Clinical and economic outcomes in thrombolytic treatment of peripheral arterial occlusive disease and deep venous thrombosis

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Purpose: **Over the past 2 decades the use of thrombolytic therapy in the management of peripheral occlusive diseases, most notably peripheral arterial occlusion (PAO) and deep venous thrombosis (DVT), has become an accepted and potentially preferable alternative to surgery. We examined the period when urokinase was in short supply and subsequently unavailable, to explore potential differences in clinical outcome and economic effect between urokinase and recombinant tissue plasminogen activator (rt-PA).**

Material and methods: **Data were obtained from the Premier Perspective Database, a broad clinical database that contains information on inpatient medical practices and resource use. The study population included all patients hospitalized in 1999 and 2000 with a primary or secondary diagnosis of PAO or DVT. Incidence was calculated for common adverse events, including bleeding complications, intracranial hemorrhage, amputation, and death. Cost data were also abstracted from the database, and are expressed as mean ± SD.**

Results: **Demographic variables were similar in the urokinase and rt-PA groups. The rate of bleeding complications was similar in the urokinase and rt-PA groups. There were no intracranial hemorrhages in the urokinase group, compared with a rate of 1.5% in the rt-PA PAO group ($P = .087$) and 1.9% in the rt-PA DVT group ($P = .175$). The in-hospital mortality rate was lower in the urokinase-treated PAO subgroup (3.6% vs 8.5%; $P = .026$), but a similar finding in the DVT subgroup did not achieve statistical significance (4% vs 9.8%; $P = .069$). While pharmacy costs were greater in the urokinase-treated group ($5472 ± $5579 vs $3644 ± $6009, $P < .001$; PAO subgroup, $11,070 ± $15,409 vs $6150 ± $12,398, $P = .003$), overall hospital costs did not differ significantly between the 2 groups. This finding appears to be explained by a shorter hospital stay and reduced room and board costs in the urokinase-treated group.**

Conclusion: **There were significant differences in outcome in patients with PAO and DVT who received treatment with urokinase and rt-PA. While pharmacy costs were significantly greater when urokinase was used, reduction in length of stay accounted for similar total hospital costs compared with rt-PA. These findings must be considered in the context of the retrospective nature of the analysis and the potential to use dosing regimens that differ from those in this study. (J Vasc Surg 2004;40:971-7.)**

Thrombolytic therapy has been used in patients with peripheral arterial occlusion (PAO) and deep venous thrombosis (DVT) to recanalize the occluded vascular segment. While there exist several available thrombolytic agents, urokinase emerged as the cornerstone thrombolytic agent for management of acute limb ischemia.[1,2] In early 1999 Abbott Laboratories temporarily suspended production of Abbokinase to focus on issues raised by the United States Food and Drug Administration during a 1998 inspection of the Abbokinase manufacturing process.[3] Its withdrawal left clinicians with thrombolytic alternatives with which they were considerably less familiar and for which dosing regimens and delivery techniques had not been well established for noncoronary uses.[4] Subsequently physicians have been investigating multiple dosing protocols and various administration methods of alternative thrombolytic therapies, such as recombinant tissue plasminogen activator (rt-PA), in an attempt to find a safe and effective treatment for their patients.[5] The clinical literature suggests that this investigation with new dosing protocols remains ongoing and that no standard dosing protocol for rt-PA has been nationally established.[6]

This retrospective analysis examined health care resource use, outcomes, and costs associated with various treatments in patients with PAO or DVT between January 1999 and December 2000. Urokinase was unavailable in the United States during much of the study period. The objective of the analysis was to compare urokinase with rt-PA in the management of peripheral occlusive diseases. In addition, analyses were conducted to determine predictors of length of hospital stay and associated costs.

METHODS

Data for this study were obtained from Premier Perspective Comparative Database. Premier is a healthcare alliance collectively owned by more than 200 independent hospitals and healthcare systems in the United States. Pre-

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mier's owners include not-for-profit hospital and healthcare systems. The Premier database is a widely used source for severity-specific data, and has been used with a Center for Medicare and Medicaid Services Hospital Quality Incentive Demonstration Project.[7-9] Data collection was paid for by Abbott Laboratories, independently collected by Premier, and independently analyzed by us. Data were submitted quarterly by 199 participating hospitals. Each hospital provided service level information by hospitalization day, including detailed data on medications dispensed, such as name, dosage, and unit cost. Other information collected included patient primary and secondary diagnoses, primary and secondary procedures, payer, incidence of complications, length of stay, and cost of care by cost accounting department.

Inclusion and exclusion criteria. The study population included all patients hospitalized between January 1, 1999, and December 31, 2000, with a primary or secondary diagnosis of PAO or DVT, using the 3M Health Information System All Patient Refined DRG software (3M APR-DRG).[10,11] Patients who were readmitted with the same principal diagnosis to the same hospital or health system within 30 days were also included. Patients who received more than 1 type of thrombolytic during their hospitalization, while rare, were excluded from study.

Statistical analysis. Patients were categorized according to treatment and severity of disease. Patients given urokinase or rt-PA either solely or before surgery were categorized into respective urokinase or rt-PA groups. Patients were also categorized according to severity of illness, as defined by 3M APR-DRG classification of severity based on secondary diagnoses, interaction of secondary diagnoses, age, principal diagnosis, and presence of certain nonoperative procedures. Within each APR-DRG, patients were categorized into 4 disease severity levels that explain resource use (1 = mild, 2 = moderate, 3 = major, 4 = severe).[10]

Data are separately presented for the PAO group and the DVT subgroups. Incidence and means are presented for hospital and patient characteristics. Information on hospital characteristics was obtained from the 1999 American Hospital Association Annual Survey. Incidence was calculated for common adverse events, including bleeding complications, intracranial hemorrhage, amputation, and death. Data were not available to differentiate major and minor bleeding complications other than intracranial hemorrhage. Means were determined for hospital length of stay and total costs. Length of stay was calculated by summing the number of days from admission to discharge. The total hospital costs included room and board, and all services or medications received during the hospitalization. All services were assigned an allocated fixed and variable cost, which reflected different cost structures based on hospital size, teaching status, region, and relative wages paid to employees. The statistical methods used included the χ^2 test and the Fisher exact test for differences in proportions, and the *t* test for differences in means. Data are presented as mean ± SD unless otherwise indicated. *P* values were considered significant when the 2-sided value was $<.05$.

RESULTS

Hospital characteristics. Overall, 20,275 hospitalizations from 199 hospitals were identified during the study period. A total of 7172 patients (35.37%) were identified with either PAO (n = 5717, 28.20%) or DVT (n = 1455, 7.18%). Of these patients, 1460 (20.4%) received a thrombolytic agent, including urokinas in 289 patients (19.8%) and rt-PA in 1171 patients (80.2%). Most of these admissions originated from hospitals in the southern (57.6%) and midwestern (22.3%) regions of the United States. For hospitalizations identified in the PAO and DVT study groups, most occurred in nonteaching hospitals (80.6%) in urban settings (88.2%) with a minimum of 200 beds.

Patient demographic data. Demographic data for the study population are presented in Table I. There were no differences in age or gender in the urokinase or rt-PA treatment groups. There were no significant intragroup differences in the types of hospitals (teaching or nonteaching) or the location of the hospitals by geographic region. Patients in the urokinase-treated group were, however, more often covered by Medicare (PAO subgroup only), and were more frequently from an urban hospital (DVT subgroup only). Of importance, severity of illness appeared higher in the rt-PA–treated DVT subgroup, with a greater incidence of the higher level APR-DRG categories.

Event rates. Rates for key events associated with PAO and DVT, and use of thrombolytic agents are presented in Table II.The mortality rate was significantly lower in the urokinase-treated group with PAO (3.6% vs 8.5%; $P = .026$). Intracranial hemorrhage was not reported in any of 192 patients with PAO who received urokinase, but did occur in 8 of 529 patients (1.5%) in the rt-PA group, a difference that did not attain statistical significance ($P = .087$). None of the 97 patients with DVT patients who received urokinase had an intracranial hemorrhage, compared with 12 of 642 patients (1.9%) in the rt-PA group, a difference not statistically significant ($P = .175$). There were no differences in rate of amputation in the urokinase or rt-PA treatment groups with PAO or DVT. The rate of readmission within 30 days was significantly higher in the urokinase-treated group with DVT, occurring in 25 of 97 patients (26%) compared with 104 of 642 patients (16.2%) who received rt-PA ($P = .021$).

Resource use and cost. Trends toward shorter length of stay in the urokinase-treated group did not attain statistical significance. Within the PAO subgroup, mean length of stay for patients given urokinase was 9.0 ± 9.8 days, compared with 10.0 ± 25.0 days in the rt-PA group ($P = .433$), and within the DVT group, mean length of stay for patients given urokinase was 11.7 ± 14.4 days, compared with 14.4 ± 19.6 days in the rt-PA group ($P = .107$) (Table III).

Mean total hospital costs are presented in Table IV. Pharmacy costs were higher in the urokinase-treated PAO and DVT subgroups ($P < .001$ and $P = .003$, respectively).

Table I. Demographic and severity of illness characteristics of patients with peripheral arterial occlusion and deep venous thrombosis, receiving urokinase or rt-PA

	PAO					*DVT*				
	Urokinase n = 192		*rt-PA n = 529*			*Urokinase n = 97*		*rt-PA n = 642*		
	n	*%*	*n*	*%*	P	*n*	*%*	*n*	*%*	P
Gender					.973					.277
Male	99	52	272	51.4		47	48	293	45.6	
Female	93	48	257	48.6		50	52	349	54.4	
APR severity level					.805					.011*
1	21	10.9	54	10.2		20	21	124	19.3	
2	90	46.9	231	43.7		44	45	193	30.1	
3	62	32.2	191	36.1		17	18	183	28.5	
4	19	9.9	53	7.4		16	16	142	22.1	
Payer source					.017*					.231
Medicare	90	46.9	290	54.8		26	27	234	36.5	
Managed care	25	13	56	10.6		17	18	93	14.5	
Other	77	40.1	183	34.6		54	56	315	49.1	
Type of hospital					.511					.886
Teaching	27	14.1	85	16.1		23	24	148	23.1	
Non-teaching	165	85.9	444	83.9		74	76	494	76.9	
Location of hospital					.106					.601
Midwest	29	15.1	116	21.9		27	28	153	23.8	
South	126	65.6	298	41.3		56	58	362	56.4	
North	6	3.1	14	2.6		4	4	39	6.1	
West	31	16.1	101	19.1		10	10	88	13.7	
Hospital setting					.107					.001*
Urban	462	87.3	176	91.7		95	98	554	86.3	
Rural	67	12.7	16	8.3		2	2	88	13.7	
Age (mean ± SD)	63 ± 16.0		63.7 ± 15.7		.915	51.5 ± 17.5		53.7 ± 18.7		.267

PAO, Peripheral arterial occlusion; *DVT,* deep venous thrombosis; *UK,* urokinase.
*Statistically significant.

Table II. Complication rates in patients with peripheralarterial occlusion and deep venous thrombosis, receiving urokinase or rt-PA

	PAO					*DVT*				
	UK n = 192		*rt-PA n = 529*			*UK n = 97*		*rt-PA n = 642*		
	n	*%*	*n*	*%*	P	*n*	*%*	*n*	*%*	P
Bleeding	9	4.7	18	3.4	.422	2	2	13	2	.981
Intracranial hemorrhage	0		8	1.5	.087	0		12	19.1	.175
Amputation	13	6.8	38	7.2	.849	1	(1%)	7	1.1	.958
Mortality	7	3.6	45	8.5	.026*	4	4	63	9.8	.069
30-day readmission	24	12.5	55	10.4	.424	25	26	104	16.2	.021*

PAO, Peripheral arterial occlusion; *DVT,* deep venous thrombosis; *UK,* urokinase.
*Statistically significant.

Nevertheless, the total cost of hospitalization was similar, irrespective of the thrombolytic agent used. This observation may relate to a relatively shorter length of stay in the urokinase group, accounting for reduced room and board expenses ($P = .128$ and $P = .014$ in the PAO and DVT subgroups, respectively).

Length of stay predictors. In the PAO group, longer length of stay was associated with greater severity of illness, increased use of low molecular weight heparin (LMWH), urban hospitals, hospitals in the southern region, emergent admissions, and patients with Medicaid. Male sex was associated with a shorter length of stay; Medicare insurance was associated with a longer length of stay. In the DVT group, longer length of stay was associated with greater severity of illness, increased use of LMWH, urban and teaching hospitals, and hospitals in the northeast region.

Total cost predictors. In the PAO group, higher costs were associated with greater severity of illness, use of both glycoprotein IIb or glycoprotein IIIa inhibitors and LMWH, urban and teaching hospitals, hospitals in the

Table III. Length of hospital stay in patients with peripheral arterial occlusion and deep venous thrombosis (DVT), receiving urokinase or rt-PA

		Days	P
PAO	UK	9.0 ± 9.8	
	rt-PA	10.0 ± 25.0	.433
DVT	UK	11.7 ± 14.4	
	rt-PA	14.4 ± 19.6	.107

PAO, Peripheral arterial occlusion; *DVT,* deep venous thrombosis; *UK,* urokinase.

western region, emergent cases, and patients with Medicaid, and, specifically in combination with surgery, thrombolytic drug use. Older age, hospitals with fewer beds, hospitals in the mortheast region, and patients with HMO insurance were predictive of lower costs. Within the DVT group, higher costs were associated with greater severity of illness, increased LMWH use, urban and teaching hospitals, hospitals in the northeast region, and, specifically relative to surgery, the use of urokinase. Somewhat of a surprise, older age was associated with lower costs.

Analysis of the pharmacy cost component of total costs indicated that the wholesale acquisition cost in 1998 to treat PAO and DVT combined with urokinase ($2068) and rt-PA ($1650) differed by approximately $500 per course of treatment. The costs include wasted drug, which commonly occurs when a complete vial is not used. However, additional costs allocated to the pharmacy department differed considerably more dramatically. Mean pharmacy cost for urokinase versus rt-PA was $8000 and $5153, respectively. Mean contribution to total hospital cost of selected services associated with hospitalization are detailed in Table IV. For example, in this study, the pharmacy total contribution to hospital costs was 32% for urokinase compared with 22% for rt-PA. There was inadequate detail in the database (eg, infusion rate, partial vial use) to explain this difference in pharmacy cost.

Analysis by severity of illness. A separate analysis was performed using the 4 APR-DRG categories (Tables V and VI). While the diminished sample sizes of the subgroup analysis decreased the power of the analysis, differences were particularly important in patients with DVT patients, a group with significant disparities in the frequency of APR-DRG subgroups.

DISCUSSION

The findings of this analysis indicate that conversion in clinical practice from urokinase to rt-PA for treating peripheral occlusive diseases is not without incident, as evidenced by differences in the rates of outcome variables such as mortality, hospital costs, and length of stay. Clearly, the most appropriate means to assess differences between 2 pharmacologic agents is with performance of blinded, randomized trials. Heretofore, there were only 2 prospective, randomized studies that compared urokinase with rt-PA. The first study found few differences between the agents, but was underpowered.[12] The second study, the Surgery vs Thrombolysis for Ischemic Lower Extremity trial, again failed to find significant differences between the urokinase-treated and rt-PA–treated groups. In contrast, a retrospective study published in 2002 suggested that rt-PA, while effective, was associated with excessive bleeding in contrast to historic experience with urokinase.[13] Other large retrospective studies have corroborated these findings. In a retrospective study conducted over 9 years at the Cleveland Clinic Foundation the clinical course of 653 consecutive patients treated for lower extremity vascular occlusions with catheter-directed urokinase or rt-PA was compared.[14] The authors concluded that thrombolysis with urokinase appeared safer with urokinase than with rt-PA, with a lower incidence of hemorrhagic complications. Bleeding complications have been reported to be more frequent in patients given rt-PA compared with those given urokinase, perhaps because of its more pronounced effect in lowering fibrinogen; accumulation of large amounts of fragment X, a high molecular weight clottable fibrinogen degradation product; or its higher fibrin specificity and affinity.[15-19]

While retrospective reviews of data are limited in their ability to ascribe causality to seemingly consequential events, the findings of this analysis underscore the importance of focusing on underlying issues. Since 1999 the dosage of rt-PA used to treat peripheral occlusive disease have been lowered, in part because of complications such as bleeding that were demonstrated as its clinical use expanded.[4] It was impossible to cull dosing information from the database used in the present study. Clearly, rt-PA dosage used during the period of this study were higher than those used today. Similarly, however, urokinase dosage used today is likely significantly lower than that used during the period of study, a change primarily related to the cost of the agent. Concomitant heparin therapy has also changed over the last few years. Clinicians are now less likely to use therapeutic heparinization during thrombolytic infusions, a feature common to both urokinase and rt-PA.[5] Thus, while practice changes including lower thrombolytic and heparin dosing regimens represent an inherent limitation of the present analysis, this evolution was common to both of the agents studied. Further, a recent literature review suggests that the bleeding complications are not dose-related over the range of dosages used clinically.[20] Lower dosage of rt-PA did not appear to reduce the incidence of major hemorrhage during thrombolytic therapy; there was no correlation between the incidence of complications and rt-PA dosage. This finding, while not intuitive, is similar to the failure to detect dose-related differences in the risk for bleeding with recombinant urokinase or recombinant prourokinase.[21,22] Despite these observations, however, we must caution that the observations of the present study cannot be directly applied to instances in which different regimens of administration are used.

During the study urokinase was associated with a higher acquisition cost than was rt-PA. However, there are other issues that contribute to potentially distorted cost

Table IV. Resource utilization in patients treated with urokinase or rt-PA for peripheral arterial occlusion and deep venous thrombosis

	PAO					*DVT*				
	UK		*rt-PA*			*UK*		*rt-PA*		
Component	*$*	*% of Total*	*$*	*% of Total*	P	*$*	*% of Total*	*$*	*% of Total*	P
Pharmacy	5,472 ± 5,579	28.4	3,644 ± 6,009	19.3	<.001*	11,070 ± 15,409	35.7	6,150 ± 12,398	23.9	.003*
Room & board	4,652 ± 5,434	24.2	5,719 ± 13,352	30.4	.128	5,885 ± 1,152	19.0	9,155 ± 648	35.5	.014*
Imaging	1,976 ± 1,692	10.3	2,061 ± 1,906	10.9	.586	2,307 ± 2,530	7.4	1,705 ± 1,960	6.6	.027*
Laboratory	878 ± 1,216	4.6	868 ± 1,449	4.6	.926	1,691 ± 4,567	5.5	1,393 ± 2,155	5.4	.528
Surgical	2,087 ± 4,027	10.8	1,850 ± 2,288	9.8	.440	2,103 ± 71,114	6.8	1,458 ± 4,503	5.7	.388
Central supply	1,991 ± 2,562	10.3	2,036 ± 2,623	10.8	.836	2,484 ± 4,354	8.0	2,375 ± 6,872	9.2	.833
Emergency department	108 ± 163	0.6	122 ± 158	0.6	.323	70 ± 121	0.2	117 ± 182	0.5	.001*
Other	2,074 ± 3,419	10.8	2,534 ± 8,641	13.5	.308	5,416 ± 20,771	17.5	3,407 ± 7,095	13.2	.347
Total	19,239 ± 16,066	100.0	18,833 ± 31,564	100.0	.822	31,026 ± 51,090	100.0	25,760 ± 41,358	100.0	.335

*Statistically significant.

Table V. Outcome by severity of illness (APR-DRG levels) in patients with peripheral arterial occlusion treated with urokinase or rt-PA

APR-DRG Severity		*No.*	*Bleeding* *n*	*%*	*ICH* *n*	*%*	*Mortality* *n*	*%*	*LOS*	*Amputation* *n*	*%*	*30-Day readmit* *n*	*%*	*Total hospital costs ($)*	*Pharmacy costs ($)*
1	UK	21	0		0		0		4.4 ± 2.2	0		2	10	12,376 ± 7,188	4,380 ± 6,793
	rt-PA	54	1	2	0		0		5.0 ± 2.8	0		5	9	11,994 ± 4,974	2,471 ± 1,790
	P		.53		—		—		.401	—		.972		.825	.218
2	UK	90	6	7	0		0		6.0 ± 4.2	0		13	14	14,381 ± 7,957	4,449 ± 4,352
	rt-PA	231	5	2.2	0		1	4	6.2 ± 4.3	8	3.5	23	10	13,396 ± 7,696	2,968 ± 4,280
	P		.046*		—		.532		.599	.074		.252		.308	.006*
3	UK	62	3	5	0		3	5	10.5 ± 8.5	9	15	5	8	21,294 ± 14,553	5,922 ± 4,950
	rt-PA	191	11	5.8	2	1	22	11.5	9.4 ± 7.4	20	10.5	21	11	16,534 ± 10,170	3,283 ± 3,037
	P		.783		.419		.126		.334	.385		.509		.019*	<.001*
4	UK	19	0		0		4	21	23.9 ± 19.0	4	21	4	21	43,128 ± 29,339	10,058 ± 8,533
	rt-PA	53	1	2	6	12	22	42	34.1 ± 73.3	10	18	6	11	57,789 ± 87,777	9,092 ± 14,645
	P		.547		.126		.111		.356	.836		.293		.292	.732

ICH, Intracranial hemorrhage; *LOS,* length of stay; *UK,* urokinase.
*Statistically significant.

differences. For example, higher drug acquisition cost does not always lead to higher total hospital cost, and more expensive drugs may be associated with lower total cost and length of stay. With the reintroduction of urokinase, compared with higher dosage of infusions of urokinase prevalent through 1999, lower dosage and combination therapy dosing options may come into clinical practice. Thrombolytic therapy with urokinase is clinically superior and cost effective compared with streptokinase, despite lower acquisition cost of streptokinase.[23-25]

Retrospective database analyses of the type used in this evaluation have their limitations. Causality is difficult to ascribe. In addition, statistical differences in retrospective reviews are based on the quality of the data entered into and abstracted from the database. Differences in severity of illness may not have been completely addressed by the APR-DRG subgroup analysis performed in the present study. Perhaps the greatest confounder in this evaluation, however, is the timing of the analysis. The window of time selected for the analysis intended to provide a comparison of 1998 data, before shortage and suspension of sale of urokinase in the market and the period in which the product was unavailable. Although the intent was in part to consider the effect of this event, relatively little baseline data were available to truly characterize the established use of urokinase before suspension of production. However, the clinical literature supports the safe and effective use of urokinase, and validates many of the findings in this analysis.

In summary, we observed significant differences in outcome in patients with PAO and DVT treated with urokinase and rt-PA. Mortality was lower in patients with PAO treated with urokinase. Pharmacy costs were significantly greater when urokinase was used, but reduction in length of stay accounted for similar total hospital costs compared with rt-PA. These differences between urokinase

Table VI. Outcome by severity of illness (APR-DRG levels) in patients with deep venous occlusion treated with urokinase or rt-PA

APR-DRG Severity		*No.*	*Bleeding*		*ICH*		*Mortality*		*LOS*	*30-Day readmit*		*Total hospital costs ($)*	*Pharmacy costs ($)*
			n	*%*	*n*	*%*	*n*	*%*		*n*	*%*		
1	UK	20	0		0		0		5.9 ± 3.4	4	20	13,589 ± 7,693	5,615 ± 4,790
	rt-PA	124	0		0		0		5.6 ± 3.1	18	14.5	11,122 ± 6,356	3,117 ± 3,194
	P			—		—		—	.650		.527	.120	.035*
2	UK	44	1	2	0		1	2	7.5 ± 5.3	13	30	20,824 ± 14,303	9,007 ± 7,663
	rt-PA	193	2	10	0		1	0.5	8.1 ± 5.4	36	18.7	13,726 ± 10,941	3,239 ± 3,435
	P			.508		—		.251	.547		.107	.003*	<.001*
3	UK	17	1	6	0		0		10.1 ± 5.9	4	24	21,998 ± 27,082	11,639 ± 24,662
	rt-PA	183	4	2.2	5	2.7	13	7.1	12.1 ± 8.8	32	17.5	19,302 ± 16,653	5,524 ± 12,350
	P Value			.350		.490		.256	.200		.535	.692	.327
4	UK	16		0		0	3	19	32.4 ± 25.2	4	25	63,223 ± 73,250	22,959 ± 21,686
	rt-PA	142	7	4.9	7	4.9	49	34.5	33.7 ± 33.2	18	12.7	90,460 ± 76,863	13,560 ± 20,037
	P			.364		.364		.204	.879		.177	.320	.080

ICH, Intracranial hemorrhage; *LOS*, length of stay; *UK*, urokinase.
*Statistically significant.

and rt-PA are potentially important, but a prospective randomized comparative trial is needed to validate the findings. However, the likelihood of funding for such a study appears marginal. It is important that the observations of this retrospective analysis be evaluated in the context of practice changes that have occurred over the last few years, which include lower dosing regimens for the thrombolytic agent and concomitant heparin therapy. With the relaunching of urokinase, clinicians and formulary decision makers who represent the clinical, pharmacy, and financial perspectives are obligated to consider and track not just the relative differences in drug acquisition cost, but the overall costs incurred by their hospitals.

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