

## Intracoronary fibrinolysis: An effective yet underutilized therapeutic strategy in clinical practice

To the Editor,





Over the past years, glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitors have been mostly used as bail-out regimens in the setting of high-risk percutaneous coronary interventions (PCIs) (1). In their recently published article, Doğan et al. (2) reported a case of acute myocardial infarction (AMI) associated with bonsai use in a young male presenting with massive thrombus formation in the proximal and distal portions of the left anterior descending (LAD) artery on coronary angiogram (CAG) (2). He was managed with tirofiban (an intracoronary bolus followed by systemic infusion) on top of heparin and dual antiplatelet therapy (2). However, we strongly hold the opinion that intracoronary fibrinolysis (with or without low dose GpIIb/IIIa inhibitors) might be regarded as the first-line strategy in this case (and in other similar clinical scenarios) owing to its more substantial therapeutic benefit. Accordingly, we would like to comment on this interesting case and discuss the clinical indications of intracoronary fibrinolysis along with potential causes regarding the underuse of this effective strategy compared with GpIIb/IIIa antagonism in clinical practice.

It is well known that systemic fibrinolytic therapy has been largely replaced by primary PCI in the setting of ST-segment elevation myocardial infarction (STEMI) (1). However, intracoronary fibrinolysis still maintains its clinical significance as a particular reperfusion modality and has been mostly recommended as an adjunct to manual thrombus aspiration (MTA) and/or PCI in patients with massive intracoronary thrombus formation in an effort to enhance MTA success and also to prevent serious complications including coronary no-reflow phenomenon and stent thrombosis after coronary stenting (1). Moreover, intracoronary fibrinolysis might, per se, serve as the primary strategy in the management of non-atherosclerotic intracoronary thrombus formation associated with specific conditions including stent thrombosis, Kawasaki disease, coronary embolism, and substance abuse (cocaine, etc.) (1, 3, 4). Importantly, intracoronary thrombus formation associated with the above-mentioned conditions are generally characterized by the abundance of fibrin meshwork and trivial amount of platelet aggregates potentially making these clots more amenable to fibrinolytic therapy rather than GpIIb/IIIa antagonism (1). In previous studies, fibrinolytics, including streptokinase, alteplase, urokinase, and tenecteplase, were reported to be associated with favorable outcomes when they were administered via intracoronary route over several minutes usually in doses ranging from ½ to ¼ of their systemic doses (1). Moreover, intracoronary administration of low doses of urokinase and abciximab (in a consecutive manner) was previously reported as a promising option in this setting (1).

Importantly, intracoronary fibrinolytics (followed by low-dose GpIIb/IIIa inhibitors and/or PCI, where necessary) are well known to achieve a more substantial thrombus resolution when administered in the early stages of thrombus formation. Accordingly, the patient was reportedly an early presenter (admitted at the 3<sup>rd</sup> hour of his chest pain). Therefore, he also seems to be a candidate for intracoronary fibrinolysis following the initial CAG. Accordingly, was there an absolute contraindication to fibrinolytic therapy in the patient. Moreover, thrombus in the proximal LAD seemed to persist (though significantly regressed) on the repeat CAG (at 36 hours), and this could potentially lead to recurrent acute coronary syndromes (ACSs) in the longterm. Therefore, plain balloon angioplasty (prolonged inflation at subnominal pressures) and/or MTA and/or extended infusion of tirofiban (over 24 h) might have been reasonable options to manage this residual thrombus following repeat CAG. Specifically, we also wonder about the authors' future strategy for their patient (repeat coronary imaging for re-evaluation in the longterm, etc.).

On the other hand, there also exists a couple of reasons as to why most cardiologists feel reluctant to use intracoronary fibrinolytics even in the presence of absolute indications and, instead, prefer GpIIb/IIIa inhibitors (with or without PCI) in most cases: First, fibrinolytic therapy is generally deemed to be indicated exclusively in the setting of total coronary occlusions mostly associated with STEMI. However, use of intracoronary fibrinolysis is not strictly confined to the STEMI setting and also applies to the other ACS forms [including non-ST segment elevation acute coronary syndromes (NSTEMIs)] and even non-ACS settings (1, 3, 5). In other terms, total occlusion of the culprit coronary artery should not be regarded as a prerequisite for intracoronary fibrinolysis, provided that the apparent intraluminal material is strongly suggestive of a fibrin-rich thrombus (1, 3-5). Second, safety concerns regarding fibrinolytic therapy (including hemorrhagic complications) are prevalent among clinicians (1). However, intracoronary route is associated with a trivial systemic concentration of a given fibrinolytic agent, yet with a substantial accumulation of the same agent at the site of coronary thrombus (1). Accordingly, intracoronary fibrinolysis confers maximum therapeutic benefit along with minimum risk of hemorrhagic complications in clinical practice (1). Therefore, hemorrhagic risk of intracoronary fibrinolysis seems to be less significant compared with those of GpIIb/IIIa inhibitors given via systemic route. Lastly, there exists no consensus on the ideal types, appropriate doses, and infusion periods of intracoronary fibrinolytics that mostly rely on expert opinions and small-scale studies (1). This might also discourage the routine use of these agents in clinical practice.

In conclusion, intracoronary fibrinolysis appears to be an efficient and safe therapeutic strategy and is generally indicated in a variety of conditions primarily characterized by a fibrin-rich intracoronary thrombus formation. However, intracoronary fibrinolysis has been an underutilized strategy in clinical practice because of a variety of clinical misconceptions. Accordingly, interventional cardiologists need to be fully aware of this therapeutic modality along with its clinical implications in a detailed manner.

**Kenan Yalta\*** , **Cihan Öztürk\*** , **Tülin Yalta\*\*** , **Uğur Özkan\***   
Departments of \*Cardiology, and \*\*Pathology, Faculty of  
Medicine, Trakya University; Edirne-Turkey

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**Address for Correspondence:** Dr. Kenan Yalta,  
Trakya Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı,  
Edirne-Türkiye  
Phone: +90 505 657 98 56  
E-mail: kyalta@gmail.com, akenanyalta@trakya.edu.tr  
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## Author's Reply

To the Editor,

We would like to thank the author(s) for their interest and valuable comments on our manuscript entitled "A young patient with acute myocardial infarction due to bonsai treated with glycoprotein IIb/IIIa inhibitor" (1). Although, we agree that intracoronary fibrinolysis may be one of the treatment modalities in cases of intracoronary thrombus, data on clinical use are limited. As the author(s) state, there is no consensus on ideal types, appropriate doses, and infusion times of intracoronary fibrinolysis that mostly rely on expert opinions and small-scale studies (2). In addition, the treatment of acute myocardial infarction (AMI) cases owing to substance use (cocaine, marijuana, etc.) is still a matter of debate. In different studies, primary percutaneous coronary intervention (PCI), fibrinolytic, glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitors, or heparin-treatment modalities were used alone or in combination and success was achieved (3, 4). However, only a few cases of AMI caused by bonsai have been

reported in the literature, and primary PCI therapy alone or in combination with GpIIb/IIIa inhibitors was used in these cases (5, 6). In addition, AMI cases owing to substance use, which were successful with tirofiban treatment alone, have also been reported in the literature (7). In our case, after intracoronary tirofiban bolus dose, ST segment elevations and symptoms completely regressed in the electrocardiography. Therefore, primary PCI was not applied during the first procedure, and tirofiban infusion was continued. In control coronary angiography performed after 48 h, regression of the thrombus was observed. The GpIIb/IIIa inhibitors could be used as one of the treatment options for AMI caused by the use of bonsai and similar substances.

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**Ömer Doğan** , **Hasan Ali Barman** , **Mehmet Emin Gökçe** ,  
**Ayça Dönmez** , **Murat Kazım Ersanlı**   
Department of Cardiology, İstanbul University-Cerrahpaşa  
Institute of Cardiology; İstanbul-Turkey

**Address for Correspondence:** Dr. Hasan Ali Barman,  
İstanbul Üniversitesi-Cerrahpaşa Kardiyoloji Enstitüsü, Kardiyoloji Anabilim Dalı,  
İstanbul-Türkiye  
Phone: +90 506 326 19 25  
E-mail: drhasanali@hotmail.com  
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