Exploring cognitive impairment in the early stages of an out-of-hospital cardiac arrest – a consecutive case series study

Marco Mion[1], Neil Magee[1], Jean Davis[1], Kelly Farrell[1], Eleni Nikolopoulou[1], Donna Jessup[1], John Davies[1], Grigoris Karamasis[1,2], Thomas Keeble[1,2]

1 – Essex Cardio Thoracic Centre, Basildon and Thurrock University Hospitals, Essex, UK
2 – Anglia Ruskin School of Medicine, Chelmsford, UK

Summary

Cognitive deficits are common, although often mild, in out-of-hospital cardiac arrest patients. Prevalence and severity of cognitive deficits on discharge from acute hospital, however, are not systematically assessed in clinical practice, and not frequently reported in scientific literature, potentially hindering the development of appropriate follow-up care pathways for these patients. We hereby present data from a consecutive case series of 75 out-of-hospital cardiac arrest patients discharged from our hospital over a period of 16 months; for 46 of them we were able to obtain a cognitive profile around the time of discharge from hospital, with 37 of them experiencing cognitive deficits, ranging from mild to severe. Memory, verbal fluency and cognitive flexibility were the areas more frequently impaired. The patients we were able to assess did not differ for age, cerebral performance category score and time to return of spontaneous circulation from those we were unable to assess. Cognitive deficits were not associated with duration of 'no blood flow' during cardiac arrest or with age. Our results suggest that cognitive deficits in the immediate aftermath of out-of-hospital cardiac arrest are common, however these may be missed due to lack of systematic assessment and use of poorly sensitive cognitive tests.

Introduction

Out of hospital cardiac arrest (OHCA) is one of the most prevalent causes for mortality worldwide. In England alone, 31,698 individuals were treated by emergency services in 2020, with 8.3% surviving to hospital discharge ((Out-of-Hospital Carfiac Arrest Overview: England 2020). Better CPR training, early access to defibrillation and improved post-resuscitation care means survival rates are slowly improving (Yan S. et al, 2020; London Ambulance Service, 2019).

Considerable evidence exists that many patients who survive a prolonged period of critical care are at heightened risk of developing psychological, psycho-social, cognitive and behavioural problems once discharged (Rawal et al, 2017; Davies et al, 2017; Lilja 2018, Svenningsen, Langhorn, Ågård, & Dreyer, 2017). In the OHCA survivor population (mostly, but not solely, a subset of ICU survivors), psychological, cognitive and on-going physical health problems have been well documented. Cognitive deficits may be present in up to 40-50% of OHCA survivors in the first 6 to 12 months (Lilja et al, 2015; Lilja, 2017; Moulaert, 2009) affecting memory, information processing, executive functions and visuo-motor skills (Jaszke-Psonka et al., 2016; Lilja et al., 2015, Mędrzycka-Dąbrowska at al., 2018). Return to full participation in everyday life, and to work where applicable, is also lower for cardiac arrest patient compared to, for example, patients recovering from myocardial infarction, with cognitive impairment being a predicting variable of return to work (Lilja et al., 2018).

There is currently limited evidence on cognitive performance of OHCA survivors in the first few days and weeks after cardiac arrest. Executive functioning has been identified as a domain particularly affected in the very early stages (before discharge and in the first two weeks, respectively by Koller at al. 2017 and Steinbush et al. 2017), together with memory and attention (Sabedra et al 2015; Kim, Oh, Park, & Kim, 2019).

Early identification of cognitive deficits is pivotal in offering appropriate and timely support. The 'Activity and Life after Survival of a Cardiac Arrest' RCT demonstrated significant benefits in outcomes of cardiac arrest survivors after early identification and simple nurse-led treatment of cognitive and psychological problems, with additional analyses suggesting a high probability of cost-effectiveness from a societal perspective (Moulaert et al., 2014; Moulaert et al., 2016). The growing recognition of the multi-faceted nature of cardiac arrest survivorship (as discussed in Sawyer at al., 2020) is now beginning to be reflected in the development of clinics integrating cardiac, neurological and psychological follow-up (Boyce & Goossens, 2017; Agarwal et al, 2018; Mion et al., 2020).

The aim of this study was to investigate the early cognitive profile in a consecutive series of OHCA survivors over a period of 18 months and discuss the results in the context of current post-resuscitation pathways.

Methods

Inclusion criteria

All initially comatose patients suffering from an OHCA of presumed cardiac aetiology (as defined by Utstein template, see Perkins et al., 2015) admitted to the Essex Cardiothoracic Centre between November 2017 and April 2019 who made sufficient recovery to be discharged alive from ICU were included in this study. Patients suffering from an OHCA of presumed non-cardiac aetiology are not routinely seen in our centre. They were identified and informally monitored by a senior intensive care nurse, and routinely screened for delirium with the Confusion Assessment Method-Intensive Care Unit (CAM-ICU). After stepdown to a cardiology ward/high dependence unit a first contact was made with the patient (after resolution of delirium, and in preparation for discharge planning), with the aim of providing basic information around common cognitive deficits and psychological difficulties following a cardiac arrest. Verbal consent was sought for referral to neuropsychology; if obtained, the Clinical Psychologist was alerted. At this stage, patients were explained that the assessment offered involved paper and pencil testing around their memory, speed of thinking, and other cognitive skills, as well as a few questions around their mood (not included in this paper). They were told this was likely to take around 30 minutes and it could benefit their recovery if deficits were identified and referrals to appropriate post-discharge services made; however, they remained free to stop/withdraw at any time. No patient declined the assessment; however, three chose not to complete all the tests.

When patients were severely cognitively impaired, or it was dubious whether they could fully understand the purpose of the assessment, their families were involved from the early stages of their care and recovery process; assessments were only conducted after mutual agreement that this was in the patients' best interest, in accordance with the overarching principle of doing no harm and only assess relevant components.

On some occasion patients could not be contacted in time due to their rapid progress along the pathway and quick discharge; in these cases, an attempt was made to contact them after discharge, via telephone call and/or letter, to offer an outpatient appointment as soon as practicable (Appendix 1).

Ethical approval was sought and obtained from the BTUH Research & Development department and this research was classified as service evaluation study.

Cognitive assessment

A first appointment was arranged by the Clinical Psychologist on the cardiology ward before discharge whenever this was possible. Due to the heterogeneity of presentations (ranging from disorder of consciousness to a normal cognitive profile) and to patients' tolerance of the assessment, it was not possible to use a single cognitive battery; we therefore focussed on obtaining a cognitive profile and an indication of severity of impairment, using a small set of tests, scored according to published normative criteria where available.

The main battery consisted of the ACE-III (Addenbrooke's Cognitive Examination- III – a brief cognitive test that investigates different cognitive domains), the Trail Making Test part B (a test of visual scanning, processing speed and cognitive flexibility), and the Frontal Assessment Battery (a short battery designed to assess executive functioning). This battery covered a wide range of cognitive functions, including those known to be affected in OHCA patients after 6 to 12 months (memory, processing speed, executive functioning and visuo-motor skills).

A minority of patients (3) were deemed too frail, fatigued or cognitively impaired (e.g. they displayed severe memory deficits on the ward) to engage in the full battery; in this case the MoCA was used instead (Montreal Cognitive Assessment – a brief cognitive screening tool, usually administered in 15 minutes and recommended by ERC guidelines). Patients with more significant cognitive impairment and unable to respond to verbal commands, or in a disorder of consciousness state were monitored using serial administration of the Coma Recovery Scale-Revised or the Glasgow Coma Scale (see Table 1 for a summary of the assessment tools used).

Table 1 – List of cognitive assessments administered to patients

MoCA N=3	ACE-III, FAB, TMT Part A and B (3 patients did not complete the TMT, and 2 did not complete the FAB) N=34	Functional outcome measures (Coma Recovery Scale- R – CRS-R; Glasgow Coma Scale - GCS) N=9

ACE-III - Addenbrooke's Cognitive Examination-III (ACE-III)
FAB - The Frontal Assessment Battery
TMT Part A and B - The Trail Making Test
MoCA – Montreal Cognitive Assessment

For all patients we calculated a CPC (Cerebral Performance Category) score, based only on discharge reports and progress notes, to estimate neurological outcome at the point of discharge from our hospital.

In scoring the assessments we used the following thresholds and criteria for impairment:

- < 88 on the ACE-III (a threshold for probable neurocognitive disorder in community dwelling-individuals, mostly validated in the assessment of dementia)**;**
- A score of ≤ 12 on the FAB. This has been suggested as a cut-off to identify frontal dysfunction in several neurodegenerative conditions (Dubois et al.,2000)
- A score below the age-adjusted 10% percentile on the TMT B, which is suggestive of deficits in processing speed/ cognitive flexibility (according to normative data in age-matched, community-dwelling individuals, Tombaugh, 2004)
- MoCA 18-25 for mild impairment; 10 to 17 for moderate impairment (https://www.mocatest.org/faq/)

Patients were ranked according to the number of tests where they performed below the cut-off, and for the purpose of this study were categorized as following:

- No score below cut-off – normal cognitive profile
- One or two scores below cut-off (or MoCA between 18 and 25)– mild impairment
- Three or four scores below cut-off (or MoCA between 10-17)– moderate impairment
- Patients that were unable to respond to verbal command and to engage in cognitive assessment were monitored using the CRS-R and GCS and categorized as moderately/severely impaired.

For all patients who underwent cognitive testing, severity of cognitive impairment as defined in this study was cross tabulated with the independently calculated CPC score, to investigate if the two approaches measured a similar construct (neurological outcome) and possible differences in sensitivity to cognitive impairment. A summary of patients' scores on cognitive testing, qualitative assessments and categorization of cognitive profile (normal, mild impairment, moderate impairment, moderate/severe impairment) is provided in Appendix 2

The level of cognitive impairment, according to the criteria outlined above, was entered into a multinomial regression as a dependent variable to investigate the role of time to return of spontaneous circulation (ROSC).–and Age in predicting cognitive outcome. Analyses were conducted using Jamovi (The Jamovi Project (2020).

Results

Between November 2017 and April 2019, a total of 120 initially comatose patients were admitted to the cardio-thoracic centre following an OHCA, with 75 (62.5%) surviving to hospital discharge (Men = 63; Women = 12); the median age was 64 years (range 30 – 86; IQR 18.5), and the median length of stay in our hospital was 16 days (range 4 – 58; IQR 9.5). Cardiac aetiology was confirmed based on inpatient diagnosing testing for 73 of them (2 patients had suffered a cardiorespiratory arrest secondary to pulmonary embolism). No patient had any previous history of psychosis or dementia; one patient had multiple sclerosis and two had a past medical history of stroke, with one having made a full cognitive/physical recovery (reported in a previous discharge report), and the other having some persisting memory deficits but no physical impairment. One patient suffered a minor stroke in the context of their OHCA. Of these 75 patients, 51 were discharged home, whereas 24 needed further inpatient rehabilitation. More data around the cardiac arrest, including initial heart rhythm, estimated time since return of spontaneous circulation (ROSC) when available, CPC score as well as details around discharge destination, are provided in Appendix 3.

Of the surviving 75 patient 3 were transferred to another hospital for emergency treatment early in their admission, and 26 were not seen due to a quick discharge from hospital and no reply to telephone calls/letters with invitation for an early outpatient review.

Of the remaining 46 patients, 30 underwent standardized testing prior to discharge (median = 5 days pre-discharge, range 0 – 25; IQR 6) 7 soon after discharge (median = 37 days post-discharge, range 10 – 75, IQR 26) and for 9 we could only complete a serial administration of the Coma Recovery Scale-Revised or the Glasgow Coma Scale up to the point of discharge, due to severity of their cognitive impairment.

In this study, patients with a short length of stay were more likely to be missed or decline participation if contacted after discharge (patient not assessed: mean length-of-stay 14.6 days (range 5-26); assessed patient 20.7 days (range 5-58); $t(2.29)$; $p=0.025$). These two groups however did not differ for age (not assessed: mean 63.8 years; assessed 61 years; $t(-0.908)$, $p=0.367$), time to ROSC (not assessed mean 21.8 minutes; assessed 22.3 minutes; $t(0.126)$; $p=0.90$) or CPC score at discharge (Mann-Whitney $U=621$, $p=0.550$)

When adopting the criteria reported in the methods section, of the 46 patients we assessed 9 (19.6%) experienced no cognitive deficits; 13 (28.2%) could be considered as suffering mild cognitive impairment, 15 (32.6%) moderate cognitive impairment and 9 (19.6%) moderate to severe cognitive impairment (disorder of consciousness; generalized cognitive impairment; ongoing confabulation).

At a group level, performance on the ACE-III where this was available (n=34) suggests that most points were lost in the memory and fluency subtests (Table 2). In the TMT part B, 17 of 31 patients (55%) scored below the age-adjusted cut-off score. 6 of the 32 patients who completed the FAB (19%) scored below the cut-off.

	Attention	***Memory***	***Verbal Fluency***	***Language***	***Visuospatial***
Mean	15.2	18.4	8.2	23.9	14.1
Median	16	18	7	25	15
Range	(8-18)	(5-26)	(2-14)	(18-26)	(7-16)
Maximum possible score	18	26	14	26	16

Table 2 – Mean score, median score and range of scores in each subtest of the ACE-III for the 34 patients completing this assessment.

In the subset of patients we assessed, we cross-tabulated the severity of cognitive impairment according to our own criteria against the CPC score independently calculated based on discharge reports. Agreement was excellent for patient classified as not impaired/mildly impaired (all CPC 1 – good neurological outcome) and moderately/severely impaired (all CPC 3 or 4 – poor neurological outcome), but less so for patient in the 'moderate impairment' category (Table 3).

CPC at discharge (discharge notes)	***No Impairment (cognitive assessment)***	***Mild Impairment (cognitive assessment)***	***Moderate Impairment (cognitive assessment)***	***Moderate/Severe Impairment (cognitive assessment)***	***Total (cognitive assessment)***
1	10	13	7	0	30
2	0	0	6	0	6
3	0	0	2	4	6
4	0	0	0	4	4
Total	10	13	15	8	46

Table 3 – Patients' level of cognitive impairment as identified using our criteria cross-tabulated against CPC scores independently calculated based on discharge reports.

For this group, we also ran a multinomial regression with severity of cognitive impairment (as described above) as dependent variable, and Time to ROSC, Age and time to ROSC x Age interaction as factors to investigate their possible role on cognitive outcome. No significant correlation was found between any of these factors and severity of cognitive impairment (Time to ROSC $\chi^2 = 4.05$; $p=0.256$; Age $\chi^2 = 5.52$; $p=0.137$; Time to ROSC*Age $\chi^2 = 3.61$; $p=0.307$).

Discussion

In this study we aimed to assess the early cognitive outcome of out-of-hospital cardiac arrest survivors in a case consecutive series.

Our data suggest a high incidence of cognitive deficits around the time of discharge from hospital (only around 20% of the group we assessed did not experience any deficits in the tests administered). For some survivors this may be the result of a transitory metabolic encephalopathy, with a favourable outcome (Berisavac et al., 2017; Czyż-Szypenbejl K et al, 2019); however for others it may suggest a degree of brain damage and the possibility of persisting deficits, whose impact on day to day functioning would need to be assessed individually. In this study, many patients experienced deficits with delayed verbal memory and verbal fluency in the ACE-III, and information processing/cognitive flexibility in the TMT B. More significant executive dysfunction, as identified by the FAB, was less common. This is in line with previous research into early cognitive deficits after OHCA (Sabedra A. et al, 2015; Koller at al., 2017; Steinbush et al., 2017; Kim, Oh, Park, & Kim, 2019) and also with the deficits identified in delayed memory and information processing 6 to 12 months after an OHCA (Jaszke-Psonka et al., 2016; Lilja et al., 2015) ,

When we compared the level of cognitive deficits against the CPC score (calculated independently), all patients classified as not impaired or mildly impaired fell in CPC1 and all of those classified as moderately/severely impaired fell between CPC 3 and 4; patients classified as moderately impaired, however, showed a wider range of neurological outcomes (from CPC 1 to CPC 3). It is possible that the more granular approach here presented could better identify the degree of impairment of this group of patients; the CPC has indeed been criticized for its poor sensitivity in detecting cognitive impairment, in addition to originating from the healthcare provider and failing to take into account the survivor's perspective (Sawyer et al., 2020). We suggest that patients presenting with multiple mild cognitive deficits, even when the neurological outcome appears unremarkable, could benefit from close monitoring and early follow-up after discharge.

In the 46 patients we were able to assess, time to ROSC, age and interaction between the two were not related to the level of cognitive impairment at this very early point after OHCA (mostly <1 month). The lack of a correlation between time to ROSC and cognitive outcome is at odds with a recent study finding a significant negative correlation between time to ROSC, age, length of stay and performance on the MMSE (mini mental state examination) prior to discharge from ICU (Kim, Oh, Park, & Kim, 2019); it is worth however mentioning that almost all survivors in this study had favourable case features such as shockable initial cardiac rhythm, bystander CPR and witnessed cardiac arrest, all factors that can potentially reduce the impact of longer resuscitation times (Reynolds et al., 2016). Our patients were also assessed closer to the point of discharge, usually a few days after step-down from ITU. Importantly, this finding suggests that age, time to ROSC and the interaction between the two should not be relied upon to decide which patients should undergo a cognitive assessment before discharge.

A key strength of this study was the attempt to systematic screen for cognitive deficits after an OHCA in a case consecutive series of patients. In our clinic this provided an opportunity to deliver tailored psychoeducation to patients and their families on the early effects of surviving a cardiac arrest, including (but not limited to) normalization of distressing experience of memory loss and difficulty with cognitive flexibility, to facilitate psychological adjustment. As survivors and their families are unlikely to be able to fully engage in psychoeducation during this period (due to ongoing high levels of distress and ongoing cognitive problems, Sawyer et al. 2020) they were given an ad-hoc information leaflet to read this information in their own time, before and after discharge, (https://www.suddencardiacarrestuk.org/shop/sudden-cardiac-arrest-uk-leaflet/), a link to an online resources group created by our team (http://www.lifeaftercardiacarrest.com), and a telephone call one week after discharge by a specialist nurse part of our team to provide the opportunity to discuss any serious concerns.

There were however some limits in this study. The lack of a register to quickly identify OHCA survivors, the fast-paced nature of hospital discharges and the limited extent of funded research time meant that some patients were discharged before they could be seen on the ward. In addition, 26 of the 33 patients we contacted after discharge did not respond to our phone calls/letters (22) or declined the assessment (4). We tried to mitigate this lack of data by calculating a CPC score for every OHCA survivor based on discharge report and progress notes and investigating possible differences between the group of patients. We found that patients not assessed in this study had a shorter length of stay in hospital, but did not differ in age, time to ROSC or CPC score at discharge from hospital from the patients we assessed, suggesting the two groups may be comparable.

Another limitation of our study is the test battery we used to investigate cognitive status. The decision to adopt this battery rather than the MoCA, as recommended by ERC guidelines for follow-up assessment, was guided by the observation that the MoCA does not assess processing speed, which is an area often affected after OHCA (Steinbush et al 2017; Jaszke-Psonka et al., 2016). In addition, a flawless performance on the MoCA in other acute neurological conditions can often be associated with impaired cognitive performance on more in-depth neuropsychological assessment (Chan et al, 2014). Future studies could be aimed at validating a short cognitive battery focused on the domains most commonly affected after an OHCA and compare its performance against the MoCA; in addition, longitudinal studies focusing on pre-discharge cognitive assessment and mid/long term follow up (between 3 and 12 months) are also warranted in our opinion to better understand early predictors of persisting cognitive deficits (as in Steinbush et al 2017). In our study, every patient was offered a more detailed neuropsychological assessment at 3-months post-discharge to investigate their cognitive profile, however only 13 patients completed it and this data is not included in this paper.

As this study was aimed at investigating a very wide range of possible cognitive outcomes, different assessments had to be conducted where necessary. Patients with very severe cognitive impairment who were unable to respond to verbal commands or in a disorder of consciousness state were assessed with observational scales; the remaining patients were all candidates for the full battery, however for three patients a clinical decision was made to administer the MoCA as they were frail, very fatigable and displayed significant memory deficits on the ward. Although this approach limits the ability to directly compare performance within the group, we believe that the criteria we proposed to evaluate severity of early cognitive outcome allow for a meaningful grading of severity of cognitive impairment. It also shows good agreement with the independently calculated CPC scores.

Another limitation of this study is the lack of a control group. OHCA survivors share risk factors both with patients suffering myocardial infarction (MI) only (e.g. coronary artery disease), and with patients receiving critical care for other reasons (sedation, hypoxia, hypoxaemia, etc.). Although recent studies have suggested that OHCA survivors experience specific and additional cognitive deficits compared to MI survivors (Lilja et al., 2015), investigations are needed as to whether they differ from those of patients admitted to ICU following other critical-care related complications.

Conclusions

The results of this study suggest that cognitive deficits in the early stages of surviving an OHCA are very common, with the domains of memory, verbal fluency and processing speed/cognitive flexibility more significantly impaired, in line with the evidence currently available in the literature.

In this study age and time to ROSC did not predict cognitive outcome; relying on these variables alone to choose who should undergo cognitive testing could therefore risk missing survivors with more subtle cognitive impairment., We provide novel evidence that a short battery aimed at assessing memory, cognitive flexibility and processing speed is well tolerated by a majority of OHCA survivors able to engage in formal testing, and can identify cognitive deficits in patients with a good neurological outcome who might however benefit from cognitive rehabilitation or other care options after discharge.

Funding Details and Disclosure Statements

This work was supported by SADS UK (https://www.sadsuk.org.uk/). The authors report no conflict of interest.

Bibliography

Agarwal S, Presciutti A, Anbarasan D, Golding L, Pavol M. (2018) NeuroCardiac Comprehensive Care Clinic Seeks to Define and Detect Neurological, Psychiatric, and Functional Sequelae in Cardiac Arrest Survivors. *Circulation*. 2018;138:A302

Berisavac, I., Jovanović, D., Padjen, V., Ercegovac, M., Stanarčević, P. J., Budimkić-Stefanović, M., … Beslać-Bumbaširević, L. (2017). How to recognize and treat metabolic encephalopathy in Neurology intensive care unit. *Neurology India*; *65*: 123-128. https://doi.org/10.4103/0028-3886.198192

Boyce, L. W., & Goossens, P. H. (2017). Rehabilitation after cardiac arrest: Integration of neurologic and cardiac rehabilitation. *Seminars in Neurology*; *37*: 94–102. https://doi.org/10.1055/s-0036-1593860

Chan E, Khan S, Oliver R, Gill SK, Werring DJ, Cipolotti L. (2014). Underestimation of cognitive impairments by the Montreal Cognitive Assessment (MoCA) in an acute stroke unit population. *J Neurol Sci.* 2014; 343:176-9. http://doi: 10.1016/j.jns.2014.05.005

Czyż-Szypenbejl K, Mędrzycka-Dąbrowska W, Kwiecień-Jaguś K, Lewandowska K. (2019). The Occurrence of Postoperative Cognitive Dysfunction (POCD) - Systematic Review. *Psychiatr Pol*. 28;53:145-160. http://doi: 10.12740/PP/90648.

Davies S., Rhys M., Voss S., Greenwood R., Thomas M., Benger J. Psychological wellbeing in survivors of cardiac arrest, and its relationship to neurocognitive function. *Resuscitation; 111*: 22-25. https://doi.org/10.1016/j.resuscitation.2016.11.004

Dubois B., Slachevsky A., Litvan I., Pillon B. (2000). The FAB: a frontal assessment battery at bedside. *Neurology*; 55:1621-1626. https://doi:10.1212/wnl.55.11.1621

Hawkes, C., Booth, S., Ji, C., Brace-McDonnell, S. J., Whittington, A., Mapstone, J., … Perkins, G. D. (2017). Epidemiology and outcomes from out-of-hospital cardiac arrests in England. *Resuscitation*; *110*: 133–140. https://doi.org/10.1016/j.resuscitation.2016.10.030

Kim, S. H., Oh, S. H., Park, K. N., & Kim, T. H. (2019). Cognitive Impairment among Cardiac Arrest Survivors in the ICU: A Retrospective Study. *Emergency Medicine International*; 1–9. https://doi.org/10.1155/2019/2578258

Koller AC, Rittenberger JC, Repine MJ, Morgan PW, Kristan J, Callaway CW; Post-Cardiac Arrest Service. (2017). Comparison of three cognitive exams in cardiac arrest survivors. *Resuscitation*; 116:98-104. https://doi: 10.1016/j.resuscitation.2017.04.011.

Islam, S., Hampton-Till, J., Watson, N., Mannakkara, N. N., Hamarneh, A., Webber, T., … Keeble, T. R. (2015). Early targeted brain COOLing in the cardiac CATHeterisation laboratory following cardiac arrest (COOLCATH). *Resuscitation*; *97*: 61–67. https://doi.org/10.1016/j.resuscitation.2015.09.386

Jaszke-Psonka, M., Piegza, M., Ścisło, P., Pudlo, R., Piegza, J., Badura-Brzoza, K., … Gorczyca, P. W. (2016). Cognitive impairment after sudden cardiac arrest. *Kardiochirurgia i Torakochirurgia Polska*; *13*: 393–398. https://doi.org/10.5114/kitp.2016.64893

Lilja, G., Nielsen, N., Friberg, H., Horn, J., Kjaergaard, J., Nilsson, F., … Cronberg, T. (2015). Cognitive Function in survivors of out-of-hospital cardiac arrest after target temperature management at 33℃ Versus 36℃. *Circulation*. https://doi.org/10.1161/CIRCULATIONAHA.114.014414

Lilja, G. (2017). Follow-up of cardiac arrest survivors: Why, how, and when? a practical approach. *Seminars in Neurology*; *37*: 88–93. https://doi.org/10.1055/s-0036-1593859

Lilja, G., Nielsen, N., Bro-Jeppesen J., Dunford H., Friberg H., … Cronberg, T. (2018). Return to work and participation in society after out-of-hospital cardiac arrest. *Circulation*. https://doi.org/10.1161/CIRCOUTCOMES.117.003566

London Ambulance Service (2019). Cardiac arrest annual report: 2018-2019. https://www.londonambulance.nhs.uk/wp-content/uploads/2020/01/Cardiac-Arrest-Annual-Report-2018-2019.pdf. Accessed on 1st February 2021.

Mędrzycka-Dąbrowska WA, Czyż-Szybenbejl K., Kwiecień-Jaguś K., Lewandowska K. Prediction of cognitive dysfunction after resuscitation - a systematic review. *Postepy Kardiol Interwencyjnej*. 2018;14:225-232. https://doi: 10.5114/aic.2018.78324.

Mion, M., Al-Janabi, F., Islam, S., Magee, N., Balasubramanian, R., Watson, N., … Keeble, T. R. (2020). Care after REsuscitation: Implementation of the United Kingdom's First Dedicated Multidisciplinary Follow-Up Program for Survivors of Out-of-Hospital Cardiac Arrest. *Therapeutic Hypothermia and Temperature Management*; *10*: 53–59. https://doi.org/10.1089/ther.2018.0048

Moulaert, V. R., Verbunt, J. A., Cm Van Haastregt, J., Wade, D. T. (2009). Cognitive impairment in survivors of out-of-hospital cardiac arrest: A systematic review. *Resuscitation*; 89: 297-305. https://doi.org/10.1016/j.resuscitation.2008.10.034

Moulaert, V. R., Cm Van Haastregt, J., Wade, D. T., Van Heugten, C. M., & Verbunt, J. A. (2014). "Stand still …, and move on", an early neurologically-focused follow-up for cardiac arrest survivors and their caregivers: a process evaluation. *BMC Health Services Research*, *14*. https://10.1186/1472-6963-14-34

Moulaert, V. R. M., Goossens, M., Heijnders, I. L. C., Verbunt, J. A., & Heugten, C. M. va. (2016). Early neurologically focused follow-up after cardiac arrest is cost-effective: A trial-based economic evaluation. *Resuscitation*; *106*: 30–36. https://doi.org/10.1016/j.resuscitation.2016.06.015

Out-of-Hopital Cardiac Arrest Overview: England 2020. Out-of-Hospital Cardiac Arrest Outcomes (OHCAO) Project Annual Epidemiology and Outcomes. https://warwick.ac.uk/fac/sci/med/research/ctu/trials/ohcao/publications/epidemiologyreports/ohca_epidemiological_report_2020_-_england_overview.pdf. Accessed November 13th, 2021.

Perkins G., Jacobs I., Nadkarni V., Berg R., Bhanji F., Biarent D., …. Utstein Collaborators. Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: A Statement for Healthcare Professionals From a Task Force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. *Resuscitation;* 201:96:328-40. https://doi: 10.1016/j.resuscitation.2014.11.002.

Rawal G., Yadav S., Kumar R. (2017). Post-intensive care syndrome: an overview. J Transl Int Med; 5: 90-92. https://doi:10.1515/jtim-2016-0016

Reynolds, J. C., Grunau, B. E., Rittenberger, J. C., Sawyer, K. N., Kurz, M. C., & Callaway, C. W. (2016). Association between Duration of Resuscitation and Favorable Outcome after Out-of-Hospital Cardiac Arrest: Implications for Prolonging or Terminating Resuscitation. *Circulation*;*134*: 2084–2094. https://doi.org/10.1161/CIRCULATIONAHA.116.023309

Sabedra AR, Kristan J, Raina K, Holm MB, Callaway CW, Guyette FX, Dezfulian C, Doshi AA, Rittenberger JC. (2015). Neurocognitive outcomes following successful resuscitation from cardiac arrest. *Resuscitation*;90:67-72. https://doi: 10.1016/j.resuscitation.2015.02.023.

Sawyer KN, Camp-Rogers TR, Kotini-Shah P, Del Rios M, Gossip, Moitra VK et al. (2020). Sudden Cardiac Arrest Survivorship: A Scientific Statement From the American Heart Association.

Circulation;141:e654-e685. https://doi.org/10.1161/CIR.0000000000000747

Svenningsen, H., Langhorn, L., Ågård, A. S., & Dreyer, P. (2017). Post-ICU symptoms, consequences, and follow-up: an integrative review. *Nursing in Critical Care*; *22*: 212–220. https://doi.org/10.1111/nicc.12165

Steinbusch C., van Heugten C., Rasquin S., Verbunt J., Moulaert V. (2017). Cognitive impairments and subjective cognitive complaints after survival of cardiac arrest: A prospective longitudinal cohort study. *Resuscitation; 120: 132-137.* https:// 10.1016/j.resuscitation.2017.08.007

The Jamovi project (2020). *jamovi* (Version 1.2) [Computer Software]. Retrieved from https://www.jamovi.org

Tombaugh, T. N. (2004). Trail Making Test A and B: Normative data stratified by age and education. *Archives of Clinical Neuropsychology*; *19*: 203–214. https://doi.org/10.1016/S0887-6177(03)00039-8

Yan, S., Gan, Y., Jiang, N. *et al.* The global survival rate among adult out-of-hospital cardiac arrest patients who received cardiopulmonary resuscitation: a systematic review and meta-analysis. *Crit Care* 24, 61. https://doi.org/10.1186/s13054-020-2773-2