Heart J* 2005;150:102–108.
2. Kolansky DM, Shah AJ, Mannion T, et al. FilterWire distal embolic protection device for vein graft stenting: Initial single-center experience. *Clin Cardiol* 2005;28:556–560.
3. van Gaal WJ, Choudhury RP, Porto I, et al. Prediction of distal embolization during percutaneous coronary intervention in saphenous vein grafts. *Am J Cardiol* 2007;99:603–606.
4. Casserly IP, Abou-Chebl A, Fathi RB, et al. Slow-flow phenomenon during carotid artery intervention with embolic protection devices: Predictors and clinical outcome. *J Am Coll Cardiol* 2005;46:1466–1472.
5. Hellings WE, Ackerstaff RG, Pasterkamp G, et al. The carotid atherosclerotic plaque and microembolization during carotid stenting. *J Cardiovasc Surg (Torino)* 2006;47:115–126.
6. Edwards MS, Craven BL, Stafford J, et al. Distal embolic protection during renal artery angioplasty and stenting. *J Vasc Surg* 2006;44:128–135.
7. Henry M, Klonaris C, Henry I, et al. Protected renal stenting with the PercuSurge GuardWire device: A pilot study. *J Endovasc Ther* 2001;8:227–237.
8. Karnabatidis D, Katsanos K, Kagadis GC, et al. Distal embolism during percutaneous revascularization of infra-aortic arterial occlusive disease: An underestimated phenomenon. *J Endovasc Ther* 2006;13:269–280.
9. Shammas NW, Dippel EJ, Coiner D, et al. Preventing lower extremity distal embolization using embolic filter protection: Results of the PROTECT Registry. *J Endovasc Ther* 2008;15:270–276.
10. Suri R, Wholey MH, Postoak D, et al. Distal embolic protection during femoropopliteal atherectomy. *Catheter Cardiovasc Interv* 2006;67:417–422.
11. Wholey MH, Toursarkissian B, Postoak D, et al. Early experience in the application of distal protection devices in treatment of peripheral vascular disease of the lower extremities. *Catheter Cardiovasc Interv* 2005;64:227–235.
12. Shammas NW, Dippel EJ, Gayton L, et al. Safety and effectiveness of the Power-Pulse spray and rheolytic thrombectomy in treating patients with recent onset of claudication and limb ischemia. *J Endovasc Ther* 2008 (In print).
13. Kasirajan K, Haskal ZJ, Ouriel K. The use of mechanical thrombectomy devices in the management of acute peripheral arterial occlusive disease. *J Vasc Interv Radiol* 2001;12:405–411.
14. Siablis D, Karnabatidis D, Katsanos K, et al. Outflow protection filters during percutaneous recanalization of lower extremities' arterial occlusions: A pilot study. *Eur J Radiol* 2005;55:243–249.
15. Shammas NW. Embolization in lower extremity percutaneous interventions: Recommendations and strategies for embolic filter protection use. *Vascular Disease Management* 2008;5:22–26.
16. Shammas NW, Dippel EJ, Shammas GA, et al. Utilization of GpIIb/IIIa inhibitors in peripheral percutaneous interventions: Current applications and in-hospital outcomes in a tertiary referral center. *J Invasive Cardiol* 2008;20:266–269.