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| Question |
| **Should [Emergent or early CAG with PCI if indicated] vs. [Delayed CAG or no CAG] be used for [Unresponsive adults (> 18 years old) with return of spontaneous circulation (ROSC) after cardiac arrest without ST-segment elevation on ECG]?** |
| **Population:** | [Unresponsive adults (> 18 years old) with return of spontaneous circulation (ROSC) after cardiac arrest] |
| **Intervention:** | [Emergent or early CAG with PCI if indicated] |
| **Comparison:** | [Delayed CAG or no CAG] |
| **Main outcomes:** | Survival at 24 hours-RCTs; Survival to hospital discharge-RCTs; Survival to hospital discharge-no STEMI-RCTs; Survival to hospital discharge-shockable-RCTs; Survival at 30 days-NRCTs; Survival at 90 days-RCTs; Survival at 1 -3 years-NRCTs; Favorable Neurologic Outcome at ICU discharge -RCTs; Favorable Neurologic Outcome at hospital discharge-NRCTs; Favorable Neurologic Outcome at hospital discharge-noSTEMI-NRCTs; Favorable Neurologic Outcome at hospital discharge-shockable-NRCTs; Favorable Neurlogic Outcome at 90 days-RCTs; Favorable Neurologic Outcome at 90 days-noSTEMI-RCTs; Favorable Neurologic Outcome at 90 days-shockable-RCTs; PCI ITT-RCTs; PCI PP-RCTs; Successful PCI ITT-NRCTs; Successful PCI PP-NRCTs; CABG ITT-RCTs; Stroke-ICH-NRCTs; Stroke-ICH-RCTs; Recurrent arrest; Sepsis; Pneumonia; Bleeding; Renal replacement therapy; Acute renal failure; Brady arrhytmias-Pacing; Shock; Survival to hospital discharge-STEMI-NRCTs; Favorable Neurologic Outcome at hospital discharge-STEMI-NRCTs; |
| **Setting:** |  |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** |  |

# Assessment

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| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know | Survival from cardiac arrest is low (~10%). The majority of cardiac arrests are of presumed cardiac etiology amendable to cardiac intervention. Specifics around the use of coronary angriography such as timing, patient populations etc. are not well defined. Patients without ST-segment elevation on ECG are less likely to have a lesion amendable to coronary angiography and percutaneous coronary intervention, compared to patients with ST-segment elevation on ECG. There are, however, patients within this group who require CAG.  | Stable, non-cardiac arrest patients suffering a myocardial infarction without ST-segment elevation on ECG do not require urgent coronary angiography.  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial●Small○ Moderate○ Large○ Varies○ Don't know | Improving patient outcomes after cardiac arrest is of utmost importance. The impact of urgent coronary angiography, however, appears to vary by population. While urgent angiography may be most important in post-cardiac arrest patients with STE on ECG we did not find improved survival or neurological outcome in patients without STE on ECG or with initial shockable cardiac arrest rhythms.  |  |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Large○ Moderate● Small○ Trivial○ Varies○ Don't know | We did not find any evidence of adverse events including, rearrest, bleeding, infection with early coronary angiography compared to delayed coronary angiography.  | Coronary angiography for post-cardiac arrest patients requires considerable resource utilization, cost and may detract from other important intervetnsions such as TTM in undifferentiated post-cardiac arrest patients.  |
| Certainty of evidenceWhat is the overall certainty of the evidence of effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Very low● Low○ Moderate○ High○ No included studies | The certainty of evidence is low for post-cardiac arrest patients with no STEMI on ECG. The effect estimate for survival comes from a single RCT stopped early for futility (OR 1.33 95% CI 0.60 to 2.93) [Kern 2020] and an RCT examining patients with no STEMI and an initial shockable rhythm (OR 0.85, 95% CI 0.60 to 1.22) [Lemkes 2019]. Both studies have confidence intervals for the effect estimate that span 1.00. Further, observational studies and RCTs show effects in opposite directions for survival and neurological outcome.  |  |
| ValuesIs 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 uncertainty or variability○ No important uncertainty or variability | Survival and neurological outcome are both patient-oriented outcomes that are considered highly important for cardiac arrest research. COSCA statement [Haywood 2018] include these as core outcomes for reporting of cardiac arrest. |  |
| Balance of effectsDoes 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 | While the outcome of survival would be valued more than the undesirable effects the effect estimate and certainty of evidence suggests no benefit for early CAG for cardiac arrest patients, patients without STEMI on ECG, and patients with VF as an initial presenting rhythm. This evidence, however, comes from a single RCT where unstable patients were excluded.  |  |
|  Resources requiredHow 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 | Costs were not evaluated in this systematic review. Resource costs, however, are substantial for this intervention and will most likely vary across countries. This would include both costs to the prehospital system and in-hospital system. |  |
| Certainty of evidence of required resourcesWhat 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 include any studies to determine the certainty of evidence around the cost associated with early CAG.  |  |
| Cost effectivenessDoes 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 include any studies that examined the cost-effectiveness of this intervention.  |  |
| EquityWhat 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 |  |  |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | The intervention is widely accepted in non-cardiac arrest patients and in post-cardiac arrest patients with ST-segment elevation no ECG. We did not find evidence to suggest that urgent CAG should also be applied to other groups of post-cardiac arrest patients.  |  |
| FeasibilityIs the intervention feasible to implement? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes○ Yes● Varies○ Don't know | Feasibility of this intervention may vary between jurisdictions. While the intervention is a common treatment for both post-cardiac arrest and non-cardiac arrest patients the feasibility of early angiography for post-cardiac arrest patients would depend on system resources to transport patients to a centre capable of performing the intervention and on the accessibility of a PCI centre. This will vary across regions.  |  |

# Summary of judgements

|  | **Judgement** |
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| **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 |
| **Feasibility** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |

# Type of recommendation

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| 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

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| Recommendation |
| When coronary angiography is considered for comatose post-arrest patients without ST elevation, we suggest that either an early or a delayed approach for angiography is reasonable. (weak recommendation, low certainty of evidence) |
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| Justification |
| In making the above recommendations, the taskforce weighed the fact that we did not find sufficient evidence to demonstrate improved outcomes with early angiography for post cardiac arrest patients without ST-segment elevation regardless of presenting cardiac arrest rhythm (shockable or non-shockable). Patients in cardiogenic shock post arrest were excluded from all studies and there is unlikely to ever be sufficient clinical equipoise to support a randomized trial of delayed intervention in the shock cohort. There may be subgroups of patients without ST-segment elevation with high-risk features that would benefit from earlier coronary angiography. Importantly this review examined the timing of coronary angiography if it was done, and did not compare to no coronary angiography. It may be that survival and functional survival may not be the right outcomes to measure harm or benefit from an intervention that adjusts the timing of PCI in post arrest patients. We know that the majority of patients admitted to hospital after cardiac arrest do not die from cardiac complications and most die as a result of neurologic injury. There are no significant differences in adverse event rates with either time interval.  |

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| Subgroup considerations |
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| Implementation considerations |
| The ability to implement coronary angiography for post-cardiac arrest patients will vary across systems. It will depend on prehospital resources, distance to cath lab and ability of hospitals to perform intervention. Regional variations may also differ in terms of whether patients are transported directly from the field (“Bypass directive”) or if they are transported to local hospitals and then transferred to a cardiac centre at a later time (“inter-facility transfer”).  |

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| Monitoring and evaluation |
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| Research priorities |
| * Future trials should consistently define what are the comparable time intervals to treatment for early compared to late angiography and PCI.
* Whether early coronary angiography improves survival/survival with favorable neuro outcome for post-arrest patients with ST elevation
* Whether angiography, compared to no angiography, improves outcomes in post-arrest patients
* Whether angiography and PCI may improve outcomes in the no ST elevation cohort who present in shock
* No studies identified evaluated this question for cardiac arrest in the in-hospital setting.
* No RCTs compared angiography and PCI vs thrombolysis and early vs late time to treatment interval.
* Most randomized trials have focused on short term survival and functional outcomes so data on longer term outcomes is relatively more limited.
* Relatively few studies examining health related quality of life (HRQoL) outcomes
* There may be newer or alternative endpoints such as functional or biochemical measures that may show a benefit with timing of coronary angiography in cardiac arrest patients
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