**Question:** Does Low or normal neuron specific enolase (NSE), S-100B, neurofilament light (NfL), Tau, GFAP or UCH-1 compared with lack of low or normal levels, predict favorable neurologic outcome at 90-180 days for patients comatose after cardiac arrest?

| **Certainty assessment** | **Certainty** | **Importance** |
| --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** |
| NSE (<17ug/L) |
| 5 | Observational studies (2245 patients) | seriousa | not serious | seriousc | seriousb | Heterogeneity and risk of bias did not allow pooling of studies to generate effect estimates. Different time-points assessed. | very low | CRITICAL |

####  Low levels of S100-B (<0.61 ug/L-0.105 ug/L)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 2 | Observational study (717 patients) | seriousa | seriousf | seriousc | seriousb | Heterogeneity and risk of bias did not allow pooling of studies to generate effect estimates. | Very low | CRITICAL |

#### Low levels of Neurofilament light (NfL) (<30-250 pg/ml)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 3 | Observational study (1047patients) |  seriousa | seriousf | seriousc | seriousb | Heterogeneity and risk of bias did not allow pooling of studies to generate effect estimates. | Very low | CRITICAL |

#### Low levels of TAU (<1.55 pg/ml)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 2 | Observational study (806 patients) |  seriousa | seriousf | seriousc | seriousb | Heterogeneity and risk of bias did not allow pooling of studies to generate effect estimates |  very low | CRITICAL |

#### Low levels of GFAP (<22 pg/ml)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 2 | Observational study (801 patients) |  seriousa | seriousf |  seriousc | seriousb | Heterogeneity and risk of bias did not allow pooling of studies to generate effect estimates |  very low | CRITICAL |

#### Low levels of UCH-1 (<327 pg/ml)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | Observational study (693 patients) |  seriousa | not applicable | seriousc | seriousg |  | very low | CRITICAL |

#### Explanations

a. Risk of bias varied from high to low across studies. Most studies limited by self-fulfilling prophecy. NfL studies looked at frozen samples not available to the clinical team, so less limited by sellf-fulfilling prophecy.

b. Wide range of sensitivities and specificities between studies

c. Most available data (90%) is from patients with OHCA of likely cardiac origin, so may not apply to a large percentage of cardiac arrest patients. Indirectness not present if considering OHCA patients with cardiac etiology

d. Sensitivity ranged from 37 to 69% and specificity from 74% to 89%

e. Sensitivity ranged from 74-88% and specificity from 86-100%

f. Different cutoffs determined to predict favorable outcome in different studies

g. Single study with variable sensitivity and specificity at different time points