# QUESTION

|  |  |
| --- | --- |
|  |  |
| **POPULATION:** | Among adults who are in cardiac arrest due to PE or suspected PE in any setting (P), |
| **INTERVENTION:** | does any specific alteration in treatment algorithm (eg, fibrinolytics, or any other) (I), |
| **COMPARISON:** | compared with standard care (according to 2015 treatment algorithm) (C), |
| **MAIN** | Survival with Favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days AND/OR 1 year, Survival only at |
| **OUTCOMES:** | discharge, 30 days, 60 days, 180 days AND/OR 1 year, ROSC (O) |
| **SETTING:** | Any setting |

**ASSESSMENT**

|  |
| --- |
| **Problem**Is the problem a priority? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * No
* Probably no
* Probably yes
 | Pulmonary Embolism is a (possibly) reversible cause of cardiac arrest and represents 2- 7% of all causes of OHCA {Javaudin 20191167} {Böttiger 2008 2651}. Overall mortality | eCPR is a relatively new therapy concept for CA caused by PE, andthis was not included in the |
| * **Yes**
 | is high, and chances for ROSC and survival can be significantly higher when the embolus | systematic review for 2015.. At the |
| * Varies
* Don't know
 | is removed from the pulmonary artery. Thus, treatment options for cardiac arrestsecondary to pulmonary embolism include administration of fibrinolytics, surgical | moment, this is only available forcertain patients in certain designated centres. |
|  | embolectomy, and percutaneous mechanical thrombectomy. |  |
| **Desirable Effects**How substantial are the desirable anticipated effects? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Trivial
* **Small**
* Moderate
* Large
* Varies
* Don't know
 | Fibrinolysis, surgical embolectomy, and percutaneous mechanical thrombectomy can lead to higher rates of ROSC and finally survival (treatment option for a reversible cause of cardiac arrest, ERC 2015).New evidence since 2015: | French study is registry data of patients with OHCA who were transported to hospital and had diagnosis of PE |

|  |  |  |
| --- | --- | --- |
|  | In a large observational trial, survival at 24 hours was comparable (66% in the thrombolysis group and 63% in the control group, p = .76). {Javaudin 2019 1167}Survival at 30 days was significantly better in fibrinolysis group 9/58 (16%) vs. 12/188 (6%) ; (p=0.005; adjusted log-rank test). {Javaudin 2019 1167}Survival with good neurological outcome (CPC 1-2) on day 30 was not significantly better in the thrombolysis group: six (10%) vs nine (5%) in the control group (adjusted relative risk, 1.97; 95% CI, 0.70-5.56). {Javaudin 2019 1167}A small observational study showed that ROSC was comparable in both groups (tPA 9/19 = 47.4% vs control 11/23 =47.8%, p=0.98) {Yousuf 2016 190} and also. survival to discharge was comparable (2/19 =10.5% vs 2/23 =8.7%; p=1.00) {Yousuf 2016 190}NO new results were identified for surgical embolectomy, and for percutaneous mechanical thrombectomy. | Absolute numbers for 24h survival were not provided |
| **Undesirable Effects**How substantial are the undesirable anticipated effects? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Large
 | In the most recent studies, death from hemorrhage did not occur more often in thrombolysis group than in the control group (6% vs 5%; P = .73) {Javaudin 2019 1167}, and major bleeding complications were not more frequent (5.3% tPA vs. 4.3% control; p=1.00) {Yousuf 2016 190}.The results from TROICA study – which is the largest study with thrombolysis during cardiac arrest –suggest that there is a certain risk for bleeding in the thrombolysis group (any intracranial hemorrhage2.7 vs 0.4 %, RR 6.95 (1.59–30.41) , p=0.006), but major bleeding complications did not occur more often in thrombolysis group (symptomatic intracranial hemorrhage 0.8% vs 0%, RR 8.93 (0.48– 165.45), p=0.13; major non-intracranial hemorrhage 7.7% vs 6.4; RR 1.21 (0.77–1.88), p=0.48; Ischemic stroke 0.8% vs. 0.6%; RR 1.32 (0.30–5.88), p=1.00). {Böttiger 2008 2651}. | Patients die from PE cardiac arrest |
| * Moderate
 | rather from the treatment. |
| * **Small**
 |  |
| * Trivial
 | If fibrinolysis used in patient without |
| * Varies
 | PE, there is a risk of bleeding |
| * Don't know
 |  |
| **Certainty of evidence**What is the overall certainty of the evidence of effects? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * **Very low**
* Low
* Moderate
* High
* No included studies
 | Very low. Only one RCT. Small observational studies with high risk of bias. |  |

|  |
| --- |
| **Values**Is there important uncertainty about or variability in how much people value the main outcomes? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Important uncertainty or variability
* Possibly important uncertainty or variability
* Probably no important uncertaintyor variability
* **No important uncertainty or variability**
 | No |  |
| **Balance of effects**Does the balance between desirable and undesirable effects favor the intervention or the comparison? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Favors the comparison
* Probably favors the comparison
* Does not favor either the intervention or the comparison
* **Probably favors the intervention**
* Favors the intervention
* Varies
* Don't know
 | The presented results probably favors the intervention when PE is highly suspected. | Given the high mortality from cardiac arrest from PE, a small benefit would be of value |
| **Resources required**How large are the resource requirements (costs)? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Large costs
* Moderate costs
* Negligible costs and savings
* Moderate savings
* Large savings
* Varies
* **Don't know**
 | We did not identify studies addressing the costs. For fibrinolysis, the costs must be considered as moderate. | Optimal strategy (dose, drug choice) for use of fibrinolysis is uncertain |
| **Certainty of evidence of required resources**What is the certainty of the evidence of resource requirements (costs)? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |

|  |  |  |
| --- | --- | --- |
| * Very low
* Low
* Moderate
* High
* **No included studies**
 | We did not identify any studies comparing costs between the interventions. |  |
| **Cost effectiveness**Does the cost-effectiveness of the intervention favor the intervention or the comparison? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Favors the comparison
* Probably favors the comparison
* Does not favor either the intervention or the comparison
* Probably favors the intervention
* Favors the intervention
* Varies
* **No included studies**
 | We did not identify any studies addressing cost-effectiveness. |  |
| **Equity**What would be the impact on health equity? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * Reduced
* Probably reduced
* Probably no impact
* Probably increased
* Increased
* Varies
* **Don't know**
 | There is no research evidence on the impact on health equity. |  |
| **Acceptability**Is the intervention acceptable to keystakeholders? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * No
* Probably no
* Probably yes
* **Yes**
 | Currently part of guidelines |  |

|  |  |  |
| --- | --- | --- |
| * Varies
* Don't know
 |  |  |
| **Feasibility**Is the intervention feasible to implement? |
| **JUDGEMENT** | **RESEARCH EVIDENCE** | **ADDITIONAL CONSIDERATIONS** |
| * No
 | Fibrinolyis is already implemented; Surgical embolectomy and percutaneous mechanical thrombectomy are available at specialized | eCPR was not part of this question |
| * Probably no
 | centres only (no new studies identified). | as has been addressed in CoSTR |
| * Probably yes
 |  | 2019 |
| * **Yes**
 |  |  |
| * Varies
 |  |  |
| * Don't know
 |  |  |

**SUMMARY OF JUDGEMENTS**

|  |  |
| --- | --- |
|  | **JUDGEMENT** |
| **PROBLEM** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **DESIRABLE EFFECTS** | **Trivial** | **Small** | Moderate | Large |  | Varies | **Don't know** |
| **UNDESIRABLE EFFECTS** | Large | **Moderate** | **Small** | Trivial |  | Varies | **Don't know** |
| **CERTAINTY OF EVIDENCE** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **VALUES** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | **No important uncertainty or variability** |  |  |  |
| **BALANCE OF EFFECTS** | Favors the comparison | **Probably favors the comparison** | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **RESOURCES REQUIRED** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | **Don't know** |
| **CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **COST EFFECTIVENESS** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **EQUITY** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **ACCEPTABILITY** | No | Probably no | **Probably yes** | **Yes** |  | Varies | Don't know |

|  |  |
| --- | --- |
|  | **JUDGEMENT** |
| **FEASIBILITY** | No | Probably no | **Probably yes** | **Yes** |  | Varies | Don't know |

**TYPE OF RECOMMENDATION**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Strong recommendation against the intervention**○ | **Conditional recommendation against the intervention**○ | **Conditional recommendation for either the intervention or the comparison**○ | **Conditional recommendation for the intervention****●** | **Strong recommendation for the intervention**○ |

**CONCLUSIONS**

##  Recommendation

* **We suggest administering fibrinolytic drugs for cardiac arrest when PE is the suspected cause of cardiac arrest (weak recommendation, very low certainty of evidence).**
* **We suggest the use of fibrinolytic drugs or surgical embolectomy or percutaneous mechanical thrombectomy for cardiac arrest when PE is the known cause of cardiac arrest (weak recommendation, very low certainty of evidence).**

##  Justification

We updated our systematic review from the 2015 guidelines, and we found no new evidence to change the existing recommendations.

Although the overall certainty in the evidence is very low, the current evidence suggests administering fibrinolytic drugs for cardiac arrest when PE is the suspected cause of cardiac arrest. There is no new evidence to support a change to these guidelines.

Newer case series and cohort studies report that eCPR – alone or in combination with one or more of the standard therapies fibrinolysis, surgical embolectomy and/or percutaneous mechanical thrombecomy – may be an effective therapy for CA caused by PE. There is not enough evidence to make a recommendation at the time being. Further studies are required to evaluate this therapy for CA due to PE.

*For the role of eCPR on patients with cardiac arrest due to pulmonary embolism, we refer to the ILCOR CoSTR 2019: 'We suggest that ECPR may be considered as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings in which it can be implemented (weak recommendation, very low certainty of evidence).'[2019 ILCOR CoSTR] {Soar 2019 145}{ Soar 2019 e826}*

##  Subgroup considerations

Subgroups comparing different drugs for fibrinolysis exist, but there is not enough evidence to support either of the drugs.

##  Implementation considerations

Since fibrinolytic drugs are already in use in most systems, we see no substantial concerns related to implementation of this. The option for eCPR depends on the availability in hospital. Diagnosis of PE in cardiac arrest not straight forward.

The optimal dosing regimen is unknown.

##  Monitoring and evaluation

Since fibrinolysis is an implemented therapy, we see no substantial concern regarding this therapy.

##  Research priorities

The overall certainty in the evidence is very low.

**References**

Böttiger BW, Arntz HR, Chamberlain DA, Bluhmki E, Belmans A, Danays T, Carli PA, Adgey JA, Bode C, Wenzel V; TROICA Trial Investigators; European Resuscitation Council Study Group. Thrombolysis during resuscitation for out-of-hospital cardiac arrest. N Engl J Med. 2008;359(25):2651-62.

Doerge HC, Schoendube FA, Loeser H, Walter M, Messmer BJ. Pulmonary embolectomy: review of a 15-year experience and role in the age of thrombolytic therapy. Eur J Cardiothorac Surg. 1996;10(11):952-7.

Fava M, Loyola S, Bertoni H, Dougnac A. Massive pulmonary embolism: percutaneous mechanical thrombectomy during cardiopulmonary resuscitation. J Vasc Interv Radiol. 2005;16(1):119-23.

Janata K, Holzer M, Kürkciyan I, Losert H, Riedmüller E, Pikula B, Laggner AN, Laczika K. Major bleeding complications in cardiopulmonary resuscitation: the place of thrombolytic therapy in cardiac arrest due to massive pulmonary embolism. Resuscitation. 2003;57(1):49-55.

Javaudin F, Lascarrou JB, Le Bastard Q, Bourry Q, Latour C, De Carvalho H, Le Conte P, Escutnaire J, Hubert H, Montassier E, Leclère B; Research Group of the French National Out-of-Hospital Cardiac Arrest Registry (GR-RéAC). Thrombolysis During Resuscitation for Out-of-Hospital Cardiac Arrest Caused by Pulmonary Embolism Increases 30-Day Survival: Findings From the French National Cardiac Arrest Registry. Chest. 2019;156(6):1167-1175.

Konstantinov IE, Saxena P, Koniuszko MD, Alvarez J, Newman MA. Acute massive pulmonary embolism with cardiopulmonary resuscitation: management and results. Tex Heart Inst J. 2007;34(1):41-5.

Kürkciyan I, Meron G, Sterz F, Janata K, Domanovits H, Holzer M, Berzlanovich A, Bankl HC, Laggner AN. Pulmonary embolism as a cause of cardiac arrest: presentation and outcome. Arch Intern Med. 2000;160(10):1529-35.

Soar J, Maconochie I, Wyckoff MH, Olasveengen TM, Singletary EM, Greif R, et al. 2019 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces. Circulation. 2019;140(24):e826-e80.

Soar J, Maconochie I, Wyckoff MH, Olasveengen TM, Singletary EM, Greif R, et al. 2019 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Resuscitation. 2019;145:95-150.

Yousuf T, Brinton T, Ahmed K, Iskander J, Woznicka D, Kramer J, Kopiec A, Chadaga AR, Ortiz K. Tissue Plasminogen Activator Use in Cardiac Arrest Secondary to Fulminant Pulmonary Embolism. J Clin Med Res. 2016;8(3):190-5.