

# KPR SIRASINDA TROMBOLİTİK TEDAVİ

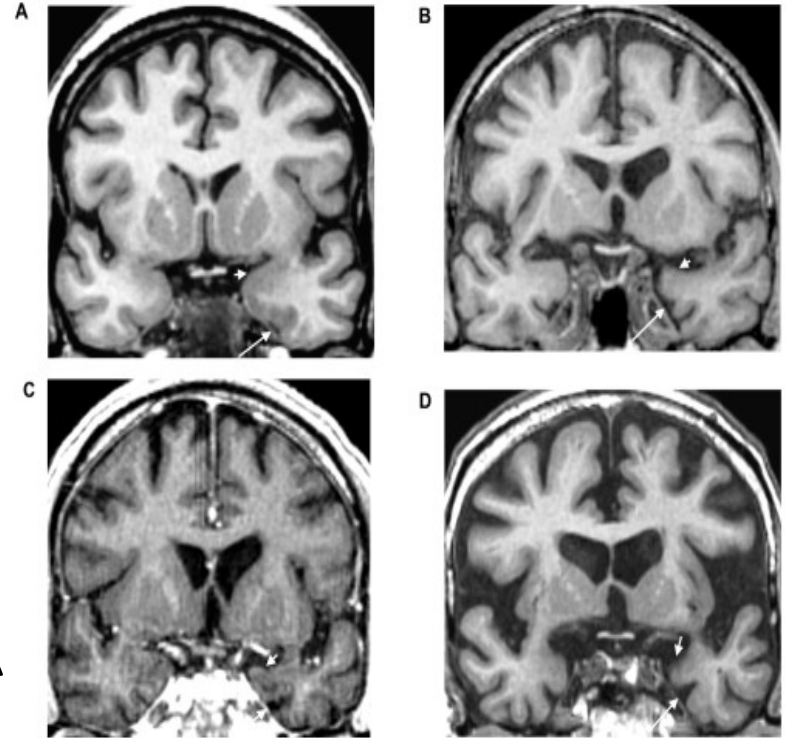


**Dr ERTAN SÖNMEZ**  
**ACİL TIP A.B.D**

# **KPR'de trombolitik neden düşünülmüş?**

- 1- Kardiyak arrestlerin %50-70'i PE veya AMI'ya bağlı
- 2- Dolaşımın durmasına bağlı intravasküler mikrotrombüslerin oluşması.

- Mikrosirkülasyonda pıhtılaşma görülmesi 4-5 dakika iken makrosirkülasyonda 20 dakika kadar.
- Bu sürenin hipotermide 40 dakikaya uzaması KPR de neden hipotermimin gerektiğini açıklar.



## pathophysiology of coagulopathy after CA

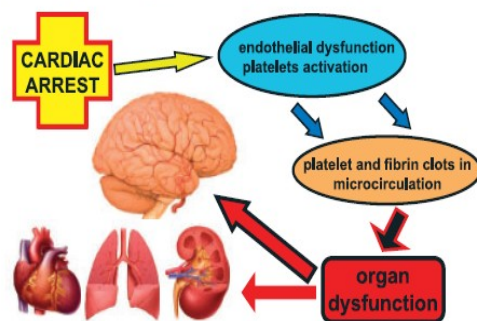


Fig. 2. Pathophysiology of microcirculatory dysfunction of vital organs after CA.

thrombin and enable fibrin deposition under the picture of systemic activation of coagulation (1, 2) which is not sufficiently counterbalanced by properly activated endogenous fibrinolytic

Maca J et al. Thrombolysis and cardiac arrest

(after ROSC) detected in blood serum by elevated levels of soluble fibrin monomers (sm-fibrin), thrombin antithrombin complex (T-AT), PAI-1 and finally also decreased activity of protein C/protein S (PC/PS) complex. Moreover, often long-lasting elevated blood level of PAI-1, in context with impaired fibrinolysis, is sometimes considered responsible for late organ hypoperfusion (2, 7) even hours from CA.

### Role of thrombolysis (rationale)

Intravascular obstruction by blood clot, no matter what type of vessel is affected, can be resolved by several treatment strategies. Aside from recently mostly used direct angiologic intervention, which is usually considered to be the best option for many patients, there is also available a bit older conservative approach with the help of highly effective drugs as causal or preventive medication. Importance of such therapeutic approach is especially highlighted in situations, when radical angiologic intervention is contraindicated or not available in due time. There are several drug groups affecting hemostasis in the sense of inhibition or



- Trombolitikler pulmoner emboli ve AMI da başarılı bir şekilde kullanılmakta.
- Normalde dolaşımda oluşan mikrotrombüsler endojen fibrinolitikler ile parçalanırken KPR'de bu denge bozuluyor.
- Bu nedenle KPR sırasında trombolitiklerle başta beyin olmak üzere mikrotrombüslerin zarar verebileceği amaçlanıyor.

**Thrombolysis and other drugs during cardiopulmonary resuscitation**

Fabian Spöhr<sup>a</sup>, Volker Wenzel<sup>b</sup> and Bernd W. Böttiger<sup>a</sup>

<sup>a</sup>Department of Anaesthesiology and Postoperative

Purpose of review



Anesthesiol Intensivmed Notfallmed Schmerzther. 2008 Mar;43(3):226-30; quiz 231. doi: 10.1055/s-2008-1070974.

## [Emergency medicine and myocardial ischaemia - thrombolysis during cardiopulmonary resuscitation - available data and recommendations].

[Article in German]

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### Abstract

Patients suffering cardiac arrest still have a poor prognosis. Up to the present, no drug therapy has shown to improve longterm survival after cardiac arrest. Acute myocardial infarction (AMI) or massive pulmonary embolism (PE) are the underlying causes for sudden cardiac arrest in 50-70 % of patients. Thrombolysis is an effective and causal therapy in patients with AMI or PE. Therefore, combining cardiopulmonary resuscitation (CPR) with thrombolysis may be a promising therapeutic approach. Experimental studies have demonstrated that thrombolytic therapy during CPR is not only a causal treatment for coronary or pulmonary arterial thrombi, but may also improve microcirculatory reperfusion after cardiac arrest. Although numerous case series and ~~small clinical studies showed evidence for the success of thrombolytic therapy during CPR,~~ a large randomised study did not confirm these results. Thrombolysis during CPR today can not be recommended as a standard therapy in patients suffering cardiac arrest. However, it should be considered if a massive PE is supposed to be the cause of cardiac arrest or if conventional CPR has not been successful in a patient with presumed thrombotic cause of cardiac arrest. The expected bleeding risk is outweighed by the potential benefit of this therapy in selected patients.

PMID: 18350476 [PubMed - indexed for MEDLINE]

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[Thrombolysis in cardiopulmonary resuscitation] [Hamostaseologie. 2007]

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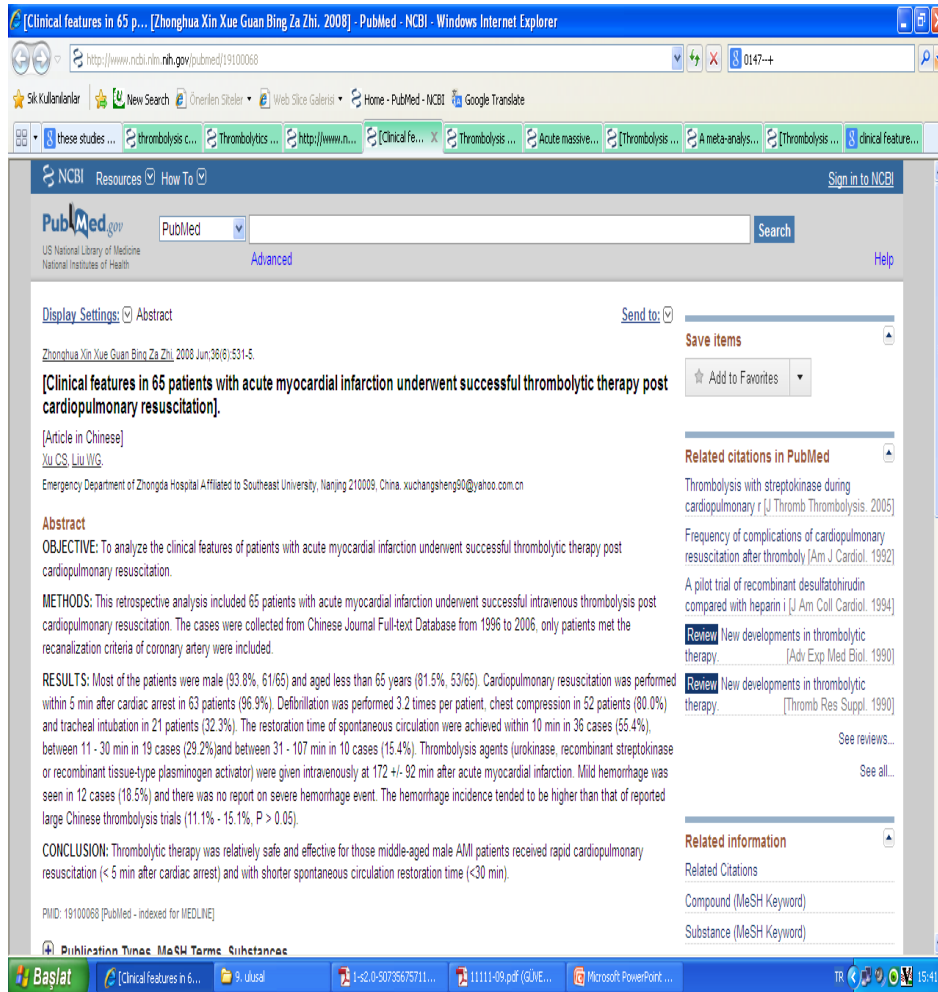
**Review** Thrombolytic therapy during cardiac arrest [Minerva Anestesiol. 2003]

**Review** Thrombolytic therapy during cardiac arrest [Curr Opin Crit Care. 2001]

**Review** Thrombolytics in CPR. Current recommendations [Minerva Anestesiol. 2005]

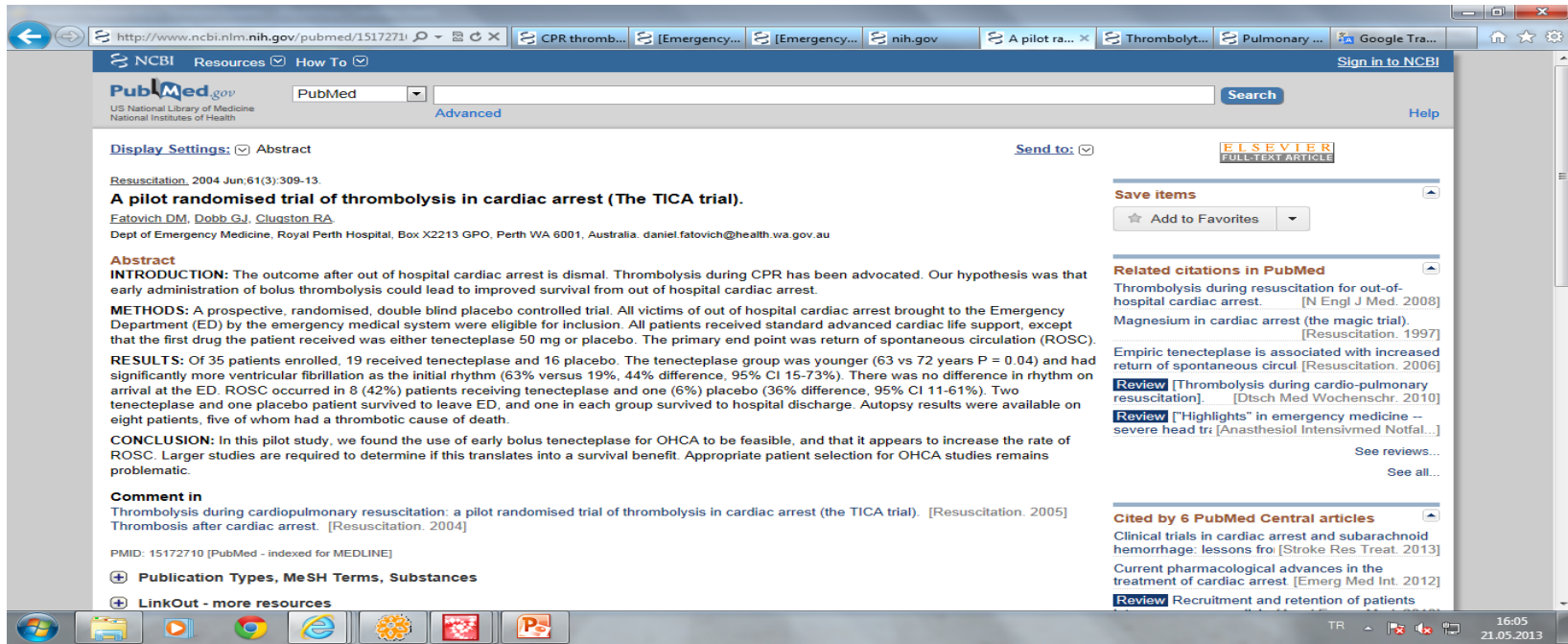
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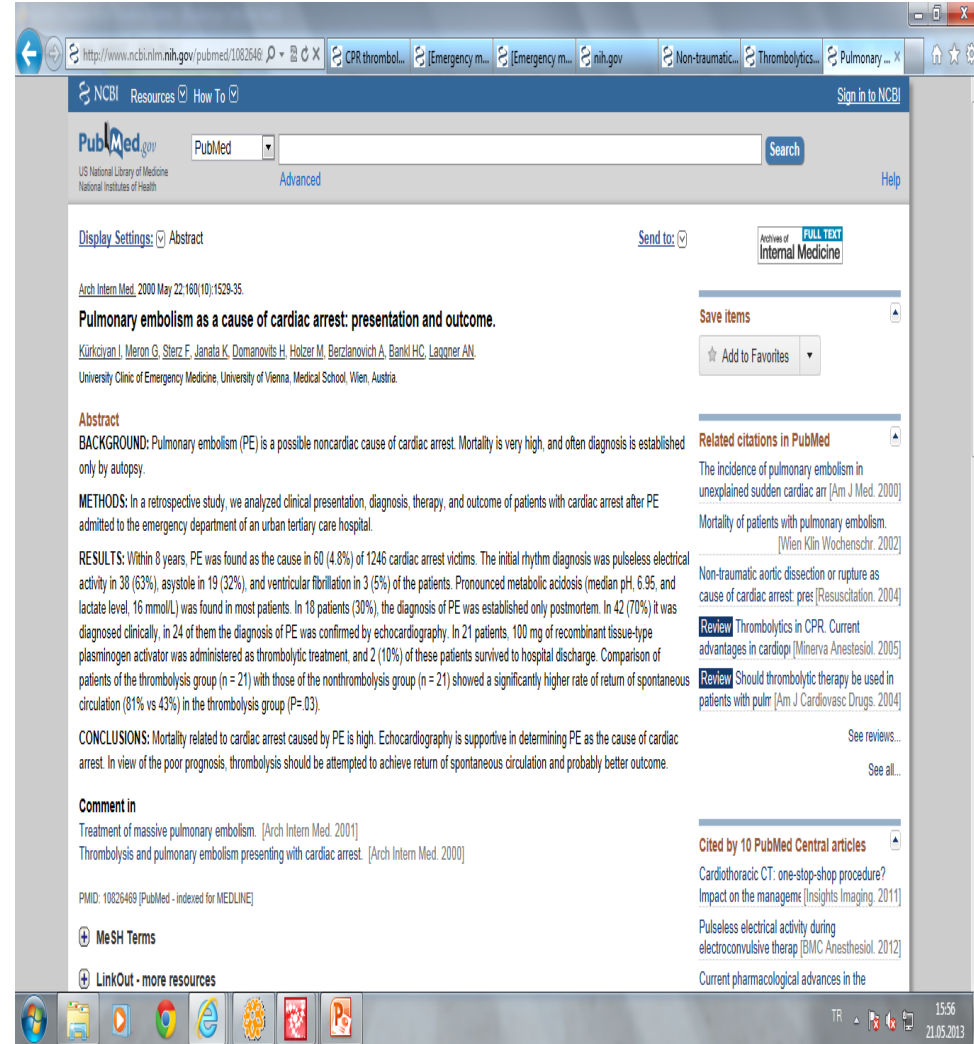
- Retrospektif bir çalışmada akut mi sonrası arrest olan 65 hastada KPR sonrası trombolitik tedaviler başarılı şekilde uygulanmıştır.
- %18 inde orta





- Randomize bir çalışmada hastane dışı arrest olan 35 hastanın 19'unda tenekteplaz ve 16'sında plasebo ile KPR yapılmış.
- Spontan Dolaşımın Geri Dönmesi (SDGD) 8 hastada %42 oranla sağlanmış.

- Bir retrospektif çalışmada massif pulmoner emboliye bağlı kardiyak arrest olan 21 hastada KPR esnasında trombolitik uygulanmış ve kontrol gurubuna göre SDGD'de önemli fark görülmüſ (%81-



## CASE REPORT

Korean Circ J 2007;37:663-665

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# Thrombolytic Therapy during Cardiopulmonary Resuscitation in a Patient with Cardiac Arrest

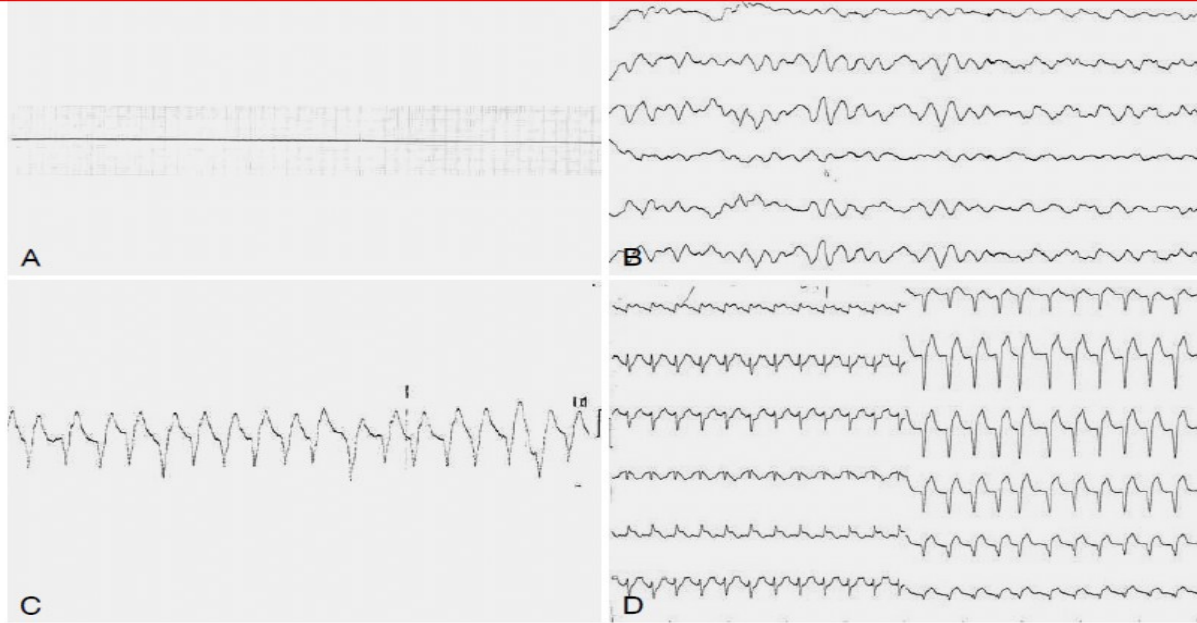
Woong Kim, MD, Young-Jo Kim, MD, Won-Jae Lee, MD, Sang-Hee Lee, MD, Geu-Ru Hong, MD, Jong-Seon Park, MD, Dong-Gu Shin, MD and Bong-Sup Shim, MD

*Division of Cardiology, Department of Internal Medicine, Yeungnam University Medical Center, Daegu, Korea*

## ABSTRACT

Thrombolytic therapy during cardiopulmonary resuscitation is not routinely recommended, but 50-70% of cardiac arrests are caused by either acute myocardial infarction or massive pulmonary embolism. Thrombolytic therapy can be a reasonable treatment modality for a patient suffering with cardiac arrest in an emergency situation and whose diagnosis is not known. We report here on a case with cardiac arrest and the diagnosis was not known. The patient was refractory to conventional cardiopulmonary resuscitation, and he was treated with a bolus injection of a thrombolytic agent. He recovered completely without complications. (Korean Circ J 2007;37:663-665)

**KEY WORDS:** Thrombolytic therapy; Cardiopulmonary resuscitation; Heart arrest.



**Fig. 1.** The serial electrocardiogram was recorded from the emergency room admission to the recovery after thrombolytic therapy. A: initial electrocardiogram at ER shows no electrical activity. B: ventricular fibrillation developed during cardiopulmonary resuscitation. C: pulseless activity still remained when tenecteplase 40 mg was injected during cardiopulmonary resuscitation. D: the electrocardiogram recorded 2 hours later after cardiopulmonary resuscitation. The vital signs became stable. ER: emergency room.

- 43 yaş erkek hasta 1 saatlik göğüs ağrısı sonucu hastaneye giderken 5 dakikalık arrest ve asistolide, pupilleri dilate olarak acile ulaşıyor.
- Geleneksel KPR' ye dirençli (25 dak) olan vakaya trombolitik uygulanıyor ve nörolojik sekelsiz tam iyileşme sağlanıyor. 1yıl sonraki kontrollerinde sağlıklı.



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[Emerg Med J.](#) 2006 Mar;23(3):e19.

## **Bolus thrombolytic infusion during prolonged refractory cardiac arrest of undiagnosed cause.**

[Sheth A](#), [Cullinan P](#), [Vachharajani V](#), [Conrad SA](#).

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### **Abstract**

Acute myocardial infarction (AMI) and pulmonary embolism (PE) account for about 70% of cardiac arrest. Although thrombolytic therapy is an effective therapy for both AMI and PE, it is not routinely recommended during cardiopulmonary resuscitation (CPR) for fear of life threatening bleeding complications. Numerous case reports and retrospective studies have suggested a beneficial effect of thrombolytics in cardiac arrest secondary to AMI and PE; however, we present a case of successful use of bolus thrombolytics during CPR in a patient with undifferentiated cardiac arrest (undiagnosed cause) after prolonged conventional resuscitation without success.

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- 19 yaşında guillain barre hastası solunum sıkıntısıyla interne ediliyor.
- 7 gün süreyle entübe olarak günlük plazma exchange tedavisi alıyor.
- Extübe edilince ani solunum sıkıntısı ve göğüs ağrısı sonrası arrest gelişiyor.
- 18 dakikalık KPR'de NEA ritminde değişiklik görülmeyen hastaya bolus 100 U rh-TPA uygulanıyor.
- 3 dakika sonra SDGD ve yeni gelişen bir sağ dal



## Low-dose tenecteplase during cardiopulmonary resuscitation due to massive pulmonary embolism: a case report and review of previously reported cases

David Václav Fred Hefer<sup>a</sup>, Aman Munir<sup>b</sup> and Hassan Khouli<sup>c</sup>

The case of a 29 year-old man who suffered a cardiac arrest due to a massive pulmonary embolism while he was undergoing surgical repair of a complex tibial plateau fracture is presented. After 70 min of unsuccessful cardiopulmonary resuscitation a bolus of 20 mg tenecteplase was given, with a return of spontaneous circulation 2 min after administration of the drug. Pulmonary embolism was subsequently demonstrated on a pulmonary angiogram. To our knowledge this is the first report to show that the use of a low dose of tenecteplase might be useful to achieve the return of spontaneous circulation in the resuscitation of patients with cardiac arrest secondary to massive pulmonary embolism. Previously reported cases are reviewed. *Blood*

*Coagul Fibrinolysis* 18:691 –694 © 2007 Lippincott Williams & Wilkins.

*Blood Coagulation and Fibrinolysis* 2007, 18:691–694

**Keywords:** cardiac arrest, cardiopulmonary resuscitation, pulmonary embolism, tenecteplase, thrombolysis

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Accepted 24 May 2007

- Tibia plato kırığı olan 29 yaşında erkek hasta da operasyonun 15. dakikasinda ani gelişen taşikardi, tansiyon düşüklüğü ve saturasyon düşüklüğü sonrası arrest olmuş.
- 70 dakika süren KPR'ye yanıt alınamayan hasta da pulmoner emboli düşünülerek 20 mg düşük doz tenektoplaz verilmiş. 2 dakika sonra SDGD görülmüş.
- Çekilen EKO'da sağ boşluklar geniş, BT anjioda her iki alt lob pulmoner arterde pulmoner emboli görülmüş.

**2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction :  
A Report of the American College of Cardiology Foundation/American Heart Association  
Task Force on Practice Guidelines**

WRITING COMMITTEE MEMBERS\*, Patrick T. O'Gara, Frederick G. Kushner, Deborah D. Ascheim, Donald E. Casey, Jr, Mina K. Chung, James A. de Lemos, Steven M. Ettinger, James C. Fang, Francis M. Fesmire, Barry A. Franklin, Christopher B. Granger, Harlan M. Krumholz, Jane A. Linderbaum, David A. Morrow, L. Kristin Newby, Joseph P. Ornato, Narith Ou, Martha J. Radford, Jacqueline E. Tamis-Holland, Carl L. Tommaso, Cynthia M. Tracy, Y. Joseph Woo and David X. Zhao

*Circulation*. 2013;127:e362-e425; originally published online December 17, 2012;

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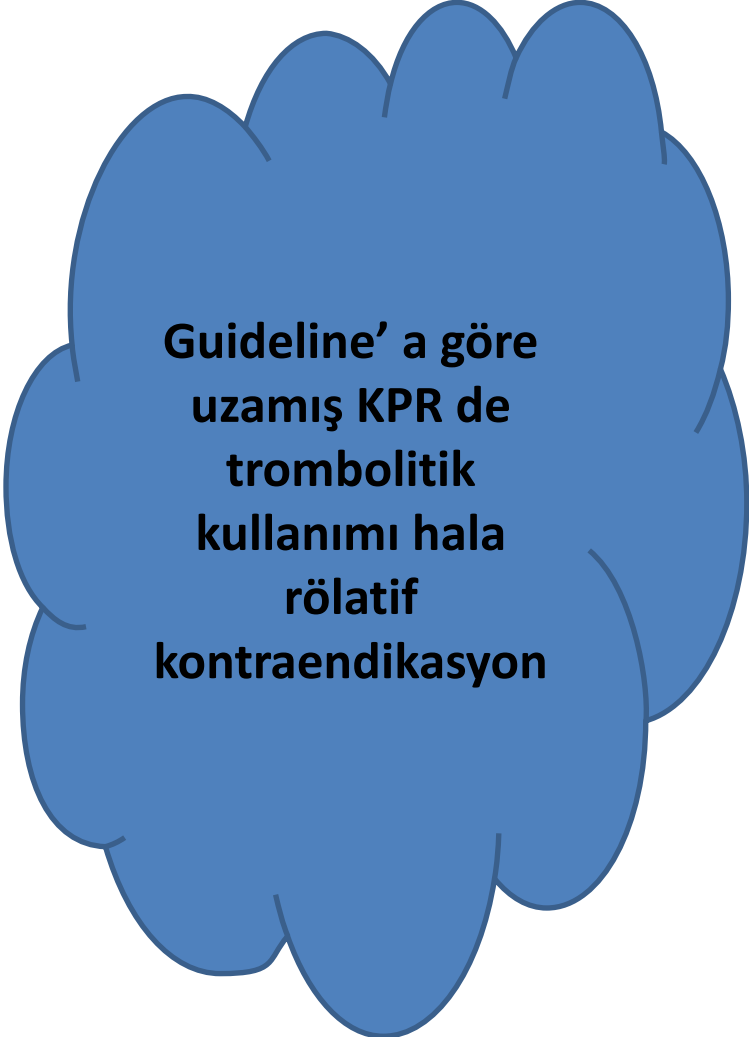
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- Guideline da hastane öncesi fibrinolitik tedavinin önemi vurgulanmıştır.
- İlk Medikal Temas (FMC ) ve Perkütan Anjiyografik Girişim (PCI) zamanı 120 dakikayı geçecek ise fibrinolitik tedavi endikasyonu vardır. *(81,306–311 (Level of Evidence: A)*
- Semptomların başlamasından itibaren özellikle kırsal alanda eğitilmiş acil servis sistemi veya hastane hekimiyle bağlantılı olarak hastane öncesi fibrinolitik tedavi verilmesinin

### Relative contraindications

- History of chronic, severe, poorly controlled hypertension
- Significant hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)
- History of prior ischemic stroke >3 mo
- Dementia
- Known intracranial pathology not covered in absolute contraindications
- Traumatic or prolonged (>10 min) CPR
- Major surgery (<3 wk)
- Recent (within 2 to 4 wk) internal bleeding
- Noncompressible vascular punctures
- Pregnancy
- Active peptic ulcer
- Oral anticoagulant therapy



**Guideline’ a göre  
uzamış KPR de  
trombolitik  
kullanımı hala  
rölatif  
kontraendikasyon**

# Thrombolysis and other drugs during cardiopulmonary resuscitation

Fabian Spöhr<sup>a</sup>, Volker Wenzel<sup>b</sup> and Bernd W. Böttiger<sup>a</sup>

<sup>a</sup>Department of Anaesthesiology and Postoperative

Purpose of review

- 30 yıldan fazla KPR de trombolitik kullanımı bir çok vakada sürpriz güzel sonuçlar verdiği gösterilmiş.
- Şimdilerde massif pulmoner emboli ve AMI ya bağlı arrest vakalarda KPR sırasında trombolitiklerin prospektif çalışmalarda kanıt değeri düşük olmakla birlikte faydası gösterilmiştir.
- Bu konuda yapılan çalışmaların çoğu retrospektif olup 2 çalışma hastane dışı

# **Thrombolysis and other drugs during cardiopulmonary resuscitation**

Fabian Spöhr<sup>a</sup>, Volker Wenzel<sup>b</sup> and Bernd W. Böttiger<sup>a</sup>

<sup>a</sup>Department of Anaesthesiology and Postoperative

**Purpose of review**

- Hastane dışı arrestlerde yapılan kontrollü çalışmada normal KPR ye 15 dakika yanıtsız 40 hastaya Alteplaz (rt-PA) ile KPR uygulanmış. 50 hastaya normal KPR uygulanmış.
- Trombolitik uygulanan grupta SDGD %68 iken normal KPR'de %44 görülmüş. Hastaneye ulaşabilmeleri ise %58'e %30 oranında daha iyi olmuş.
- 24 saatlik survi ve hastaneden taburculuk daha iyi bulunmakla birlikte çalışma istatistiksel



# Thrombolysis and other drugs during cardiopulmonary resuscitation

Fabian Spöhr<sup>a</sup>, Volker Wenzel<sup>b</sup> and Bernd W. Böttiger<sup>a</sup>

<sup>a</sup>Department of Anaesthesiology and Postoperative

Purpose of review

**Table 1** Prospective studies on thrombolysis during cardiopulmonary resuscitation after out-of-hospital cardiac arrest

	Design	Number of patients (thrombolysis/control)	Endpoint	Results (thrombolysis/control)	CPR-related severe bleeding (thrombolysis/control)
Böttiger <i>et al.</i> [19]	Historical controls	401/150	Admission ICU	58%/30%	0/0
Fatovich <i>et al.</i> [20]	Double-blind, Placebo-controlled	19/16	ROSC	42%/6%	Not recorded
Bozeman <i>et al.</i> [21]	Historical controls	50/113	ROSC	26%/12%	1/0
Abu-Laban <i>et al.</i> [22]	Double-blind, Placebo-controlled	117/116	Hospital discharge	1/0	2/0

CPR, cardiopulmonary resuscitation; ICU, intensive care unit; ROSC, restoration of spontaneous circulation.



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# A meta-analysis of cardiopulmonary resuscitation with and without the administration of thrombolytic agents<sup>☆</sup>

Xin Li<sup>a</sup>, Qing-ling Fu<sup>b</sup>, Xiao-li Jing<sup>a</sup>, Yu-jie Li<sup>a</sup>, Hong Zhan<sup>a</sup>,  
Zhong-fu Ma<sup>a</sup>, Xiao-xing Liao<sup>a,\*</sup>

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<sup>b</sup> Department of Anatomy, The University of Hong Kong, 21 Sassoon Road, Hong Kong, PR China

- Kardiyak arrestlerin en sık nedenleri AMI ve P.E olması bununla birlikte arrest sırasında mikrotrombuslerin oluşması nedeniyle KPR 'de trombolitiklerin etkisi araştırılmıştır.
- Bu meta-analizde, KPR de trombolitiklerin etkisini görmek için 1966-2004 yılları arasında medline veritabanlı klinik çalışmalara bakılmış.
- Sekiz çalışma bulunmuş ve bunlarda SDGD, 24 saatlik survi, hastaneden taburculuk ve uzun dönem nörolojik iyileşme anlamlı derecede



**EMA**  
Emergency Medicine Australasia



*Emergency Medicine Australasia* (2011) 23, 282–285

doi: 10.1111/j.1742-6723.2011.01422\_13.x

## MEDICATIONS



# Medications in Adult Cardiac Arrest. ARC and NZRC Guideline 2010

Australian Resuscitation Council, New Zealand Resuscitation Council

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- İki randomize çalışma KPR’de fibrinolitiklerin kısa veya uzun vadede iyi sonuçları artırmadığını göstermiş.
- Bir çalışma kardiyak arrestte **rutin** trombolitik kullanımının intrakraniyal kanama riskini artırdığını düşündürmüştü.
- 7 çalışma standart tedavilerden fayda görmemiş arrestli hastada fibrinolitiklerin faydasını göstermemiş ancak birçok sınırlayıcı faktörler içerir.
- Fibrinolitiklerin hastane içi veya dışı

# AKUT MI TROMBOLİTİK TEDAVİSİ

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Dosya Düzenle Görünüm Belge Araçlar Pencere Yardım

20 / 52 %110 Bul

References.

**Table 15 Doses of fibrinolytic agents**

	Initial treatment	Specific contraindications
Streptokinase (SK)	1.5 million units over 30–60 min i.v.	Prior SK or anistreplase
Alteplase (tPA)	15 mg i.v. bolus 0.75 mg/kg over 30 min (up to 50 mg) then 0.5 mg/kg over 60 min i.v. (up to 35 mg)	
Retepase (r-PA)	10 units + 10 units i.v. bolus given 30 min apart	
Tenecteplase (TNK-tPA)	Single i.v. bolus: 30 mg if <60 kg 35 mg if 60 to <70 kg 40 mg if 70 to <80 kg 45 mg if 80 to <90 kg 50 mg if ≥90 kg	

i.v. = intravenous.

in non-cerebral bleeding complications. The net clinical benefit (absence of death, non-fatal infarction and intracranial haemorrhage) favoured enoxaparin.<sup>160,161</sup> Finally, fondaparinux was shown in the large OASIS-6 trial to be superior to placebo or UFH in preventing death and reinfarction,<sup>118,164</sup> especially in patients who received streptokinase.

In a large trial with streptokinase,<sup>176</sup> no mortality reduction was observed at 30 days, but significantly fewer reinfarctions were seen with bivalirudin (a direct antithrombin, given for 48 h), compared with UFH, though at the cost of a modest and non-significant increase in non-cerebral bleeding complications. Bivalirudin has not been studied with fibrin-specific agents. Thus there is no evidence in support of direct thrombin inhibitors as an adjunct to fibrinolysis.

Tenecteplase, aspirin, enoxaparin and clopidogrel comprise the antithrombotic combination that has been most extensively studied as part of a pharmacoinvasive strategy, viz. Trial of Routine Angioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in acute myocardial infarction (TRANSFER),<sup>168</sup> NORwegian study on District treatment of ST-Elevation Myocardial Infarction

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ESC GUIDELINES

European Heart Journal (2012) 33, 2569–2619  
doi:10.1093/eurheartj/ehc215

**ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation**

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC)

Authors/Task Force Members: Ph. Gabriel Steg (Chairperson) (France)\*, Stefan K. James (Chairperson) (Sweden)\*, Dan Atar (Norway), Luigi P. Badano



# AKUT PUMONER EMBOLİ TROMBOLİTİK TEDAVİSİ

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Akut Pulmoner Embolide Tanı ve Tedavi Kılavuzu

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yoluyla vazodilatörler uygulanabilir.<sup>226</sup> Küçük klinik çalışmalardan elde edilen verilere göre, nitrik oksit inhalasyonu, PE'li hastalarda hemodinamik durum ve gaz alışverişini düzeltebilir.<sup>227-229</sup> PE'ye ikincil gelişen pulmoner hipertansiyon tedavisinde inhale aerosol şeklinde kullanılan prostasiklin ile ilgili az veri bulunmaktadır.<sup>226,230,231</sup>

DeneySEL ön veriler, akut PE'de levosimendanın, pulmoner vazodilatasyon oluşturmakla birlikte RV kasılabilirliğini artırması sonucu, sağ ventrikül-pulmoner arter bağlantısını yeniden düzenleyebileceğini düşündürmektedir.<sup>232</sup>

PE'de endotelin antagonistleri ve fosfodiesteraz-5 inhibitörleri kullanımına olan ilgi giderek artmaktadır. DeneySEL çalışmalarda, endotelin reseptörlerinin antagonizması, masif PE'nin neden olduğu pulmoner hipertansiyonun şiddetini azaltmıştır.<sup>233,234</sup> Sildenafil infüzyonu da, deneySEL PE'de pulmoner arter basıncındaki artışı düşürmüştür.<sup>235,236</sup>

PE'li hastalarda hipoksemi ve hiperkapniye sık rastlanır; ancak bunların ağırlığı, olguların çoğunda orta derecedir. Açık foramen ovale, sağ atriyum basıncının sol atriyum basıncını aşması sonucu ge-

**Tablo 13 Pulmoner embolide onaylanmış trombolitik rejimler**

Streptokinaz	250 000 IU yüklenme dozu olarak 30 dakikada, takiben 100 000 IU/saat 12-24 saatte
	Hızlı rejim: 1.5 milyon IU, 2 saatte
Ürokinaz	4400 IU/kg yüklenme dozu olarak, 10 dakikada, takiben 4400 IU/kg/saat 12-24 saatte
	Hızlı rejim: 3 milyon IU, 2 saatte
rtPA	100 mg, 2 saatte
	ya da 0.6 mg/kg, 15 dakikada (maks. doz 50 mg)

rtPA = rekombinan doku plazminojen aktivatörü.

yakın zamanlı randomize çalışmalarda<sup>247,248</sup> 2 saat içinde infüze edilen 100 mg rtPA'nın, 12 ya da 24 saat içinde 4400 IU/kg/saat hızla infüze edilen ürokinaza göre, daha hızlı anjiyografik ve hemodinamik düzelme sağladığı, ürokinaz infüzyonu sonunda ise sonuçların farklı-

European Heart Journal (2008) 29, 2276-2315  
doi:10.1093/eurheartj/ehn310

**ESC KILAVUZLARI**

**Akut Pulmoner Embolide Tanı ve Tedavi Kılavuzu**

**Avrupa Kardiyoloji Derneği (ESC) Akut Pulmoner Emboli Tanı ve Tedavisi Görev Grubu**

**Yazarlar/Görev Grubu Üyeleri:** Adam Torbicki, Başkan (Polonya)\*, Arnaud Perrier (İsviçre), Stavros Konstantinides (Almanya), Giancarlo Agnelli (İtalya), Nazareno Galis (İtalya), Piotr Pruszczyk (Polonya), Frank Bengel (ABD), Adrian J.B. Brady (İngiltere), Daniel Ferreira (Portekiz), Thibault Vignati (Fransa), ...

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25.08.2013

# Akılda tutulması gereken noktalar:

- Rutin KPR'yi uygulama sırasında arada SDGD durumunda EKG veya EKO bulgularına göre erken tedavi şansımızı kullanabiliriz.

*(ST elvasyonu, sağ veya sol dal bloğu, sağ ventrikül dilatasyonu, PAB artışı)*

- Ayrıcalık: PCI lab varsa ve hemodinami stabilleşirse
- Arrest öncesi semptom veya bulguların AMI veya PE'yi düşündürmesi bizi cesaretlendirmeli.

teşekkürler