Intra-arrest thrombolytic

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- Prolong Cardiac Arrest (CA) is associated with an activation of blood coagulation.
- In 1950s Crowell et al. firstly reported an intravasculary coagulation during CA.
- Callaway et al. showed endothelial damage after CA.
- Budrham et al detected left ventricular thrombus by TEE in 86% of swine following 6 min of untreated VF.
- Varrale et al reported intracardiac thrombus at 20-30 min after CA in humans.

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RESUSCITATION

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A pilot randomised trial of thrombolysis in cardiac arrest (The TICA trial)

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Abstract

Introduction: The outcome after out of hospital cardiac arrest is dismal. Thrombolysis during CPR has been advocated. Our hypothesis was that early administration of bolus thrombolysis could lead to improved survival from out of hospital cardiac arrest. *Methods*: A prospective, randomised, double blind placebo controlled trial. All victims of out of hospital cardiac arrest brought to the Emergency Department (ED) by the emergency medical system were eligible for inclusion. All patients received standard advanced cardiac life support, except that the first drug the patient received was either tenecteplase 50 mg or placebo. The primary end point was return of spontaneous circulation (ROSC). *Results*: Of 35 patients enrolled, 19 received tenecteplase and 16 placebo. The tenecteplase group was younger (63 vs 72 years $P = 0.04$) and had significantly more ventricular fibrillation as the initial rhythm (63% versus 19%, 44% difference, 95% CI 15–73%). There was no difference in rhythm on arrival at the ED. ROSC occurred in 8 (42%) patients receiving tenecteplase and one (6%) placebo (36% difference, 95% CI 11–61%). Two tenecteplase and one placebo patient survived to leave ED, and one in each group survived to hospital discharge. Autopsy results were available on eight patients, five of whom had a thrombotic cause of death. *Conclusion*: In this pilot study, we found the use of early bolus tenecteplase for OHCA to be feasible, and that it appears to increase the rate of ROSC. Larger studies are required to determine if this translates into a survival benefit. Appropriate patient selection for OHCA studies remains problematic.
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TICA

- 35 patients
- 19 received 50 mg tenecteplase, 16 received plasebo
- Early bolus tenecteplase was feasible for OHCA and
- They found that the rate of ROSC increased.

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European Journal of Clinical Investigation (2005) 35, 315–323

International multicentre trial protocol to assess the efficacy and safety of tenecteplase during cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest: The Thrombolysis in Cardiac Arrest (TROICA) Study

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Abstract

Prehospital cardiac arrest has been associated with a very poor prognosis. Acute myocardial infarction and massive pulmonary embolism are the underlying causes of out-of-hospital cardiac arrest in 50–70% of patients. Although fibrinolysis is an effective treatment strategy for both myocardial infarction and pulmonary embolism, clinical experience for this therapy performed during resuscitation has been limited owing to the anticipated risk of severe bleeding complications. The TROICA study is planned as one of the largest randomized, double-blind, placebo-controlled trials to assess the efficacy and safety of prehospital thrombolytic therapy in cardiac arrest of presumed cardiac origin. Approximately 1000 patients with cardiac arrest will be randomized at approximately 60 international study centres to receive either a weight-adjusted dose of tenecteplase or placebo after the first dose of a vasopressor. Patients can be included if they are at least 18 years, presenting with a witnessed cardiac arrest of presumed cardiac origin, and if either basic life support had started within 10 min of onset and had been performed up to 10 min or advanced life support is started within 10 min of onset of cardiac arrest. Primary endpoint of the study is the 30-day survival rate, and the coprimary endpoint is hospital admission. Secondary endpoints are the return of spontaneous circulation (ROSC), survival after 24 h, survival to hospital discharge, and neurological performance. Safety endpoints include major bleeding complications and symptomatic intracranial haemorrhage.

Keywords Cardiopulmonary resuscitation, clinical study, myocardial infarction, prehospital, pulmonary embolism, randomized, thrombolysis.

TROICA

- The largest, randomised, double blind placebo-controlled trial
- Approximately 1000 patients from 60 international centers
- Patients were ≥18 years and they had witnessed CA presumed cardiac origin.
- The two group had similar rates of ROSC
- 24 hour survival
- survival to hospital discharge
- 30 day mortality
- neurologic outcomes
- The patients received tPA had more intracranial hemorrhages.

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Tissue Plasminogen Activator Use in Cardiac Arrest Secondary to Fulminant Pulmonary Embolism

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Abstract

Background: Tissue plasminogen activator (tPA) is used emergently to dissolve thrombi in the treatment of fulminant pulmonary embolism. Currently, there is a relative contraindication to tPA in the setting of traumatic or prolonged cardiopulmonary resuscitation > 10 minutes because of the risk of massive hemorrhage.

Methods: Our single-center, retrospective study investigated patients experiencing cardiac arrest (CA) secondary to pulmonary embolus. We compared the effectiveness of advanced cardiac life support with the administration of tPA vs. the standard of care consisting of advanced cardiac life support without thrombolysis. The primary endpoint was survival to discharge. Secondary endpoints were return of spontaneous circulation (ROSC), major bleeding, and minor bleeding.

Results: We analyzed 42 patients, of whom 19 received tPA during CA. Patients who received tPA were not associated with a statistically significant increase in survival to discharge (10.5% vs. 8.7%, P = 1.00) or ROSC (47.4% vs. 47.8%, P = 0.98) compared to the control group. We observed no statistically significant difference between the groups in major bleeding events (5.3% in the tPA group vs. 4.3% in the control group, P = 1.00) and minor bleeding events (10.5% in the tPA group vs. 0.0% in the control group, P = 0.11).

Conclusion: This study did not find a statistically significant difference in survival to discharge or in ROSC in patients treated with tPA during CA compared to patients treated with standard therapy. However, because no significant difference was found in major or minor bleeding, we suggest that the potential therapeutic benefits of this medication should not be limited by the potential for massive hemorrhage. Larger prospective studies are warranted to define the efficacy and safety profile of thrombolytic use in this population.

embolism; Thrombolytic therapy; Tissue plasminogen activator

Introduction

Venous thromboembolism, a condition that includes both deep vein thrombosis and pulmonary embolus, is estimated to affect up to 900,000 patients per year in the United States. Within this group, approximately 60,000 - 100,000 patients die from complications [1]. Fulminant pulmonary embolism can lead to cardiac arrest (CA) in 41% of patients [2]. CA secondary to pulmonary embolus often leads to sudden decompensation and is a major predictor of mortality. The most common presentations of massive pulmonary embolus as a cause of CA are asystole and pulseless electrical activity [3-5]. Once CA has occurred, cardiopulmonary resuscitation (CPR) should be immediately initiated. Among the viable treatment options for fulminant pulmonary embolism, thrombolytic agents have received the most attention because of their availability, rapid administration and action, and theoretical pathophysiologic benefits. Current guidelines for the treatment of non-massive pulmonary embolus involve the use of anticoagulants such as heparin. Tissue plasminogen activator (tPA) is indicated to treat massive pulmonary embolus, a pulmonary embolus causing sustained hypotension, pulselessness, or bradycardia. However, a relative contraindication exists for the use of tPA during traumatic or prolonged (> 10 min) resuscitation efforts.

Our study was designed to examine the efficacy and safety of thrombolytic use in patients experiencing CA as a result of pulmonary embolism.

- One sıngle center, retrospective, CA secondary to PE
- 42 patients, 19 received tPA
- There was no statistically significant difference in ROSC and survival to hospital discharge.
- However, also there was no significant difference in minor or major bleeding complications.

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Case Report

Thrombolysis during continuous chest compression in a patient with cardiac arrest due to pulmonary embolism: prolonged CPR–induced spinal cord injury

Pulmonary embolism (PE) is a life-threatening condition, and cardiac arrest is the most serious clinical circumstance. Clinical practice guidelines recommend systemic thrombolysis for high-risk or massive PE patients as the primary treatment. However, there are insufficient data to argue for or against the routine use of thrombolytic therapy during cardiac arrest. We report a 47-year-old man with acute PE complicated by cardiac arrest with pulseless electrical activity. Intravenous thrombolytic therapy with 1.5 million U of urokinase was performed by a constant infusion pump within 30 minutes during continuous mechanical chest compression with LUCAS (Jolife AB, Lund, Sweden). After 46 minutes of cardiopulmonary resuscitation, return of spontaneous circulation was achieved, and the patient eventually survived to discharge. Unfortunately, he had an irreversible spinal cord injury due to prolonged cardiopulmonary resuscitation and traumatic injury.

peripheral saturation of oxygen 84%. Based on these findings, he wa presumptively diagnosed with acute PE.

While the patient was transferred from the ED to the cardiac car unit, he had a witnessed cardiac arrest with pulseless electrical activit (Fig. 1A). Continuous chest compression was preformed immediatel and a single dose of epinephrine 1 mg was administered intravenousl The ECG monitor demonstrates wide QRS complex pulseless electric activity, and there was still no cardiac output (Fig. 1B). He was intubate with ventilation support, and 1.5 million U of urokinase was given by constant infusion pump within 30 minutes while continuous mechan cal chest compression with LUCAS (Jolife AB, Lund, Sweden) device sup port. After another 16 minutes of CPR, return of spontaneous circulatio was achieved for the first time, and the heart's rhythm was also restore to sinus rhythm with blood pressure increasing to 130/84 mm Hg Bedside echocardiographic examination was performed again, whic

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Case Report

Extracorporeal cardiopulmonary resuscitation in bedside echocardiography–diagnosed massive pulmonary embolism

Abstract

Acute pulmonary embolism (PE) is one of the major causes of inhospital cardiac arrest as well as out-of-hospital cardiac arrest. Bedside diagnosis of acute PE in the emergency department (ED) can be challenging, especially in a cardiac arrest setting. Even if the early diagnosis of an acute massive PE had been made, hemodynamic instability may be worsened unless obstructive shock gets resolved. We present a case of a 46-year-old woman who developed pulseless electrical activity (PEA) after complaining of weakness and dyspnea in an ambulance, presumptively diagnosed as acute PE by bedside focused echocardiography. She received thrombolytic therapy and was rescued by extracorporeal cardiopulmonary resuscitation for recurrent PEA arrest in the ED. Focused bedside echocardiography provides a rapid diagnostic adjunct, and extracorporeal cardiopulmonary resuscitation can be a valuable rescue therapy for PEA arrest from massive PE.

However, PEA developed repeate
achieved, which required prolon
complex PEA at a rate of approxi
observed over a 60-minute interva
level reported during CPR was 279
Refractory PEA arrest with a pote
massive PE persisted despite stand
support. Hence, a decision was m
active chest compressions in the ED

Under ultrasound guidance, extr
(ECMO) catheters were inserted i
modified Seldinger technique. Extr
support was initiated using the En
Tokyo, Japan). After initiation of ECM
ness but was hemodynamically unst
fluid boluses, inotropes, and vasopre

Does Thrombolysis Have a Place in the Cardiopulmonary Resuscitation of Patients With Acute Pulmonary Embolism? A Case of Successful Thrombolysis During Pulmonary Embolism Induced Cardiopulmonary Arrest

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Objective: Pulmonary embolism often causes cardiac arrest. When this occurs, thrombolytic therapy is not routinely administered. There are multiple reasons for this, including difficulty with rapidly adequately diagnosing the embolus, the lack of good data supporting the use of thrombolytics during resuscitation, the belief that thrombolytic therapy is ineffective once a patient has already arrested, the difficulty of obtaining thrombolytics at the bedside rapidly enough to administer during a code, and the increased risks of bleeding, particularly with ongoing chest compressions. In this case report, we present a patient who was successfully treated with thrombolytic therapy during pulmonary embolism–induced cardiopulmonary arrest and discuss the role of thrombolytics in cardiopulmonary resuscitation.

Design: Case report.

Setting: Surgical ICU in a comprehensive cancer center.

Patient: A 56-year-old man who developed hypotension, dyspnea, hypoxia, and pulseless electrical activity 10 days after resection of a benign colon lesion with a right hemicolectomy and primary end-to-end anastomosis.

Interventions: After a rapid bedside echocardiogram suggesting pulmonary embolus, thrombolytic therapy was administered during cardiopulmonary resuscitative efforts.

Measurements and Main Results: The patient had a return of spontaneous circulation and showed improvement in repeat echocardiographic imaging. He had a prolonged course in the ICU and hospital, but eventually made an essentially complete clinical recovery.

Conclusion: As bedside echocardiographic technology becomes more rapidly and readily available, the rapid diagnosis of pulmonary embolism and use of thrombolytics during cardiopulmonary resuscitation may need to be more routinely considered a potential therapeutic adjunctive measure. (*Crit Care Med* 2016; 44:e300–e303)

Key Words: cardiac arrest; cardiopulmonary resuscitation; pulmonary embolism; thrombolysis; venous thromboembolism

Pulmonary embolism (PE) commonly causes cardiovascular collapse and is amenable to a variety of therapies, including thrombolysis in hemodynamically unstable patients. Currently, no treatment is offered in Advanced Cardiovascular Life Support (ACLS) protocols for this potentially deadly disease (1). This is likely due to several factors. First, diagnosing the PE needs certain tests and studies that are not often available during cardiopulmonary resuscitation (CPR). Second, no randomized study has proven the efficacy of thrombolysis in cardiovascular resuscitation (2). Third, it is often believed that by the time of diagnosing PE during an

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Case Report

Successful use of intra-arrest thrombolysis for electrical storm due to acute myocardial infarction☆

Abstract

Acute vascular thrombotic disease, including acute myocardial infarction and pulmonary embolism, accounts for 70% of sudden outpatient cardiac arrest. The role of intra-arrest thrombolytic administration aimed at reversing the underlying cause of cardiac arrest remains an area of debate with recent guidelines advising against routine use. We present a case of prolonged refractory ventricular fibrillation electrical storm in a patient who demonstrated intra-arrest electrocardiographic and sonographic markers confirming acute myocardial infarction. Return of spontaneous circulation was rapidly achieved after rescue intra-arrest bolus thrombolysis. Highlights of this case are discussed in the context of the current evidence for thrombolytic therapy in cardiac arrest with specific attention to the issue of patient selection.

was intermittently achieved during pr
recurrent VF within seconds. The patient
of epinephrine, 50 mL of sodium bicarb
lidocaine, and 6 direct current shocks over
hospital arrival.

On arrival to the emergency department
sponsive and undergoing active CPR. Initial
pulmonary resuscitation was continued. H
episodes of defibrillation and received 150
amiodarone, sodium bicarbonate, calcium g
normal saline. During a rhythm analysis 33
the supraglottic airway device was repla
tube via direct laryngoscopy and confirmed
Venous point-of-care laboratory studies revea
Po_2 29, lactate 13 mmol/L, troponin 0.

Successful Management of Cardiac Arrest Due to Pulmonary Embolus Using Extracorporeal Membrane Oxygenation and Ultrasound-Accelerated Catheter-Directed Thrombolysis

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Here we present the case of a patient that suffered a cardiac arrest due to pulmonary embolus. The patient was resuscitated using extracorporeal membrane oxygenation and treated with ultrasound-accelerated catheter-directed thrombolysis during support on extracorporeal membrane oxygenation, with an excellent outcome. This case demonstrates that the use of extracorporeal membrane oxygenation and ultrasound-accelerated catheter-directed thrombolysis can be highly effective for managing select patients with pulmonary embolus and cardiac arrest.

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Thrombolytic-Enhanced Extracorporeal Cardiopulmonary Resuscitation After Prolonged Cardiac Arrest

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Subjects—Pigs

Interventions—Animals underwent 30-minute untreated ventricular fibrillation cardiac arrest followed by extracorporeal cardiopulmonary resuscitation (ECPR) for 6 hours. Animals were allocated into two experimental groups: t-ECPR, which received Streptokinase 1 MU and c-ECPR which did not receive Streptokinase. In both groups the resuscitation protocol included the following physiologic targets: mean arterial pressure (MAP) > 70 mmHg, Cerebral perfusion pressure (CerPP) > 50 mmHg, PaO_2 150 ± 50 mmHg, $PaCO_2$ 40 ± 5 mmHg and core temperature 33 ± 1 °C. Defibrillation was attempted after 30 minutes of ECPR.

Measurements and Main Results—A cardiac resuscitability score was assessed on the basis of: success of defibrillation; return of spontaneous heart beat; weanability form ECPR; and left ventricular systolic function after weaning. The addition of thrombolytic to ECPR significantly improved cardiac resuscitability (3.7 ± 1.6 in t-ECPR vs 1.0 ± 1.5 in c-ECPR). Arterial lactate clearance was higher in t-ECPR than in c-ECPR (40 ± 15% VS 18 ± 21 %). At the end of the experiment, the intracranial pressure was significantly higher in c-ECPR than in t-ECPR. Recovery of brain electrical activity, as assessed by quantitative analysis of EEG signal, and ischemic neuronal injury on histopathologic examination did not differ between groups. Animals in t-ECPR group did not have increased bleeding complications, including intracerebral hemorrhages.

Conclusions—In a porcine model of prolonged cardiac arrest, thrombolytic-enhanced ECPR improved cardiac resuscitability and reduced brain edema, without increasing bleeding complications. However, early EEG recovery and ischemic neuronal injury were not improved.

- Underlying pathologies: Pulmonary embolism, Acute MI
- Age: Younger patients
- Timing of lysis: t-PA may be administered in at least first 1 hour after CA
- Contraindications ????
- Alternative interventions: extracoporeal membrane oxygenation
- percutaneous coronary intervention

The dose and the rate of thrombolytic???

- 100 mg alteplase over 2 hours or even 90 min infusion
- 0.6-1.0 mg/kg (max 100 mg) alteplase bolus
- 15 mg rtPA bolus →50 mg over 30 min→35 mg over 60 min

- There is no consensus about the dose and the administration method (bolus or infusion or together).

In conclusion;

- Today; the risk/ benefit ratio of thrombolytic in cardiac arrest remains poorly understood.
- Rescue PCI for suspected AMI and
- ECMO for suspected PE were firstly recommended if they will be done immediately in experienced centers.
- If those interventions can not be available, thrombolytic administration will be decided in the earlier time.

Questions??????
Additions……
Experiences…..

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