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THE EFFECTIVENESS OF EMPIRIC TRANSARTERIAL GLUE EMBOLIZATION (TAGE) OF GASTRODUODENAL ARTERY (GDA) FOR BLEEDING DUODENAL ULCER: A RETROSPECTIVE STUDY

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ABSTRACT:

Purpose

To determine the efficacy of empiric transarterial glue embolization (TAGE) of gastroduodenal artery (GDA) for bleeding duodenal ulcers.

Materials and Methods

All patients treated for bleeding duodenal ulcers between June 2019 and June 2023, in a single tertiary centre (Penang General Hospital) were retrospectively identified based on interventional radiology reports. Patients with bleeding duodenal ulcers underwent empiric TAGE of GDA following endoscopic hemostasis were included.

Results

During the study period, a total of 26 patients had empiric TAGE of GDA for bleeding duodenal ulcer. A total of 25 patients with duodenal ulcers of Forrest Ia (n=5), Ib (n=12), IIa (n=4), IIb (n=3) and IIc (n=1) who successfully underwent prophylactic TAGE of GDA were included in this study. It has a high technical success rate of 96.2% (n=25). Clinical success rate amongst the 25 patients who successfully underwent empiric TAGE of GDA was 84% (n=21) with only four patients developing rebleeding and required repeated endoscopic clipping. One of the four patients succumbed secondary to refractory bleeding.

Conclusion

Empiric TAGE of gastroduodenal artery GDA can be a useful adjunct treatment option in high-risk bleeding duodenal ulcer with high technical and clinical success.

Keywords: Empiric transarterial glue embolization, gastroduodenal artery, bleeding duodenal ulcers

INTRODUCTION

Acute gastrointestinal bleeding is a common surgical emergency associated with an average mortality rate of 10% (1). Despite significant advancements in primary endoscopic and pharmacological treatments for gastrointestinal bleeding, the risk of rebleeding remains a substantial concern. Unsuccessful endoscopic interventions often necessitate surgical management. Nevertheless, in cases involving patients with multiple comorbidities and a high surgical risk profile, an angiographic approach presents an effective alternative. Angiography plays a crucial role in the diagnosis and treatment of acute gastrointestinal bleeding where the site of bleeding may be localised and be effectively treated with embolization. However, the source of upper gastrointestinal bleed is often not evident angiographically due to the intermittent nature of the bleed and the variable bleeding rate during angiography (2). Consequently, in such cases, empiric transarterial glue embolization (TAGE) may be performed in the absence of angiographic evidence of contrast extravasation. TAGE is defined as embolization without angiographic proof of contrast extravasation. In this retrospective study, we sought to evaluate the clinical outcome of empiric transarterial glue embolization of gastroduodenal artery (GDA) for patients with high-risk bleeding duodenal ulcer during the past 4 years in our centre.

MATERIALS AND METHOD

This retrospective cohort study was conducted on patients treated for bleeding duodenal ulcers between June 2019 and June 2023, in a single tertiary centre (Penang General Hospital). These patients were identified retrospectively based on interventional radiology reports. Patients with bleeding duodenal ulcers underwent empiric TAGE of GDA following endoscopic haemostasis were included. Patients with active bleeding of GDA as evidenced by contrast blush on angiogram were excluded from our study. Information was extracted from patients' medical, endoscopic and interventional radiology reports while maintaining their confidentiality. Demographics and clinical characteristics of study patients are summarised in Table 1. This study focused on exploring post empiric TAGE outcomes. Technical success of TAGE, number of patients with rebleeding, and 30-day mortality rate were recorded. Data was computed and analysed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, N.Y., USA).

Operational definitions

Technical success of TAGE is defined as complete angiographic occlusion of the suspected culprit vessel i.e. gastroduodenal artery. Technical success rate was calculated as the ratio of the number of technically successful empiric TAGE procedures to the total number of empiric TAGE. Clinical success was determined by a combination of technical success and no evidence of ongoing upper gastrointestinal bleed (as suggested by clinical, laboratory or endoscopic findings) within the first 60 days after the procedure. Clinical success rate is calculated as the ratio of the number of patients with clinically successful empiric TAGE procedures to the total number of empiric TAGE.

Operational procedure

With ultrasound guidance, the right common femoral artery was punctured with an 18G puncture needle and subsequently a 5Fr introducer sheath was inserted. Selective cannulation of celiac trunk and common hepatic artery with digital subtraction angiogram (DSA) were performed. Common diagnostic angiographic catheters utilised were 4-Fr Cobra C1 (Cordis; Miami, Florida) and Simmons Sim 1 (Cordis; Miami, Florida) catheters. Subsequently, the gastroduodenal artery was selectively cannulated with a 2.4F Renegade microcatheter from the common hepatic artery. Super-selective embolisation of branches supplying D1, D2 segments of duodenum was performed with N-butylcyanoacrylate (NBCA): Lipiodol mixture with ratio ranging from 1:2 to

1:4, with end point of achieving proximal occlusion of GDA. Post embolisation GDA angiogram was performed to assess the adequacy of embolisation.

RESULTS

Following initial endoscopic haemostasis, 26 patients were planned for TAGE of GDA. Technical and clinical success rates of angiographically negative TAGE were 96.2% and 84%. One of the patients with technical failure was due to tortuous arterial anatomy as the normal anatomy was disrupted by prior surgical repair of perforated gastric ulcer. Recurrent bleeding occurred in four (16%) patients which required further endoscopic clipping. Out of the 25 patients, 7 died within the first-30 days giving a mortality rate of 28%. The causes of death were mostly unrelated to the procedure, which include multiorgan failure (n=1), acute pulmonary embolism (n=1), severe sepsis (n=1), cerebellar stroke (n=1), no data (n=2). Only one of which died from refractory bleeding (n=1) despite surgical intervention (under-running of duodenal ulcer). We have classified our data according to high rebleeding risk (Forrest Ia), increased rebleeding risk (Forrest Ib to IIc) and low rebleeding risk (Forrest III) as proposed by a recent study to simplify Forrest classification [5]. The risk of rebleeding post embolization for each category was tabulated below.

30-day mortality rate is highest in Forrest Ia (n=2) and Ib (n=4) compared to Forrest IIa (n=1), IIb (n=1) and IIc (n=0).

DISCUSSION

Upper gastrointestinal bleed carries a significant mortality rate of 10% with peptic ulcer disease constituting majority (83.6%) of the cases in Malaysia (1,3). Common risk factors attributed to it are alcohol usage, smoking history and history of antiplatelets/ anticoagulants. Massive bleeding or refractory bleeding may lead to mortality.

However, recurrent bleeding remains an important adverse prognostic factor and contributes to morbidity and mortality. Endoscopic hemostasis and pharmacological treatments such as proton-pump inhibitors (PPI) and H2 receptor antagonists remain the mainstay treatment for bleeding peptic ulcer disease. Surgery is usually reserved for cases of massive bleeding and ulcers which are inaccessible to endoscopic control (4).

Forrest classification is widely used by endoscopists to classify peptic ulcers to identify risk of bleeding, rebleeding and mortality. Based on a recent study on reassessing the predictive value of Forrest classification for peptic ulcer rebleeding, it was found that rebleeding rates was highest for Forrest Ia (58.8%), followed by Forrest IIb (31.2%), Forrest Ib (26.0%), Forrest IIa (21.2%), Forrest IIc (15.6%) and Forrest III (6.5%) (5). In addition to that, they proposed to classify the risk of bleeding into three which are high risk of rebleeding which includes Forrest Ia, increased risk of bleeding which includes Forrest Ib-IIc and low risk of bleeding which is Forrest III ulcers (5). The results in our study show reduction in bleeding risk in both high risk and increased risk groups.

With the increased availability of interventional radiology services, empiric transarterial embolisation of gastroduodenal artery plays an important role in reducing rebleeding risk in bleeding peptic ulcer. Based on a meta-analysis evaluating 12 studies with a study population of 1329 patients, empiric transcatheter arterial embolization is associated with lower risk of rebleeding (6). In our retrospective study, the clinical success rate amongst the 25 patients with duodenal ulcers of high risk or increased risk of rebleeding (Forrest I-II) who successfully underwent empiric TAGE of GDA was 84% (n=21) with only four patients developed rebleeding and required repeated endoscopic clipping. Apart from that, GDA embolisation has a relatively high technical success rate of 70-100% with a technical success rate of 96.2% in our study.

Various embolic agents can be used in transcatheter arterial embolisation of gastroduodenal artery such as metallic coils,

polyvinyl alcohol (PVA), gelatin sponge, vascular plug and last but not least NBCA glue. In our centre, we utilise NBCA glue as our embolic agent for empiric GDA embolisation of bleeding duodenal ulcer as it is more cost effective in our settings, and it achieves faster and effective hemostasis. Based on a meta-analysis carried out by Kim et al., it demonstrates that embolisation of upper GI bleed with NBCA is associated with lower risk of rebleeding (7). Besides that, it is also effective in patients with coagulation disorder especially patients with disseminated intravascular coagulation (DIC) following massive upper gastrointestinal bleeding as the polymerization of glue does not depend on coagulation parameters of the patient (8). However, utilisation of glue as embolic material requires a steep learning curve and should be administered by experienced and skillful interventional radiologists as it may cause non-target embolisation and premature polymerization causing microcatheter blockage or retention (9). The main complication of TAGE of GDA is duodenal ischemia which may present as duodenal erosion, ulcer, necrosis in acute manner or stricture in a delayed manner (10,11).

The principal limitation of this study is the retrospective study design, which may decrease the statistical strength of the study. For instance, the difference in time between the GI bleeding and angiography, the hemodynamic parameters just prior to the angiography and presence of coagulopathy were not evaluated. Additionally, we did not compare the outcomes between surgical intervention and embolization. There was also limited data in this study regarding the complications of TAGE of GDA, and therefore not included. Besides, another limitation of this study is the small sample size which we are unable to study specifically on each population based on Forrest classification. Despite these limitations, our study remains vital in studying the clinical outcome of patients with angiographically negative bleeding duodenal ulcer post TAGE of GDA. In view of sample size limitation, further data collection and study should be focused on each group of Forrest classification to evaluate the clinical outcome of empiric TAGE with control group to avoid overtreating with empiric TAGE.

CONCLUSION

Empiric TAGE of GDA can be an effective treatment adjunct for high and increased risk bleeding duodenal ulcer with high clinical success rate and technical success rate.

CONFLICTS OF INTEREST

The authors have no potential conflicts of interest to disclose and are in agreement with the contents of the manuscript.

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TABLE LEGENDS:

Table 1: Demographics and clinical characteristics of study patients.

Sex	
Male	17 (68%)
Female	8 (32%)
Age (mean) [range]	66.12 [19-86] years
Comorbidities	
Hypertension	20 (80%)
Diabetes mellitus	13 (52%)
Dyslipidaemia	8 (32%)
Malignancy	3 (12%)
Ischaemic heart disease	4 (16%)
Liver cirrhosis	1 (4%)
Forrest classification	
Ia	5 (20%)
Ib	12 (48%)
IIa	4 (16%)
IIb	3 (12%)
IIc	1 (4%)
III	0 (0%)

Table 2: Outcomes of patients post TAGE of GDA.

Technical success	25/26 (96.2%)
Clinical outcome[a]	
Recurrent bleeding	4 (16%)
No recurrent bleeding	21 (84%)
Total 30-day mortality rate[a]	7 (28%)
Mortality due to refractory bleed	1 (4%)
Mortality due to other causes	6 (24%)
Survival at 30-day[a]	17 (68%)

[a]Only includes patients with angiographically negative technical successful TAGE of GDA.

Table 3: Number of patients with rebleeding after TAGE based on rebleeding risk (simplified Forrest classification)

Rebleeding Risk	Total number of patients, n (%)	Rebleeding Post TAGE of GDA, n (%)
High	5 (20%)	1 (20%)
Increased	20 (80%)	3 (15%)
Low	0	0

FIGURE LEGENDS:

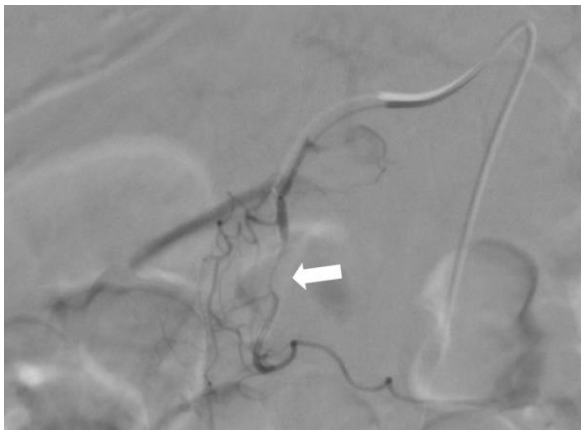

Figure 1: Selective catheterization of GDA with microcatheter demonstrating segmental spasm of GDA (arrow) which is an indirect sign of recent bleeding.

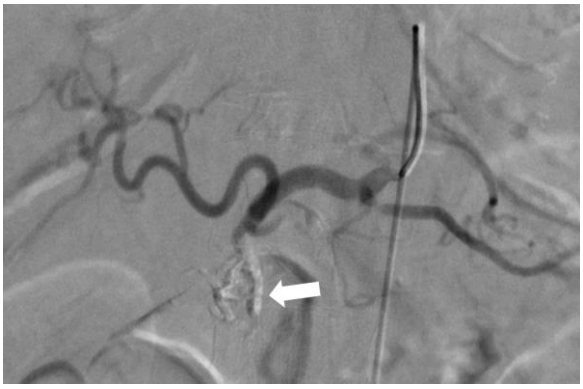

Figure 2: Post embolization angiogram demonstrates glue cast (arrow) and immediate obliteration of GDA.

ANTIPLATELETS GUIDELINES IN ENDOVASCULAR TREATMENT OF INTRACRANIAL ANEURYSMS: RECOMMENDATIONS FROM MALAYSIAN NEUROINTERVENTIONAL SOCIETY (MyNIS)

M.F.A. Kamis, I.A. Zainal; on behalf of the Malaysian Neurointerventional Society.

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INTRODUCTION

The landscape of periprocedural antiplatelet therapy has witnessed significant evolution alongside advancements in the endovascular management of intracranial aneurysms. This includes the introduction of flow-diverting stents, intracranial stents, intrasaccular devices, and stent-assisted coiling. Traditionally, a dual antiplatelet therapy (DAPT) regimen involving Aspirin and Clopidogrel has been widely adopted due to its established safety and efficacy. However, recent studies have identified alternative antiplatelet agents such as Ticagrelor, Tirofiban, or Prasugrel, which have demonstrated comparable efficacy and safety profiles. Endorsed by the Malaysian Society of Interventional Neuroradiology (MYNIS), this guideline aims to assist Interventional Neuroradiologists (INRs) and other physicians involved in treatment in selecting the most appropriate antiplatelet therapy for patients undergoing interventional procedures.

COX-1 INHIBITORS

Aspirin

Aspirin, also known as acetylsalicylic acid (ASA), functions as an irreversible inhibitor of cyclooxygenase-1 (COX-1), thereby impeding the production of thromboxane A2. Even with daily doses as low as 75 mg, Aspirin achieves complete inactivation of COX-1 within platelets due to its irreversible binding and the fact that platelets do not synthesize new proteins during their 7- to 10-day lifespan. This characteristic renders Aspirin an ideal antiplatelet agent, characterized by a stable half-life and predictable therapeutic response, particularly in preventing thromboembolism in the treatment of unruptured intracranial aneurysms. Its onset of action typically occurs within 15–30 minutes, and the plasma half-life of Aspirin is approximately 15–20 minutes.

Original trials involving intracranial flow diverters utilized daily maintenance doses ranging from 100 mg to 325 mg of Aspirin, while

a standard dosage of 325 mg per day is commonly employed for intracranial stents and flow-diverting devices. Research suggests that Aspirin may contribute to the reduction of aneurysmal degradation and inflammation of the aneurysmal wall, in addition to promoting endothelial progenitor cell mobilization. Common side effects of Aspirin administration include gastritis and ulceration attributed to its non-selective COX blockade.

$P2Y_{12}$ INHIBITORS

Clopidogrel

Clopidogrel, a thienopyridine compound, functions by irreversibly inhibiting the platelet P2Y12 adenosine diphosphate receptor, thereby reducing platelet aggregation. Additionally, it impedes platelet aggregation by other platelet agonists such as thromboxane A2 and thrombin by diminishing the amplification effect of ADP released from platelet-dense granules. With a half-life spanning 7–8 hours and an onset of action typically ranging from 2 to 4 hours, Clopidogrel is commonly administered in a loading dose of 300 to 600 mg, complemented by a daily dosage of 75 mg.

The combination of Clopidogrel with Aspirin as part of dual antiplatelet therapy (DAPT) is a widely adopted practice in endovascular aneurysm treatment. However, a major concern with Clopidogrel is its nature as a prodrug, necessitating enzymatic conversion to active metabolites for its antiplatelet effects to manifest. Consequently, loading doses are often required to achieve rapid efficacy. Various factors, including drug interactions, polymorphisms within the CYP450 enzyme family, and smoking status, can contribute to a significant proportion of individuals showing an inadequate response to Clopidogrel treatment.

Prasugrel

Prasugrel is a newer generation thienopyridine, functions by inhibiting the P2Y12 receptor and has a half-life ranging from 2 to 15 hours. In comparison to Clopidogrel, it offers a faster onset of action and increased efficacy. Prasugrel undergoes more efficient conversion to its active metabolites and exhibits reduced dependence on CYP enzymes compared to Clopidogrel. Prasugrel is primarily used for patients undergoing intracranial flow diversion, especially when Clopidogrel fails to produce an adequate response due to altered hepatic metabolism. The duration of action of Prasugrel is similar to other thienopyridines, involving irreversible binding to ADP receptors. The standard dosing regimen is a 60 mg loading dose followed by a once-daily maintenance dose of 10 mg (or 5 mg if the patient weighs less than 60 kg). Prasugrel is associated with an increased risk of major bleeding and is contraindicated in patients with acute stroke due to the increased risk of hemorrhagic transformation.

Ticagrelor

Ticagrelor is a reversible inhibitor of P2Y12 receptors, belonging to the thienopyridine class, similar to Clopidogrel and Prasugrel. It has a median onset of action of 1.3–2 hours, a half-life of 4.6–6.3 hours, and becomes undetectable in plasma after 20 hours. Unlike Clopidogrel, Ticagrelor does not require hepatic metabolism for activation, making it effective for patients with genetic resistance to Clopidogrel due to CYP2C19 enzyme alterations. Ticagrelor is considered a safe and efficacious alternative to Clopidogrel, typically administered with a

loading dose of 180 mg and a maintenance dose of 90 mg twice daily for 3–6 months.

GLYCOPROTEIN IIB/IIIA AGENTS

Tirofiban

Tirofiban, a glycoprotein IIb/IIIa receptor antagonist, binds reversibly to the GPIIb/IIIa receptor and has a plasma half-life of 2.5 hours. It is helpful in preventing platelet aggregation and thrombosis, particularly in acute ischemic stroke and during endovascular treatments. Administered intravenously, Tirofiban achieves more than 90% inhibition of ADP-induced platelet aggregation within 10–40 minutes with a 0.4 μg/kg loading infusion, followed by a maintenance infusion of 0.1 μg/kg/min. Platelet function returns to near baseline in 90% of patients within 4–8 hours after discontinuing the infusion. Similar to Eptifibatide, Tirofiban is renally cleared and requires dose adjustment in patients with impaired renal function; however, it can be effectively cleared by hemodialysis.

Eptifibatide

Eptifibatide, a cyclic heptapeptide derived from rattlesnake venom, reversibly binds to the GPIIb/IIIa receptor and has a plasma half-life of 1.5–2.5 hours. A bolus dose of 180 μg/kg achieves over 80% inhibition of platelet function within 15 minutes. An infusion of 0.5–0.75 μg/kg/min decreases platelet function after 4–6 hours, the time required to reach a steady state. This delay can be mitigated by administering a second 180 μg/kg bolus within 10 minutes after the first. Less than 50% of platelet aggregation inhibition remains 4 hours after stopping the infusion. Eptifibatide is renally cleared and requires dosage adjustment in patients with a creatinine clearance of less than 50 ml/min. It is particularly useful for proximal thrombus or in-stent occlusions during aneurysm coil embolization, with no reported hemorrhagic complications or worsening of pre-existing subarachnoid hemorrhage, although it may be less effective for distal thrombi.

CLINICAL SCENARIO

CASE 1 **Elective procedure with no intra-operative complication, e.g unruptured intracranial aneurysm for flow diverter stent placement**
Pre-procedure: Oral Aspirin 300-325mg and Clopidogrel 300-600mg given 5-7 days prior to the procedure Post-procedure: Oral Aspirin 75-100mg daily for 12 months and Clopidogrel 75mg daily for 3-6 months; *or* Oral Aspirin 75-100mg daily for 12 months and Ticagrelor 90mg BD for 3-6 months
CASE 2 **Emergency procedure with no intra-operative complication, e.g ruptured intracranial aneurysm for flow diverter stent or stent and coiling placement**
Pre-procedure: Oral Aspirin 300-325mg or IV Aspirin 500mg, and Clopidogrel 300-600mg prior to the procedure Post-procedure: Oral Aspirin 75-100mg daily for 12 months and Clopidogrel 75mg daily for 3-6 months; *or* Oral Aspirin 75-100mg daily for 12 months and Ticagrelor 90mg BD for 3-6 months

CASE 3 **Elective procedure with intra-operative thrombosis, e.g placement of flow diverter in unruptured intracranial aneurysm complicated with thrombosis.**
Pre-procedure: Oral Aspirin 300-325mg and Clopidogrel 300-600mg given 5-7 days prior to the procedure Intra-procedure: Tirofiban 12μg/kg loading infusion over 30 minutes Post-procedure: IV infusion of Tirofiban 0.1μg/kg/min for 12-24 hours; *and* Oral Aspirin 75-100mg daily for 12 months and Clopidogrel 75mg daily for 3-6 months; *or* Oral Aspirin 75-100mg daily for 12 months and Ticagrelor 90mg BD for 3-6 months

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TABLE LEGENDS:

Table 1: Summary of pharmacokinetic and pharmacodynamics of commonly used antiplatelet agents.

Antiplatelet Agents	Mechanism of action	Half-life	Onset of action	Consideration	Side effects
Aspirin	COX-1 inhibitor	15–20min in plasma	15-30min	Effect on platelets 8–10 days given irreversibility of COX inhibition	Bleeding. Gastrointestinal upset
Clopidogrel	Irreversible P2Y12 inhibitor	7-8h	2-4h	Requires hepatic metabolism, potential genetic resistance (CYP2C19 variations)	Bleeding. Marrow suppression. Thrombotic thrombocytopenic purpura
Prasugrel	Irreversible P2Y12 inhibitor	2-15h	30min	Effects last 8–10 days. Rapid onset of action due to fast conversion to active metabolites	Bleeding
Ticagrelor	Reversible P2Y12 inhibitor	4.6-6.3h	1.3-2h	Not affected by CYP polymorphisms	Bleeding. Respiratory discomfort
Tirofiban	Reversible GPIIb/IIIa receptor antagonist	2.5h	10-40min	Given IV or IA. Needs renal adjustment	Bleeding. Thrombocytopenia
Eptifibatide	Reversible GPIIb/IIIa receptor antagonist	1.5-2.5h	15min	Given IV or IA. Needs renal adjustment	Bleeding. Thrombocytopenia

Table 2: Recommended antiplatelet regimes and dosage.

Antiplatelet Agents	Dosage		Duration
	Loading	Maintenance	
Elective			
Aspirin	300-325mg	75-100mg daily	5-7 days prior, then continue minimum for 12 months
Clopidogrel	300-600mg	75mg daily	5-7 days prior, then continue for 3-6 months
Prasugrel	30-60mg	5-10mg daily	3-6 months
Ticagrelor	180mg	90mg twice daily	3-6 months
Emergency			
Aspirin	Oral: 75-325mg IV: 500mg Rectal: 120-300mg	75-100mg daily	STAT, then continue minimum for 12 months
Clopidogrel	300-600mg	75mg daily	STAT, then continue for 3-6 months
Prasugrel	30-60mg	5-10mg daily	3-6 months
Ticagrelor	180mg	90mg twice daily	3-6 months
Rescue Therapy			
Tirofiban	12μg/kg for 30 min	0.1μg/kg/min	IV or IA bolus, followed by infusion 12-24 hours
Eptifibatide	180μg/kg for 1-2 min	1-2μg/kg/min	IV or IA bolus, followed by infusion 12-24 hours