Follow up Manual
for patients in the study:

DIrect or Subacute COronary angiography in out-of-hospital cardiac arrest - a randomized Study (DISCO)

November 2019

Principal Investigator: Sten Rubertsson, Professor, MD
Responsible for Follow up visits: Ing-Marie Larsson, PhD, specialized nurse, intensive care, Ewa Wallin, PhD, specialized nurse, intensive care.

Table of Contents

Introduction

The DISCO study investigates if early angiography, (within 120 minutes from randomisation) in patients with cardiac arrest, without ST elevation on ECG, is safe to perform, improves the circulation and survival with good neurological function. Secondary outcome is neurological and cognitive function, depression and anxiety, health related quality of life, fatigue and close relative's situation. A relative is defined as someone that knows the patient well before/after the out-of-hospital cardiac arrest and observes them in daily life, typically a family member or close friend.

To be able to compare the results despite where the follow up takes place, it is important that the tests and questionnaires are introduced and performed in the same way on all study sites. Please note that the person doing the follow up at one and six months shall be blinded to which group the patient is randomized to.

Follow up data is collected at four different timepoints.
Use paper copy for each instrument to collect data. Save the original documents.

Follow-up documentation
Save the original documents. Make sure each instrument has the patients screening number, date for follow up and then register the answers in the e-CRF.
At discharge from ICU: mRS och CPC
One month: EQ-5D-5L, mRS och CPC.
Six months: Patient: EQ-5D-5L, Background, mRS, GOSE, CPC, TSQ, MoCA, SDMT, MFI-20, SHCQ, PHQ9 och GAD7. Close relative: IQCODE-CA, CBS, IES-R and EQ-5D-5L.

e-CRF Manual, user account and access to the e-CRF is given by research nurses Joanna Wessbergh joanna.wessbergh@akademiska.se and Elin Söderman elin.soderman@akademiska.se

Flow chart of the Follow Up

1. At discharge from the ICU

Clinician reported outcome (information on outcome provided by the rater/examiner)

- modified Rankin Scale (mRS)
- Cerebral Performance Category (CPC)

2. At 1 month (30 days ±7) after the cardiac arrest

Patient reported outcome (information on outcome provided by the patient)

- EuroQol health (EQ-5D-5L)

Clinician reported outcome (information on outcome provided by the rater/examiner)

- modified Rankin Scale (mRS)
- Cerebral Performance Category (CPC)

3. At 6 months (180 days ±14)

Patient reported outcome (information on outcome provided by the patient)

- Background information
- EuroQol health (EQ-5D-5L)
- Two simple questions (TSQ)
- Multidimensional Fatigue Inventory (MFI-20)
- Somatic Health Complaints Questionnaire (SHCQ)
- Patient Health Questionnaire 9 (PHQ 9)
- Generalized Anxiety Disorder 7-item scale (GAD 7)

Performance outcome (objective measures on e.g. cognitive or physical functioning

- Montreal Cognitive Assessment (MoCA)
- Symbol Digit Modalitet Test (SDMT)

Clinician reported outcome (information on outcome provided by the rater/examiner)

- Glasgow Outcome Scale - Extended (GOSE)
- modified Rankin Scale (mRS)
- Cerebral Performance Category (CPC)

Observer (proxy) reported outcome (information about outcome provided by an informant who knew the patient before and after the cardiac arrest)

- Modifierat Informant Questionnaire on Cognitive Decline Decline – Cardiac arrest version (IQCODE-CA)

Caregiver burden (information about relatives situation)

- Caregiver burden scale (CBS)
- Impact of event scale (IES)
- EuroQol health (EQ-5D-5L)

Please observe that all instruments are being used with a license or permission only for the DISCO study.

Performance procedure for the follow up. An Overview:

At discharge from the ICU

At discharge from ICU, the patient is being evaluated according to mRS and CPC.
Use the structured interview on the patient and relative. (the 9 questions, mRS-9Q) to asses mRS. Calculate the levels in the electronic calculator. The Calculator is at www.modifiedrankin.com (see instructions p11). Make sure you get enough information during your conversation, so that you can assess CPC. (see instructions p13). Save the original document and registered the answers in the eCRF

At 1 month (30 days ±7)

The patient shall be informed and must have given consent before this event take place.

The person performing the follow up shall be blinded to which randomization group the patient is allocated to. Explain to the patient and/or relative that you don't have knowledge of the study intervention and that you can't answer any questions about the study intervention.

- This follow-up is performed as a telephone interview at 30 days after the cardiac arrest. If the patient is discharged, you can send a letter to the patient including a copy of the EQ-5D-5L (see instruction p9). Start with an initial conversation and establish a good contact with the patient. Go through EQ-5D-5L and let the patient answer the questions. Use the structured interview with the patient (if possible) and/or a relative/proxy to assess mRS (the 9 questions, mRS-9Q). Calculate in the electronic calculator. The calculator is on www.modifiedrankin.com (see instruction p11). Make sure you get enough information for CPC during your conversation (see instructions p13). For patients unable to participate in the interview, information may be collected from a relative or from a proxy (health care professional) caring for the patient

- If the patient is still in the hospital, visit the patient at the ward. Start with an initial conversation and establish a good contact with the patient. Go through EQ-5D-5L and let the patient answer the questions (see instruction p9). Use the structured interview with the patient and relative (if possible) to assess mRS (the 9 questions, mRS-9Q). Calculate in the electronic calculator. The calculator is on www.modifiedrankin.com (see instruction p11). Make sure you get enough information for CPC during your conversation (see instructions p13).

Please note if the follow up is done by phone or personal visit, and where the patient is staying at the time of the follow up. Also note the source of information (patient, relative, or health care professional). Save the original document and registered the answers in the eCRF

At 6 months (180 days ±14)
The person performing the follow up shall be blinded to which randomization group the patient is allocated to.

Invitation:
Send an invitation to the patient to set up a meeting (It is important that you send information to the patient even if you set up a telephone meeting). Encourage the patient to bring a close relative to the visit. You can do this by writing: "You and a close relative) are welcome to…(day, time and place)". Inform them that the visit will take about 60-90 minutes. Remind the patient to bring hearing aid and glasses if he/she uses them.
Preferably coordinate so that the follow up with echocardiogram and blood sampling takes place on the same day, but please inform the patient that the visit will take longer.

One week before the visit, send the following instrument to the patient. Ask the patient to answer the instruments and bring them to the visit. Explain that there are no right or wrong answers, that the questions should be answered according to his/her situation and experience. The patient shall describe his/her situation over the last week.

- Multidimensional Fatigue Inventory (MFI-20)
- Somatic Health Complaints Questionnaire (SHCQ)
- Patient Health Questionnaire 9 (PHQ 9)
- Generalised Anxiety Disorder 7-item scale (GAD 7)

By sending these instruments and give the patient the opportunity to answer them in advance, shortens the visit time and decrease the risk that the patient gets too tired.

The visit:
Perform the visit in the following order:

1. Explain to the patient that you have no information about which group the patient got randomized to, and that you can't have that information. This means that you cant answer any questions about angiography that he/she may have.

2. Establish a good contact with the patient and the relative and explain the procedure with the instrument briefly. Tell them that they are going to answer some questionnaires and answer some questions about how they perceive their situation. Explain that there are no right or wrong answers, that the questions should be answered according to their situation and experience.

3. Let the patient answer the EQ-5D-5L (see instruction p9).

4. Ask questions from the background information form. (see instruction p10).

5. Use the structured interview on the patient and relative (if possible) to assess mRS, (the 9 questions, mRS-9Q). Calculate in the electronic calculator. The calculator is on www.modifiedrankin.com (see instruction p11).

6. Interview the patient (and relative) with GOS-E (see instruction p12).

7. Assess the patient with CPC. You might need to ask some additional questions to get the correct result. (see instructions p13).

8. Ask the patient ”Two simple questions” (TSQ) (see instruction p14).

9. Hand over the IQCODE-CA (see instruction p27), to the relative. Be clear to inform the relative that you would like him/her to complete the questionnaire that concerns the patient's current capacity to perform everyday activities related to mental performance and the ability to remember.

10. Hand over the CBS (see instruction p29), IES-R (see instruction p30) and EQ-5D-5L (see instruction p9) to the relative. Be clear to inform the relative that he/she shall evaluate their own situation.

11. When the relative answers the questionnaires, you can perform some tests on the patient. Inform the relative that they have to wait with any questions they might have until you are done with the patient's tests.

12. Perform the MoCA (see instruction p15).

13. Let the patient do the SDMT (see instruction p19).

14. Go through the instruments the patient did before the visit and ask if there is anything that needs to be explained in MFI-20 (see instruction p21), SHCQ (sre instruction p23), PHQ9 (see instruction p24) and GAD7 (see instruction p25).

15. Make sure all questions have been answered in EQ-5D-5L, MFI-20, SHCQ, PHQ9, and GAD7 before the patient and relative leaves. It's very important that as many questions as possible are answered.

16. Make sure all questions in IQCODE-CA, CBS, IES-R and EQ-5D-5L are answered by the relative before they leave. It's very important that as many questions as possible are answered.

17. Thank the patient and the relative for their participation and make sure they understand their valuable contribution to the study. If no relative participated at the meeting, ask for permission and contact details of whom to contact by telephone to obtain further information for the IQCODE-CA, CBS, IES-R and EQ5D-5L.

18. Complete the assessments. Save the original document and registered the answers in the eCRF. Make sure all documents have the patients screening number and date for follow up.

19. Registered the answers in the e-CRF: EQ-5D-5L (patient), Background information, mRS, GOSE, CPC, TSQ, MoCA, SDMT, MFI-20, SHCQ, PHQ9, GAD7, IQCODE-CA, CBS, IES-R and EQ5D-5L (relative).

20. Now the DISCO study follow-up tests are finished. If any problems occurred during the follow up, it's important that you know what you can help the patient with in accordance with your hospital resources. Don't hesitate to contact us with any

questions you might have regarding the follow up. We will give you the tests/instruments and we are happy to answer your questions.

Contact information

Ing-Marie Larsson
PhD, specialized nurse, intensive care
ing-marie.larsson@surgsci.uu.se

Frequently asked questions

Question: No relative can participate at the follow up visit?
Answer: Ask if it's possible to contact the relative by phone to ask some questions. If possible, explain on the phone how the IQCODE-CA, CBS, EQ-5D-5L and IES-R and send them to the relative with a prepaid and already addressed envelope so that he/she can return it to you

Q: No close relative can answer the questions?
A: If that happens, the IQCODE-CA and the other instruments to relative will be excluded (CBS, EQ5D-5L and IES-R).

Q: The patient can't answer EQ-5D-5L, MFI-20, PHQ9, GAD7, SHCQ due to cognitive impairment?
A: The relative/proxy can help the patient with this, but it must be documented that this is the case.

Q: Can the follow up visit take place in the patient's home if that is easier?
A: You can do the follow up in the patient's home, but you need to be aware that this may take much longer. Studies have shown that the patient gets higher scoring when answering the questions at home, so this may affect the results in the end. Document if the follow up takes place in the patient's home.

Q: A personal visit is not possible (the patient lives far away or can't come in for a visit).
A: Contact us for an alternative phone call follow up. This should be avoided if possible and only be used when a personal visit isn't an option, because comparison will be difficult in the end. However, a phone call follow up is better than no follow up.

Q: The patient is not able to answer the questions due to illness/reduced health?
A:: It is important that you try to perform the follow up anyway, even if the patient scores 0. It's very important that these patients are included in the results.

Q: The patient has cognitive or other problems that are revealed at the follow up?
A: Patients with revealed difficulties during the follow up are in need of more investigations to asses if these difficulties affects the patient's and close relative's everyday life. You will have to be prepared to meet these patients and have a strategy for them. If limitations in every day life are revealed the patient can be in need of rehabilitation/information, to improve functions. If the patient has anxiety/depression it is important that they get medical help, cognitive behaviour therapy etc. Even the relative may need help and support.

Q: The patient has another native language and speaks your language so poorly that the results from the cognitive tests will be hard to interpret.
A: We recommend that you don't use the relative as interpreter. It is very important that you use an authorised interpreter. Tell the interpreter to translate the questions as precisely as possible and not repeat the information unless told to do so. Tell the interpreter to use a first-person perspective when interpreting.
Inform the patient about the interpreter's confidentiality. Complete as many of the tests as possible.

Q: How shall the **the test forms after transferring data to the eCRF**

A: All original documents must be saved and stored in accordance with national rules regarding the data protection law All original documents shall be saved at every site for 15 years so that they are available for inspection by the GCP unit or local authorities.

Q: Is there a standard letter to use when booking the follow up visit?
A: No, there is not. Every study site writes their own model. It is however important that you include the information mentioned in this manual. If you want an example on how to write, please contact us.

Q: If it's not possible to do the follow up within the timeframe (180 days ±14 days) due to illness or operation?
A: Try to make it within the time frame. If not possible, the follow up is better to be performed after the timeframe (not before). Try to avoid it as much as possible.

EuroQol (EQ-5D-5L)

The EQ-5D-5L is a standardized measure of health-related quality of life consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), and a VAS scale of overall self-reported health.

Performance

1. Inform the patient to answer the questions based on how he or she experiences his or her health today.
2. On EQ-VAS, ask the patient to mark with an X on the scale that shows his or her health today. (For example, ask: "mark an X on the scale to indicate how your health is TODAY".
3. Ask the patient to write down the number shown by the X on the scale.

Assessment
Level 1 No problems
Level 2 Minor problems
Level 3 Moderate problems
Level 4 Major problems
Level 5 Extreme problems

Assessment in EQ-VAS represents 100 for best possible health and 0 worst possible health.

Alternative administration
If the patient is not able to complete the EQ-5D-5L due to cognitive disability, a relative may assist the patient, but this must be noted in the comments field in the eCRF. If there is an obvious reason for concern that the patient has provided a response that may not be accurate e.g. the patient actually lives in a nursing home but the patient states that they have no problems doing their usual activities, or when the relative does not agree with the patients answer, the relative may also complete their own version of the EQ-5D-5L based on their perception of the patient's health, in addition to the version completed by the patient. If data is totally missing, describe in the comments field potential reasons why the patient was unable to answer, and if this was related or unrelated to their health.

References
Herdman H, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et.al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality Life Res 2011; 20: 1727-1736.*

The EuroQol Group. EuroQol- a new facility for the measurement of health-related quality of life. *Health Policy 1990; 16: 199-208.*

Background information

The background information describes socio-demographic variables and contains of 11 questions. They are about marital status, education, native tongue, disabilities, previous neurological diseases, occupation, living conditions, where the follow up takes place and the patients relation to the relative joining the follow up.
Ask the questions from the questionnaire to the patient and relative and document the answers.

modified Rankin Scale (mRS)

The mRS measures overall functional outcome after a neurological insult, including degree of disability and dependence in daily activities. The reliability in the assessment improves by using structured questions.

Performance
Start by performing the structured interview with the patient and the informant. For question 1 "Do you have any symptoms that bothers you", it is important to include a broad range of symptoms that are common after a cardiac arrest such as; memory or attention issues, problems with executive functions (reduced planning or organization), fatigue, anxiety, depression or posttraumatic stress. To calculate mRS, use the electronic calculator at www.modifiedrankin.com .

Assessment

0. No symptoms
1. No significant disability despite symptoms; able to perform all usual duties and activities.
2. Slight disability; unable to perform all previous activities but able to look after own affairs without assistance.
3. Moderate disability; Requires some help but can walk without assistance.
4. Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5. Severe disability; bedridden, incontinent, and requires constant nursing care and attention.
6. Death

References
Nolan JP, Soar J, Cariou A, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines for Post-resuscitation Care 2015: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. *Resuscitation*. 2015; 95: 202-22

Patel N, Rao VA, Heilman-Espinosa ER, Lai R, Qesada RA, Flint AC. Simple and reliable determaniation of the modified Rankin Scale score in neurosurgical and neurological patients: The mRS-9Q. *Neurosurgery 2012; 71: 971-975.*

Quinn T, Dawson J, Walters M, & Lees K. Reliability of the modified Rankin Scale: A systematic review. *Stroke 2009; 40: 3393-3395.*

Rankin J. "Cerebral vascular accidents in patients over the age of 60. II. Prognosis." *Scottish Medical Journal 1957*.

Rittenberger JC, Raina K, Holm MB, Kim YJ, Callaway CW. Association between Cerebral Performance Category, Modified Rankin Scale, and discharge disposition after cardiac arrest. *Resuscitation 2011; 82: 1036-1040.*

Glasgow Outcome Scale – Extended (GOSE)

The GOSE is a functional outcome measure of overall social recovery. It addresses the level of consciousness, recovery, disability and social integration.
To increase the comparability between raters and sites, the GOSE structured interview will be used.

Performance
Use the structured interview GOS-Eand ask the questions to assess the patient's level of recovery. **Ask all questions, regardless of the answers you get**. The interview can be done with the patient, the relative, or the patient and relative together. Document who is answering the questions.

Assessment
The overall GOSE score represents 8 categories of outcome (including dead). Use the structure for scoring, provided by the structured interview. Include information from the patient, the informant, performance measures and you own general perception of the patient's outcome, In general, the lowest category reported by any source of information will indicate the total score. The GOSE categories are:

Death
Vegetative State (VS)
Lower Severe Disability (Lower SD)
Upper Severe Disability (Upper SD)
Lower Moderate Disability (Lower MD)
Upper Moderate Recovery (Lower GR)
Lower Good Recovery (Lower GR)
Upper Good Recovery (Upper GR)

References
Jennett B & Bond M. Assessment of outcome after brain damage. *Lancet 1975; 1: 480-484.*

Jennett, B., Snoek, J., Bond, M.R., Brooks, N. (1981). Disability after severe head injury: observations on the use of Glasgow Outcome Scale. *J Neurol. Neurosurg. Psychiatry, 44: 285-293.*

Smith K, Andrew E, Nehme Z, Bernard S. Quality of Life and Functional Outcomes 12 Months After Out-of-Hospital Cardiac Arrest. *Circulation*. *2015;131:174-181.*

Wilson, J.T.L., Pettigrew, L.E.L., Teasdale, G.M. (1998). Structured interview for the Glasgow Outcome Scale and the Extended Glasgow Outcome Scale: guidelines for their use. *Journal of Neurotrauma., 15 (8): 573-585.*

Cerebral Performance Category (CPC)

CPC is a commonly used scale to assess neurological function in cardiac arrest studies

Performance
Assessment is done after collecting information, about the patients functional recovery, from the patient, relative and tests.

Assessment

1. Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychological deficit.
2. Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
3. Severe cerebral disability; conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
4. Coma or vegetative state. Any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.
5. Brain death: apnea, areflexia, EEG silence etc.(dead)

Obs: If the patient is sedated, paralysed or intubated, please assess the patient based on the situation but document for example sedation, muscle relaxant or paralysis.

Reference
Jennett B & Bond M. Assessment of outcome after brain damage. *Lancet 1975; 1: 480-484.*

Two simple questions (TSQ)

The aim of the two simple questions is to capture the patient's perception of dependency in daily activities and mental recovery after the cardiac arrest.
This version also uses two follow up questions.

Performance:
The outcome assessor asks the two questions and documents the answers on the document. If the answer on question 1 is "Yes", you ask question 1b. If the answer on question 2 is "No", you ask question 2b.

Assessment
Possible answers are Yes and No.

If the patient is unable to answer the questions by themselves or needed help by the informant, this must be noted

References
Longstreth WT, Nichol G, Van Ottingham L, & Hallstrom AP. Two simple questions to assess neurological outcome at 3 months after out-of-hospital cardiac arrest: Experience from the public access defibrillation trial. *Resuscitation 2010; 81: 530-533.*

Lilja G, Nielsen N, Friberg H, Horn J, Kjaergard J, Pellis T, et.al. Cognitive function after cardiac arrest and temperature management; rationale and description of a sub-study in the Target Temperature Management. *BMC Cardiovascular disorders 2013; 13: 1-9.*

Montreal Cognitive Assessment (MoCA)

The Montreal Cognitive Assessment (MoCA) is a screening instrument for cognitive dysfunction and assesses different cognitive functions: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation.

Performance
See the Questionnaire
You need a stopwatch and the instructions in your local language. Make sure to speak load and clear. Note in the background sheet if the patient had problems with e.g. physical disability, vision or hearing to such extent that it might have interfered with their results on the MoCA test.

Below follow the instructions in English:
1. Alternating Trail-making test
Instruct the patient: ”Please draw a line going from a number to a letter in ascending order. Begin here [point to (1)] and draw a line from 1 then to A then to 2 and so on. End here [point to (E)].”
Scoring: Give points if the patient can do 1-A-2-B-3-C-4-D-5-E without crossing lines. All errors that the patient doesn’t correct immediately by themselves results in 0 points.

2. Visuoconstructional Skills (Cube):
Give the following instructions, pointing to the cube. ”Copy this drawing as accurately as you can.”
Scoring: a properly executed task gives one point:
a. The figure need to be three-dimensional.
b. All lines need to be there.
c. No extra lines have been added.
d. The lines are relatively parallel with about the same length.
All criteria’s must be fulfilled to be scored with points.

3. Visuoconstructional Skills (Clock)
Ensure that the patient does not look at his/her watch while performing the task and that no clocks are in sight. Indicate the appropriate space and give the following instructions: “Draw a clock. Put in all the numbers and set the time to 10 past 11

Scoring: One point for each of the following criteria’s:
a. Contour (1p): the watch face needs to be circular with only small deviations.
b. Numbers (1p): All numbers on the Watch must exist and no extra. They need to be in order and placed in just about the right place. Roman numbers ar ok as is numbers outside the watch face.
c. Pointers (1p): There need to be two pointers that together show the correct time. Hour pointer must be obviously shorter than the minute pointer. The pointers must be from the centre of the watch and meet in the middle.
All criteria’s must be fulfilled to be scored with points.

4. Naming:
Beginning on the left, point to each figure and say: “Tell me the name of this animal.”

Scoring: One point for the following answers: (1) lion, (2) rhinoceros, (3) camel or dromedary.

5. Memory
Read a list of five words at a rate of one per second, giving the following instructions: "This is a memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn't matter in what order you say them." Mark a check in the allocated space for each word the patient produces on this first trial. When the patient indicates that (s)he has finished (has recalled all words, or can recall no more words), read the list a second time with the following instructions: "I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time." Put a check in the allocated space for each word the patient recalls on the second trial. At the end of the second trial, inform the patient that (s)he will be asked to recall these words again by saying: "I will ask you to recall those words again at the end of the test."
Only two trials are permitted, even if the patient is not able to encode all the words within the two trials
Scoring: No points are given at this time.

6. Attention:
Forward Digit Span: Give the following instructions: "I am going to say some numbers and when I am through, repeat them to me exactly as I said them." Read the five numbers sequence at a rate of one digit per second.

Backward Digit Span: Gives the following instructions: "Now I am going to say some more numbers, but when I am through you must repeat them to me in the backward order." Read the three numbers sequence at a rate of one digit per second.

Scoring: Give one point for every number sequence that they say correct. (Attn: Correct answer backward is 2-4-7).

Vigilance: Read the list of letters at a rate of one per second, after giving the following instructions: "I am going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, do not tap your hand."

Scoring: Give one point for 0-1 errors (An error is a tap on a wrong letter or a failure to tap on the letter A)

Serial 7s: Give the following instructions: "Now, I will ask you to count by subtracting 7 from 100, and then, keep subtracting 7 from your answer until I tell you to stop." Repeat the instruction once if necessary.

Scoring: This assignment gives a maximum of 3 points
Don't give any points (0p) if the subtraction is correct, 1p if only one subtraction is correct, 2p if two or three correct subtractions and 3 p for four or five correct subtractions. Each subtraction is being assets for them self, if the patient gives the wrong answer but then subtract correct from the wrong value, it is a correct answer. For example, if the patient answers: "92-85-78-71-64" number "92" is wrong, but every following subtraction are correct. This is a total of one wrong answer and will give 3p on this assignment.

7. Sentence repetition
Give the following instructions: "*I am going to read you a sentence. Repeat it after me, exactly as I say it* [pause]: **I only know that John is the one to help today**." Following the response, say: *"Now I am going to read you another sentence. Repeat it after me, exactly as I say it* [pause]: **The cat always hid under the couch when dogs were in the room**."
Scoring: Give one point for every correct sentence. Notice if something is left out (for example "is the" or "always") and replacements (for example "John is the one who helped today", "hide" instead of "hid" etc)

8. Verbal fluency
Give the following instructions: "Now, I want you to tell me as many words as you can think of that begin with the letter F. I will tell you to stop after one minute. Proper nouns, numbers, and different forms of a verb are not permitted. Are you ready? [Pause] [Time for 60 sec.] Stop."
Scoring: Give 1p if the patient says 11 or more words in 60 seconds.
Document the answers in the margin on the form.

9. Abstraction
Ask the patient to explain what each pair of words has in common, starting with the example: "I will give you two words and I would like you to tell me to what category they belong to [pause]: an orange and a banana." If the patient responds correctly, reply: "Yes, both items are part of the category Fruits." If the patient answers in a concrete manner, give one additional prompt: "Tell me another category to which these items belong to." If the patient does not give the appropriate response (fruits), say: "Yes, and they also both belong to the category Fruits." No additional instructions or clarifications are given. After the practice trial, say: "Now, a train and a bicycle." Following the response, administer the second trial by saying: "Now, a ruler and a watch." A prompt (one for the entire abstraction section) may be given if none was used during the example.
Scoring: Only the two later assignments are being assist. Give 1p for every correct answer
The following answers are acceptable:
a. Train-Bike = transport, a way to move around, you ride them.
b**.** Ruler-watch = measuring instrument, used for measuring.
The following are not accepted Train-bike= they have wheels; Ruler-watch = they have numbers on them.

10. Delayed recall
Give the following instruction: "I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can remember." Make a check mark (√) for each of the words correctly recalled spontaneously without any cues, in the allocated space.
Scoring: Give 1p for every word that, without help, can be reproduced correctly

Optional
Following the delayed free recall trial, prompt the patient with the semantic category cue provided below for any word not recalled. Make a check mark (√) in the allocated space if the patient remembered the word with the help of a category or multiple-choice cue. Prompt all non-recalled words in this manner. If the patient does not recall the word after the category cue, give him/her a multiple choice trial, using the following example instruction, "Which of the following words do you think it was, NOSE, FACE, or HAND?"

Use the following category and/or multiple choice cues for each word, when appropriate.

FACE:	category cue: part of the body	multiple choice: nose, face, hand
VELVET:	category cue: type of fabric	multiple choice: denim, cotton, velvet
CHURCH:	category cue: type of building	multiple choice: church, school, hospital
DAISY:	category cue: type of flower	multiple choice: rose, daisy, tulip
RED:	category cue: a colour	multiple choice: red, blue, green

Scoring: **No points are allocated for words recalled with a cue.** A cue is used for clinical information purposes only and can give the test interpreter additional information about the type of memory disorder. For memory deficits due to retrieval failures, performance can be improved with a cue. For memory deficits due to encoding failures, performance does not improve with a cue.

11. Orientation
Give the following instructions: "Tell me the date today". If the patient does not give a complete answer, then prompt accordingly by saying: "Tell me the [year, month, exact date, and day of the week]." Then say: "Now tell me the name of this place, and which city it is in."

Scoring: Give 1p for every correct answer. The patient needs to say the exact date and place. One point will be removed if the patient says the wrong day or date.

TOTAL SCORE: Add all points from the right part of the form. Add one point if the patient have 12 years formal education or less. Max score is 30.

If the patient is unable to complete the written portion of the MoCA due to a physical disability such as hemiplegia or blindness the visuospatial/executive part of the test should be excluded, as it demands the ability to write demand visual capability. Do not fill in the score 0 in the eCRF, but instead leave this column empty and write in the comments why the patient could not complete this part (e.g., due to physical disability).

Assessment
Maximum score is 30.
26 points or more indicates normal function. The following cut off levels can give guidance but shall be interpreted carefully because they are not completely validated.

> 26	Normal cognitive function
26-18	Mild cognitive dysfunction
17-10	Moderate cognitive dysfunction
<10	Serious cognitive dysfunction

References
www.mocatest.org

Nasreddine ZS, Philips N.A, Bédirian V, Charbonneau S, Whitehead V, Collin I et al. The Monteral Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *J Am Geriatric Soc 2005; 53: 695-699.*

Rossetti HC, Lacritz LH, Cullum CM, Weiner MF. Normative data for the Montreal Cognitive assessment (MoCA in a population based sample. *Neurology 2011; 27: 1272-1275.*

Symbol Digit Modalities Test (SDMT)

The SDMT is a test of mental speed, sustained attention and concentration.

Performance
You need a stopwatch.
In DISCO trial oral version is being used.
You write down the patients answers on a separate test-form to be able to assess the answers and calculate the scores.
If the patient has problems with the language for some reason, the written version can be used. This must be documented. Please contact us for the correct scoring instrucition if the written version is being used.

- Give the blank test sheet to the patient and continue by reading the following instructions aloud on how to perform the test.
- Please look at these boxes at the top of the page. You can see that each box in the upper row has a little mark in it.
- Now look at the boxes in the row just underneath the marks. Each of the boxes under the marks has a number. Each of the marks in the top row is different, and under each mark in the bottom row is a different number.
- Now look at the next line of boxes [Point to the line of boxes] just under the top two rows. Notice that the boxes on the top have marks, but the boxes underneath are empty. You are to fill each empty box with the number that should go there according to the way they are paired in the key at the top of the page and tell me what the number is
- For example, if you look at the first mark, and then look at the key, you will see that the number 1 goes in the first box. So you call out the number 1 for the first box.
- Now, what number should you put in the second box? Just call it out to me. [Number 5] That´s right. So you would say number '5' to me.
- What number goes in the third box? [Number 2] Two, right. That's the idea.
- You are to fill each of the empty boxes with the numbers that should go in them according to the key and call the number out to me.
- Now, for practice, tell me the numbers that fill in the rest of the boxes until you come to the double line. "When you come to the double line, stop.".

If the patient has not understood the nature of the task, the instructions are repeated with further examples until the nature of the test is clearly understood.

Then continue with the following instructions:

- "Now when I say 'Go!' call out the numbers just like you have been doing until I say 'Stop!'
- I will write the numbers down for you.
- When you come to the end of the first line, go quickly to the next line without stopping, and so on
- If you make a mistake, tell me what you think the correct answer is. Do not skip any boxes and work as QUICKLY as you can.
- Ready? Go!

Exactly 90 seconds from starting, say: “Stop!

Mark the numbers at the separate protocol (with the correct numbers given) sheet as the patient says them.
The patient is allowed to follow the boxes with a finger.”

Assessment
The number of correct answers during 90 seconds are counted. (the test-numbers before the 90 seconds started doesn’t count). For example, 36/39 means that the patient gave 39 answers and 36 where correct and 3 where wrong. This patient gets 36 points.

Patients over 55 years of age had a lower scoring than normal population when the SDMT was tested.
The table shows the mean scoring for normal adults. (numbers in ( ) are standard deviations Generally, scoring falling -1.5 standard deviations from the mean value (for a certain age and educational level) is an indication for possible cerebral disability.

Age	**12 years or less in scool**	**13 years or more in scool**
18-24	61.31 (11.39)	69.91(12.64)
25-34	60.57 (9.14)	65.71(11.64)
35-44	59.87 (10.49)	60.95(11.32)
45-54	53.91 (10.40)	58.31(8.67)
55-64	49.03 (9.03)	54.47 (8.93)
65-78	42.05 (11.26)	52.89 (13.54)

References
Sheridan, L K., Fitzgerald, H E., Adams, K M., Nigg, J T., Martel, M M., Puttler, L I., Wong, M M & Zucker, R A. (2006). Normative Symbol Digit Modalities Test performance in a community-based sample. *Archives of Clinical Neuropsychology, 21 (23-28).*

Smith, A. (1968). The symbol-digit modalities test: A neuropsychological test of learning and other cerebral disorders. *In J.Helmuth (Ed.), Learning disorders*. Seattle: Special Child Publications.

Smith, A. (1982). *Symbol Digit Modalities test; Manual*. Los Angeles: Western psychological services, 11 th print March 2010.

Multidimensional Fatigue Inventory (MFI-20)

MFI-20 is a questionnaire that measures five different dimensions of fatigue. General fatigue, physical fatigue, mental fatigue, less motivation and less activity.

Performance
Instruct the patient to read and answer the questions and mark with a X in the box that match the feeling the patient has had for the last few days. It's important that the patient answers all questions. If done orally the instructions should be read to the patient.

Assessment
The questionnaire contains 20 questions (statements) where the patient for each and every one shall estimate how well the statement match the situation over the last few days. Every statement is graded in a 5 grade scale. Yes-1p to No 5p. Scoring has the following algorithm:

Question 1,3,4,6,7,8,11,12,15,20:
1=1 point
2=2 points
3=3 points
4=4 points
5=5 points

Question 2,5,9,10,13,14,16,17,18,19:
1=5 point
2=4 points
3=3 points
4=2 points
5=1 points

The 20 questions contain five subscales that are calculated separately and give a possible value between 4-20 for every subscale. A higher score indicates more impact of fatigue problems.

1-4	None
5-8	Mild
9-12	Moderate
13-16	Moderately Severe
17-20	Severe

You are not recommended to sum up all 20 questions. But the subscale general fatigue can be used to describe fatigue more generally.

General fatigue	Question: 1, 5, 12, 16
Physical fatigue	Question: 2, 8, 14, 20
Mental fatigue	Question: 7,11, 13, 19
Decreased motivation	Question: 4, 9, 15, 18
Decreased activity	Question: 3, 6, 10, 17

References

Falk K, Swedberg K, Gaston-Johansson F and Ekman I. Fatigue is a prevalent and severe symptom associated with uncertainty and sense of coherence in patients with chronic heart failure. *Eur J Cardiovasc Nurs 2007; 6: 99-104.*

Smets EMA, Garssen B, Bonke B and De Haes J.C.M. The multidimensional fatigue inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psycosomatic Research 1995; 39: 315-325.*

Somatic Health Complaints Questionnaire (SHCQ)

SHCQ is a disease-specific instrument and affects bodily symptoms and has mainly been used for patients with coronary artery diseases. The instrument is divided into four dimensions; out of breath, fatigue, pain and anxiety
The questionnaire contains 13 questions that are being answered on a six-graded scale, Likert Scale. It goes from: Not at all (1) to All the time (6). The patients are asked to answer how often these symptoms have occurred during the last week.

Performance
Ask the patient to answer the questions by marking with an X where the statement match how they have been feeling for the last week.

Assessment
The questions can either be calculated to a total sum of all questions (scoring 13-78) or be divided into dimensions. A higher value indicates a bigger problem.

Fatique; Question 6,7,8,10 (Scoring 4-24)
Pain; Question 1,2,9,11 (Scoring 4-24)
Out of breath; Question 3,4 (Scoring 2-12)
Restlessness/Anxiety; Question 5,12,13 (Scoring 3-18)

References
Brink E, Cliffordson C, Herlitz J, Karlsson BW. Dimensions of the Somatic Complaints Questionnaire (SHCQ) in a sample of myocardial infarction patients. *Eur J Cardiovasc Nurs 2007; 6: 27-31.*

Patient Health Questionnaire 9 (PHQ9)

PHQ-9 is a short self reporting scale, screening for depression according Diagnostic and Statistic Manual of Mental Disorders (DSM- IV) and the measure of symptom level of depression. The nine first statements in PHQ-9 match the nine criteria for depression in DSM-IV. The tenth statement is a simple scale of function. The scale for the first 9 are being scored from 0-3 and then summed.

Performance
Ask the patient to answer every question by marking with a X at the answer that match how they have felt during the last 2 weeks.

Assessment
The Questions are being added to a total score. A high value indicates that there is a big issue.

Interpretation of PHQ-9 when screening for depressive syndrome.
0-9 No actual depression exists
10-14 Grey zone
15-27 An actual depression may exist

Interpretation of PHQ-9 when assessing actual level of symptom
0-4 No/minimal depression
5-9 Mild depression
10-14 Moderate depression
15-19 Moderate severe depression
20-27 Severe depression

Reference
Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep;16(9):606-13.

Generalized Anxiety Disorder 7-item scale (GAD7)

GAD-7 is a brief self-reported scale developed to identify generalized anxiety disorder (GAD) and may be particularly useful in assessing symptom severity and monitoring change across time. The test is for guidance only and can never replace a doctor's visit and accurate diagnosis.

Performance
Ask the patients to answer all questions by marking them with a X where they match the feeling they have had during the last 2 weeks.

Assessment
The 7 Questions are being scored from 0 (Not at all) to 3 (Nearly every day) and then summed. (Total score 0-21).
The levels for Mild, Moderate and Severe anxiety is at 5, 10 and 15 points. When screening fore anxiety disorders the recommended value is 10 or more.

Reference
Spitzer, R. L., Kroenke, K., Williams, J. W., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. Archives Of Internal Medicine, 166(10), 1092-1097.

Assessments answered by relative

Observer (proxy) reported outcome (information about outcome provided by an informant who knew the patient before and after the cardiac arrest)
The Informant Questionnaire on Cognitive Declain in the Elderly-Cardiac arrest (IQCODE-CA)

Caregiver burden (information about relative's situation)
A relative is defined as someone that knows the patient well before/after the out-of-hospital cardiac arrest and observes them in daily life, typically a family member or close friend.

Caregiver burden scale (CBS)
Impact of event scale (IES)
EuroQol health (EQ-5D-5L)

The Informant Questionnaire on Cognitive Decline in the Elderly - Cardiac Arrest version (IQCODE-CA)

The IQCODE-CA is an observer-reported questionnaire on performance in everyday situations to assess decline in cognitive functions after a cardiac arrest and will be answered by a relative, someone that knows the patient well before/after the out-of-hospital cardiac arrest and observes them in daily life, typically a family member or close friend.

Tell the relative that *you would like him/her to complete a questionnaire that concerns the patient's current capacity to perform everyday activities related to mental performance and the ability to remember*. It is important to inform the relative that this is a comparison of the patient's early capacity and present time, not a measure to evaluate how good or bad the patient's abilities are (for example if the patient always have had a difficult time remembering names and the condition is unchanged, the answer will be "unchanged").

Performance

Follow up after 180 days
The purpose is to investigate if the patient's cognitive functions have been changed since the cardiac arrest.

Read through the instructions together with the relative.
Inform and encourage the relative to focus on the capacity the patient has had for the last two weeks and not the time just after discharge from hospital. It is also important to explain that the changes only refer to the time before the cardiac arrest up until now and shall not reflect a change that may have been there before the cardiac arrest (for example; if the person always had difficulties remembering names, and still has but without present decline, the answer will be "no change").
The relative marks the answer with a circle or X. Please make sure they have understood that the middle answer is neutral/unchanged status.
The question about writing letter, also includes emails.

The relative may sit outside/in another room when completing the IQCODE-CA. If the relative stays in the same room when they complete the IQCODE-CA, it is important to tell the relative that they have to wait with any questions until after you have completed the next tests (MoCA, SDMT).

Alternative administration guidelines

If the patient does not have a relative that can participate during the visit, ask the patient about contact details for a relative. On the telephone, explain the IQCODE-CA to the relative and send the questionnaire to the relative by mail to complete and return back to you (do not forget to attach a return envelope and a stamp).

If the patient does not have a relative that can answer the questions, or if they decline any contact, the patient can complete the IQCODE-CA by him/herself. This should be avoided, since the data will be difficult to interpret.

Assessment
Every questions scoring is being summed together and then divided with the total amount of questions (26). If a question is not answered, you divide the score with the total amount of answered questions. If there are more than three unanswered questions, the test should not be evaluated.

The total score is calculated as the sum of all items, divided by the number of items completed. Tests with more than three (3) uncompleted questions should *not* be evaluated. The sum score varies from 1.0-5.0. Higher scores represent greater impairment, where 3.0 indicates a neutral response with no cognitive change after the OHCA. Scores >3.04 indicate that further cognitive testing may be necessary. For individual patients, each item represented by a change may indicate the need of further discussions.

The results varies from 1-5. A higher value indicates an increased reduction.

Score 1 and 2	Better functions than before the arrest/5 years ago
Score 3	The patient has not changed
Score 4	In average there is somewhat worse
Score 5	In average it is much worse

References
Jorm AF, & Jacomb PA. The informant questionnaire on Cognitive Decline in the Elderly (IQCODE): socio demographic correlates, reliability, validity and some norms. *Psychological medicine 1989; 19: 1015-1022.*

Jorm AF. The Informant Questionnaire in Cognitive decline in the Elderly (IQCODE); a review: *International Psychogeriatrics 2004; 16: 1-19.*

Blennow Nordström, E., Lilja, G., Årestedt, K., Friberg, H., Nielsen, N., Vestberg, S., & Cronberg, T. (2017). Validity of the IQCODE-CA: An informant questionnaire on cognitive decline modified for a cardiac arrest population. *Resuscitation, 118*, 8-14.

Caregiver burden scale (CBS)

Caregiver burden scale (CBS) intends to assess perceived burden among people/caregivers of family member with disabilities.

Performance
Instruct the relative to read and answer the questions and mark with an X where the statement match. One answer to each question

Assessment
The scale contains 22 questions that is being answered with four outcomes (no not at all, no barely, yes to some extent, yes great extent) that is being graded from 1-4.
Five dimensions are being described:
Strain
Isolation
Disappointment
Emotional involvement
Environment

For every dimension a mean is being calculated;
Strain: 1, 3, 4, 5, 7, 10, 14, 19
Isolation: 8, 12, 22
Disappointment: 2, 13, 18, 20, 21
Emotional involvement: 6, 11, 16
Environment: 9, 15, 17

Reference
Elmståhl S, Malmberg B, Annerstedt L, Caregiver´s Burden of patients 3-years after stroke assessed by a novel caregiver burden scale. Arch Phys Med Rehabil 1996;77: 117-82.

Impact of event scale-Revised (IES-R)

IES-R is a 22-item self-report measure that assesses subjective distress during the last 7 days caused by traumatic events.
The answers are in relation to a specific event, which should be clarified for the informant i.e the patient's cardiac arrest. IES-R provides a snapshot of current symptoms and can measure change over time. The questions in the IES-R are intended to cover symptoms of relapsing, avoidance and over-stretching. It is not a diagnostic instrument but gives an indication of current problems.

Performance
Instruct the relative to read every statement carefully and then indicate how distressing each difficulty has been for the informant during the last 7 days with respect to the patient's cardiac arrest.

Assessment
Every statement is being graded on a five-graded scale (Not at all=0, A little bit=1, Moderate=2, Quite a bit=3, Extremely=4). The questions can either be summed to a total score or be divided into dimensions A mean value can be calculated on the hole scale or for each dimension.
Please note that if you enter the answers in the eCRF the database will do the calculations for you

Reliving: Question 1, 2, 3, 6, 9, 14, 16, 20
Avoidance: Question 5, 7, 8, 11, 12, 13, 17, 22
Overly tence: Question 4, 10, 15, 18, 19, 21

According to *Assessing Psychological Trauma and PTSD*1 it is recommended that you don't use cut-off points. However, a mean at least 1.89 on a subscale indicate a disturbance.
A mean for the whole scale, of 1.82, indicates PTSD.

References
Arnberg, F.K., Michel, P.-0., & Johannesson, K.B., Properties of Swedish Posttraumatic Stress Measures after a Disaster, Journal of Anxiety Disorders (2014). http://dx.doi.org/10.1016/j.janxdis.2014.02.005

Horowitz, M. J., Wilner, N., & Alvarez, W. (1979). Impact of Event Scale: A measure of subjective stress. Psychosomatic Medicine, 41, 209-218.

Weiss, D.S., & Marmar, C.R. (1997). The Impact of Event Scale-Revised. In J.P. Wilson, T.M. Keane (Eds.), Assessing psychological trauma and PTSD (pp. 399-411). New York: The Guilford Press.