article.1 We agree with their proposal regarding treatment strategy after percutaneous coronary intervention (PCI). As the addition of anticoagulant treatment to dual antiplatelet therapy has the potential to increase bleeding complications,2-5 routine supplementation of anticoagulant therapy after PCI should be avoided. The lack of patient safety data means that the risks of bleeding are likely to weigh more heavily in decision-making than any benefits. However, some particular clinical situations involving a hypercoagulability state (e.g. impaired cardiac function and/or atrial fibrillation) might be considered suitable for the addition of an anticoagulant. For now though, the selection of triple antiplatelet therapy (warfarin, aspirin, and thienopyridine) for patients after PCI is considered a matter of clinical judgment in respect of each individual patient based on the attending physician’s careful analysis of the perceived balance between the risk of recurrent ischaemic events and the risk of bleeding.

Although dual antiplatelet therapy without anti-coagulation therapy is the gold standard after PCI, recent reports suggest that the tissue factor-mediated pathway of thrombin generation, but not the von Willebrand factor/glycoprotein (GP) Ib- or collagen/GPVI-mediated pathway, is the major pathway leading to platelet activation after laser-induced injury in a mouse model of arterial thrombosis.6 In this model, platelet activation and adherence at the site of injury are inhibited by treatment with lepirudin (thrombin inhibitor),7 suggesting that targeting the initial thrombin generation localized in a platelet thrombus formation could be an important strategy to treat some types of arterial thrombosis. It would be worth investigating the treatment effects of anti-coagulant therapies given that the estimated risk of major bleeding appears low; including such therapies as oral activated coagulation factor X inhibitor and antagonist for protease-activating receptor-1 (the main thrombin receptor in human platelets and endothelial cells). As well, we need to determine an effective combination of antiplatelet drug(s) with these newly available anticoagulants or low-intensity warfarin for use in high-risk patients. Large-prospective cohort studies would be needed to confirm the balance between safety and the benefits of these therapies.

More importantly, our results also mean that patients with arteriothrombosis should be treated considering many aspects, as mentioned by Dr Pastor-Pérez. It is important to recognize that a treatment strategy targeting platelets and a coagulation pathway is just one of them. We need to pay attention to other traditional risk factors and the relevant clinical background that include obesity, blood pressure, diabetes mellitus, smoking, sleep apnea, physical activity, and serum cholesterol level. Reducing these risk factors would likewise greatly reduce the incidence of additional cardiovascular events, and may ameliorate thrombotic markers including platelet reactivity, plasma levels of thrombin generation, surrogate markers for endothelial dysfunction, and plasminogen activator inhibitor-1. Given the cross-sectional nature of the results in our study,1 we regret not clearly addressing whether reducing the level of these biomarkers would be directly associated with any reduction of cardiovascular events. Further detailed prospective trials would be required to clarify the issues raised here.

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Thrombolysis during cardiopulmonary resuscitation should be addressed in guidelines for pulmonary embolism

Pulmonary embolism (PE) has been probably the most misdiagnosed life-threatening disease in cardiology, and high-quality guidelines are needed and welcomed for the diagnosis of PE.7 Also, venous thrombo-embolism remains the most common preventable cause of in-hospital death.2 Shock and hypotension have been re-emphasized as clear indication for thrombolysis in PE,1 but another possible indication was not mentioned: PE was mentioned as a probable cause of cardiac arrest, although substantial interest has been growing on this topic. We found 85 papers in PubMed with key words: resuscitation, thrombolysis, and PE.

Cardiopulmonary resuscitation (CPR) was considered contraindication for fibrinolysis in previous ESC PE Guidelines.2 On the other hand, in the current European guidelines for CPR, it was stated: ‘Consider thrombolytic therapy when cardiac arrest is thought to be due to proven or suspected pulmonary embolus’.4 Additionally, international/American guidelines for CPR also recommended: ‘Adults have been successfully resuscitated following administration of fibrinolytics (tPA) after initial failure of standard CPR techniques,'
particularly when the condition leading to the arrest was acute pulmonary embolism. There is also pragmatic reason to analyse fibrinolysis in PE patients ‘peri-CPR’. Some clinical characteristics can help to identify PE as the likely cause of cardiac arrest including: respiratory distress and altered mental status before the episode, age under 65, witnessed arrest, and the presence of pulseless electrical activity as the first rhythm. With such PE patients correctly identified, fibrinolytic efficacy might be very high, with survival rate over 50%.

In conclusion, PE may cause cardiac arrest, and such patients have been candidates for thrombolysis. This deserves elaboration in PE guidelines, as done in contemporary CPR guidelines, because thrombolysis has been the most important and challenging therapeutic decision in PE.

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**Thrombolysis during cardiopulmonary resuscitation should be addressed in guidelines for cardiopulmonary resuscitation:**

**Emphy**

Dr Koracevic raised an interesting point, suggesting that thrombolysis should be recommended in patients with PE who present with cardiac arrest. Indeed, if caused by PE, cardiac arrest is indicating the highest risk of early death. And resuscitation is no longer considered an important contraindication to thrombotic therapy. The problem is in diagnosing PE in the setting of cardiac arrest.

Thrombotic treatment was suggested to increase the chances of survival in unselected patients with cardiac arrest. However, encouraging preliminary reports and a meta-analysis of eight trials including 926 patients were not confirmed by a large multicentre study. In fact, the TROICA trial was discontinued in April 2006 after enrolling over 1000 patients because the preliminary data analysis indicated that it would be unlikely to demonstrate the superiority of tenecteplase over placebo during cardiopulmonary resuscitation (CPR) in out-of-hospital cardiac arrest. Importantly, the study was not stopped due to safety issues; the intracranial haemorrhage rate was within the expected range for fibrinolytic treatment.

This, of course, does not exclude that thrombolytic treatment could still be a valid option during CPR in selected patients with cardiac arrest and particularly in those in whom pulmonary embolism is clinically suspected. The critical question is how to identify these patients. A randomized trial involving 233 patients in cardiac arrest with episodes of pulseless electrical activity, considered as potentially suggestive of PE, failed to find any benefit in the alteplase arm compared with placebo. Moreover, the prevalence of PE in patients who underwent autopsy was unexpectedly low.

One can argue that circumstances preceding the event might be useful to increase the suspicion of PE. Unfortunately, reliable information is rarely available, especially in out-patient setting; it would thus be difficult to venture any formal recommendations, also defining what kind of information and from what sources could be considered sufficient to justify thrombolysis. Even a patient currently treated for recent PE may suffer cerebral bleeding and not necessarily early recurrence.

Therefore, similar to suspected high-risk PE presenting with hypotension or shock, some objective data collection should be attempted. Van der Wouw et al. reported on the successful use of transesophageal echocardiography (TEE) in the setting of CPR both in prolonged out-of-hospital and in-hospital cardiac arrest. Interestingly, among 48 studied cases, TEE found signs suggestive of PE in six patients, while cardiac tamponade was documented in six others, aortic dissection in five, and rupture in one patient. This highlights the importance of differential diagnosis also in such dramatic circumstances.

In summary, although PE is suspected in every case of cardiac arrest, there are no specific criteria justifying the routine use of thrombolysis in the setting of CPR. There is no evidence that thrombolysis is beneficial in unselected patients, and also in those in whom pulseless electrical activity is recorded during CPR. The use of bedside echocardiography, including TEE, and venous ultrasonography should be encouraged as in other patients with suspected high-risk PE if CT angiography is not an option. Management decisions should be taken based on all collected data on a case-by-case basis.

**References**