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Clinical paper

Routine reporting of grey-white matter differentiation in early brain computed tomography in comatose patients after cardiac arrest: A substudy of the COACT trial

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Abstract

Aim: A multimodal approach is advised for neurological prognostication in comatose patients after out-of-hospital cardiac arrest (OHCA). Grey-white matter differentiation (grey-white ratio, GWR) obtained from a brain CT scan performed < 24 hours after return of circulation can be part of this approach. The aims of this study were to investigate the frequency and method of reporting the GWR in brain CT scan reports and their association with outcome.

Methods: This is a post-hoc descriptive analysis of the COACT trial. The primary endpoint was the reporting of GWR by the radiologist. Secondary endpoints were APACHE IV score, Cerebral Performance Categories at discharge and 90-day follow-up, Glasgow Coma Scale at discharge, GWR-stratified 1-year survival, and RAND-36 stratified by normal versus abnormal GWR. Associations were analysed using multivariable analysis.

Results: A total of 427 OHCA patients were included in this study, 234 (55%) of whom underwent a brain CT scan within 24 hours after ROSC. Median time between arrest and initial CT scan was 12 hours. In 195 patients (83%), the GWR was described in the reports, but always expressed qualitatively. The GWR was deemed abnormal in 57 (29%) CT scans. No differences were found in secondary endpoints between the two groups.

Conclusion: GWR was frequently described in CT scan reports. Early abnormal GWR, as assessed qualitatively by a radiologist within 24 hours after ROSC, was a poor predictor of neurological prognosis.

Keywords: Grey-white matter differentiation, Brain, CT scan, Out-of-hospital cardiac arrest, Routine reporting, Prognosis

Introduction

One of the most common causes of mortality in the western world is out-of-hospital cardiac arrest (OHCA). Only 45% of successfully resuscitated patients whose initial rhythm is pulseless ventricular tachycardia or ventricular fibrillation survive.[1] Most of these comatose OHCA survivors ultimately die from postanoxic brain injury,[2,3] which may be associated with diffuse brain oedema,[4] despite the application of targeted temperature management.

The neurological prognostication of comatose patients is done by a bundle of tests, since none of the individual tests (e.g. clinical examination, electroneurophysiology, biomarkers, and neuroimaging) are considered to be sufficiently accurate if used as sole tests.[5]

The neuroimaging component, i.e. the grey-white matter differentiation (grey-white ratio, GWR) is determined from a CT scan of the brain by a radiologist. It is used to characterise cerebral ischaemia and oedema, and is often evaluated visually and described qualitatively as a decrease of GWR.[6] The GWR refers to the presence of the interface between cerebral and cerebellar grey and white matter. Recent research has shown that diffuse loss of GWR, measured quantitatively on admission to ICU after cardiac arrest, is correlated with poor neurological outcome at 3 months.[7]

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Although the GWR seems to be correlated with neurological outcome, the use of CT brain imaging for neuroprognostication is only recommended as part of a multimodal approach.[8] The main shortcomings in measuring the GWR include the variability in the assessment and the impact of time on the development of cerebral oedema, which may occur between 1 and 24 hours after cardiac arrest.[5]

Up to now, no research has been done on assessing how often and in what way the GWR is reported in CT scan reports of the brain in post-cardiac arrest patients in routine practice. The aims of this study were to investigate the frequency and method of routine reporting the GWR in comatose patients in current clinical practice, and to determine their prognostic value after OHCA.

Methods

Study design and overview

This study was a post-hoc analysis of the Coronary Angiography after Cardiac Arrest without ST-Segment Elevation study (COACT),[9] which was an open label, multicentre randomised controlled trial. COACT compared immediate with delayed coronary angiography in comatose patients after OHCA with a shockable rhythm and without ST-segment elevation on ECG.

Patient selection

Hospitals that included at least 15 patients in the COACT trial were contacted for additional data collection. Patients were included if they had undergone a brain CT scan within the first 24 hours after ROSC, according to the current resuscitation guideline.[10] Patients were included in COACT if they had an OHCA with an initial shockable rhythm and were comatose after ROSC. Exclusion criteria were signs of ST-segment elevation, shock, or a non-coronary cause of the arrest.

Procedure

Data were collected in person from the participating hospitals, then coded in a local reusable database. As prespecified in the original study (METC 2014.273), data were collected after informed consent and approval by all relevant ethics committees had been obtained. CT reports were evaluated for comments about GWR. A subdivision was made between a qualitative and quantitative assessment. In addition, the locations of the GWR abnormalities were extracted from the report.

End points

The primary end point was the reporting of the GWR on CT reports. Secondary end points as a result of differing GWR were APACHE IV score (mortality risk score) at admission, Cerebral Performance Categories (CPC) at discharge and at 90-day follow-up, Glasgow Coma Scale (GCS) at discharge, 1-year survival, and Physical Component Score (PCS) and Mental Component Score (MCS) (the latter two items being part of the RAND-36 general health survey), at 1 year. APACHE IV, PCS and MCS were divided into tertiles, where we compared the lowest and highest tertile. All additional analyses were conducted on patients in whom the GWR had been reported.

Statistical analysis

Categorical data were analysed using the chi-square test or the Fisher's exact test when appropriate. Continuous data were analysed with the unpaired T-test. Survival rates between groups were compared using Kaplan-Meier curves. The sensitivity and specificity for CPC 3–5 at 90-day follow-up in relation to abnormal GWR was analysed using Wilson's method. Effect size was reported as odds ratio (OR) or hazard ratio (HR). Multivariable analyses were adjusted for age and COACT group randomisation. Data were shown as numbers and percentages, mean ± SD, and median [interquartile range], when appropriate. We used SPSS Statistics 25 (IBM, USA) for statistical analyses. A confidence interval of 95% was used, with a two-sided significance level of 0.05.

Results

Hospitals

The following 10 hospitals participated in this post-hoc-analysis: Amsterdam University Medical Center location VUmc, Amsterdam; Erasmus University Medical Center, Rotterdam; Amphia Hospital, Breda; Rijnstate Hospital, Arnhem; University Medical Center Groningen, Groningen; Maasstad Hospital, Rotterdam; Haga Hospital, The Hague; Medisch Spectrum Twente, Enschede; Radboud University Medical Center, Nijmegen; and Amsterdam University Medical Center location AMC, Amsterdam.

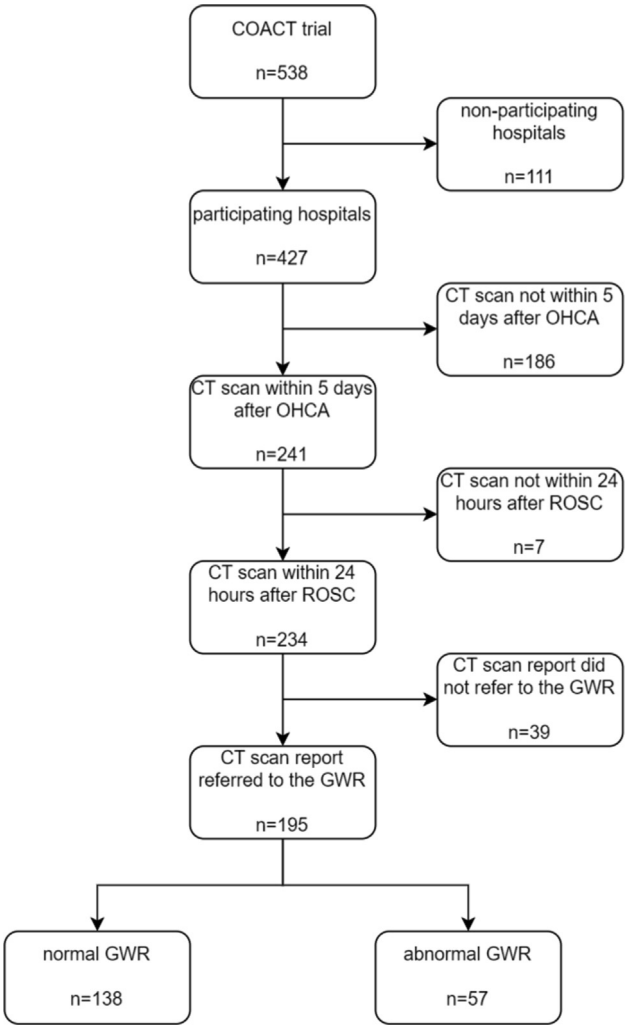

Fig. 1 – Flowchart of patient inclusion.

Patients

A total of 427 patients were included (Fig. 1). A CT scan was performed within 24 hours after ROSC in 234 patients (54.8%). This comprised 97.1% of all CT scans performed within the first 5 days after arrest (n = 241). The indication for the CT scan was to rule out traumatic brain injury (38.4%), CVA or ischaemia (25.8%), or the indication was unknown (35.8%). The median time between ROSC and initial CT scan was 12 hours.

Primary outcome

The GWR was identified in 83.3% (195/234) of patients who had a CT scan within 24 hours after ROSC. The GWR was always reported qualitatively, and expressed in a binary way: normal 138/195 (70.8%) versus abnormal 57/195 (29.2%). In 50/57 (87.7%) patients, the location of the GWR abnormality was described and the most reported location of decrease in GWR was the frontal lobe 21/50 (42.0%).

Additional analyses and secondary outcomes

Baseline characteristics are shown in Table 1. Age was significantly different between the normal and abnormal GWR groups. A significant difference was also seen between the GWR groups within the COACT group randomisation.

APACHE IV score, CPC at discharge and at 90-day follow-up, GCS at discharge, one-year survival and RAND-36 were not correlated with the presence of an abnormal early GWR (Fig. 2, Table 2).

Table 1 – Baseline characteristics of included patients.

Characteristics	GWR mentioned (n = 195)	Normal GWR (n = 138)	Abnormal GWR (n = 57)	p-values
Age (years)	63 ± 14	61 ± 13	67 ± 13	0.006
Male sex	152/195 (77.9)	110/138 (79.7)	42/57 (73.7)	0.36
Hypertension	86/193 (44.6)	55/136 (40.4)	31/57 (54.4)	0.075
Previous myocardial infarction	45/195 (23.1)	30/138 (21.7)	15/57 (26.3)	0.49
Previous CABG [α]	16/194 (8.2)	12/137 (8.8)	4/57 (7.0)	0.78
Previous PCI [β]	31/193 (16.1)	24/137 (17.5)	7/56 (12.3)	0.39
Previous CVA [γ]	9/194 (4.6)	4/137 (2.9)	5/57 (8.8)	0.13
Diabetes mellitus	20/194 (10.3)	15/137 (13.5)	5/57 (8.8)	0.65
Current smoker	47/182 (25.8)	36/129 (27.9)	11/53 (20.8)	0.32
Hypercholesterolaemia	41/192 (21.4)	26/136 (19.1)	15/56 (26.3)	0.24
Peripheral artery disease	7/194 (3.6)	5/137 (3.6)	2/57 (3.5)	1.00
Arrest witnessed	151/195 (77.4)	106/138 (76.8)	45/57 (78.9)	0.75
Time from arrest to BLS [δ] (minutes)	2 [1–5]	2 [0–5]	4 [1–5]	0.54
Time from arrest to ROSC [ε] (minutes)	12 [7–20]	10 [7–20]	15 [8–20]	0.97
Time to CT (hours: minutes)	11:55 [1:26–13:12]	11:48 [1:23–13:13]	12:26 [2:17–13:11]	0.094
Randomisation group COACT				0.029
Immediately invasive	99/195 (50.8)	77/138 (55.8)	22/57 (38.6)	
Delayed invasive	96/195 (49.2)	61/138 (44.2)	35/57 (61.4)	

Data is presented as no./total no. (%), mean ± SD or Median [IQR].

CABG [α] stands for Coronary Artery Bypass Grafting, PCI [β] stands for Percutaneous coronary intervention, CVA [γ] stands for Cerebrovascular accident, BLS [δ] stands for Basic Life Support, and ROSC [ε] stands for Return of Spontaneous Circulation.

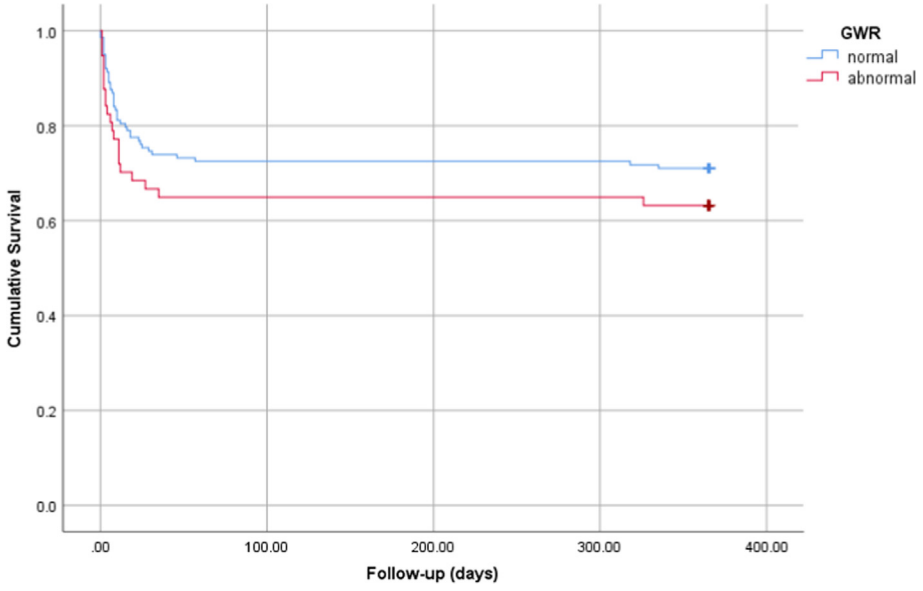

Fig. 2 – Kaplan-Meier, 1-year survival correlated to GWR.

Table 2 – Outcomes.

Outcome	GWR mentioned (n = 195)	Normal GWR (n = 138)	Abnormal GWR (n = 57)	Effect size
Secondary end points				
APACHE score IV [η]	Lowest: 75/195 (38.5)Highest: 62/195 (31.8)	Lowest: 56/138 (40.6)Highest: 43/138 (31.2)	Lowest: 19/57 (33.3)Highest: 19/57 (33.3)	OR: 1.30 (95% CI 0.615 – 2.76), p = 0.49
CPC 3–5 at discharge [ε]	54/195 (27.7)	36/138 (26.1)	18/57 (31.6)	OR: 1.31 (95% CI 0.665 – 2.57), p = 0.48
CPC 3–5 at 90 days [ε]	61/195 (31.3)	41/138 (29.7)	20/57 (35.1)	OR: 1.28 (95% CI 0.664 – 2.46), p = 0.46
GCS < 8 at discharge [ζ]	60/195 (30.8)	40/138 (29.0)	20/57 (35.1)	OR: 0.755 (95% CI 0.392 – 1.46), p = 0.40
1-year survival	134/195 (68.7)	98/138 (71.0)	36/57 (63.2)	HR: 1.43 (95% CI 0.745 – 2.74), p = 0.23
Physical Component Score	Lowest: 32/96 (33.3)Highest: 31/96 (35.4)	Lowest: 23/66 (34.8)Highest: 23/66 (34.8)	Lowest: 9/30 (30.0)Highest: 11/30 (36.7)	OR: 1.22 (95% CI 0.426 – 3.51), p = 0.71
Mental Component Score	Lowest: 32/96 (33.3)Highest: 32/96 (33.3)	Lowest: 18/66 (27.3)Highest: 21/66 (31.8)	Lowest: 14/30 (46.7)Highest: 10/30 (33.3)	OR: 0.566 (95% CI 0.209 – 1.53), p = 0.26

Data are presented as total /total no. (%) or Median [IQR], effect size is odds or hazard ratio (95% Confidence Interval lower – upper), and p-value.
Lowest and highest stands for the lowest and highest tertile as outcome of the score.
APACHE [η] stands for Acute Physiology and Chronic Health Evaluation, CPC [ε] stands for Cerebral Performance Categories, and GCS [ζ] stands for Glasgow Coma Scale.

At 90-day follow-up an abnormal GWR predicted CPC 3–5 with a sensitivity of 32.8% (95% CI: 022.3 – 45.3) and a specificity of 72.4% (95% CI: 65.5 – 80.5).

Analyses corrected for age and COACT group randomisation showed no difference when compared with primary analyses.

The role of early CT in neuroprognostication

A total of 27.9% (n = 119) of all included patients (n = 427) were withdrawn from life-sustaining therapy (LST). In 47.9% (n = 57) of all these patients a CT scan had been performed within 24 hours. Of these 57 patients, 28 had a normal GWR, 17 had an abnormal GWR, and in 12 the GWR was not reported. The reasons for withdrawal of LST in patients with a reported GWR (n = 45; 78.9% of all CT scans in this group of patients) were mainly neurological (in 68.9%; n = 31), brain death (in 11.1%; n = 5), multiple organ failure and hemodynamic failure (in 11.1% n = 5).

Discussion

In this study 54.8% of all OHCA patients had a CT scan of the brain for various reasons within 24 hours after ROSC. Of the reports on these CT scans, 83.3% contained information about the GWR, which was always reported qualitatively. This reflects current clinical practice as there are no standard operating procedures for quantitative reporting of the GWR. In addition, 38.4% of these CT scans were initially performed to rule out traumatic brain injury. Age was significantly different between the normal and abnormal GWR groups which may be relevant considering age-induced alterations in GWR.[11]

None of the secondary outcome parameters were significantly different between patients with normal and patients with abnormal GWR. An abnormal GWR was not specifically given as a reason for withdrawing LST, however, the fact that it may have contributed to a certain extent to decision-making about withdrawal of LST cannot be excluded. Abnormal GWR assessed qualitatively is therefore in itself not a strong predictor of neurological prognosis, and should remain part of the multimodal approach as advised in the guidelines.[10]

The fact that only 54.8% of the OHCA patients underwent a brain CT scan within 24 hours, which reflected 97.1% of all CT scans performed in the first 5 days after OHCA, probably means that clinicians indeed do not highly value the results from early brain imaging with CT in neuroprognostication. The question is, could standardised quantification of GWR lead to better characterisation of global ischaemic injury changes on brain CT scans, thereby improving the prognostic value?

On reviewing 17 studies Keijzer et al.[12] found GWR to be a predictor of poor outcome, and reported a specificity of 100% and a varying - but low - sensitivity (5.6–55%). Differences in results were explained by differing definitions of poor outcome, variable time intervals between cardiac arrest and CT scan, and differences in methods of measuring GWR. Caraganis et al.[13] found that substantial variability is present between radiologists in recognising decrease in GWR. This may be due to the lack of quantitative measurements or of a standardised description of the GWR. However, several studies have shown that using any quantitative measurement increases correlation with outcome when compared to qualitative reporting.[14] Chakraborty et al.[7] used an extended version of the ASPECTS scoring system[15] to define brain hypodensity. Our study did not use such

a scoring system; we found that radiologists only referred to the GWR in a subjective way, i.e. qualitatively.

In addition, as the indication for CT scan showed, the reports were not primarily focused on changes in GWR, and therefore subtle changes in GWR due to cerebral oedema or ischaemia may have been missed by the radiologist. Additionally, as our median time to CT scan was just below 12 hours, brain oedema and its accompanying decrease of GWR might not yet be visible to the radiologist. Standard time interval is an important factor in detecting a change to GWR. Hong et al.[16] found that within two hours after ROSC a CT scan does not add any value to neurological prognostication, as brain oedema may take some time to become visible. The use of a standardised description or automated evaluation of grey scales, combined with a standard time interval to CT scan, might increase the correlation with outcome. Machine learning could be even more helpful in standardising the description of global ischaemic injury changes, as a computer follows a sophisticated algorithm.[17]

The most recent Dutch guideline on post-anoxic coma, states that continuous EEG plays a more significant role than the CT scan of the brain, in the neurological prognostication of comatose patients.[18] According to Ruijter et al.[19] continuous EEG is a reliable predictor of outcome. The EEG has a sensitivity of 0.47 at 12 hours after cardiac arrest (and 0.30 at 24 hours), and a specificity of 1.00 (at both 12 and 24 hours) in comatose patients following OHCA.[19] Loss of boundary between grey and white matter with a qualitative description had a sensitivity of 0.81, and a specificity of 0.92 for an unfavourable outcome.[20] In our study we found a sensitivity of 32.8% and a specificity of 72.4% for CPC 3–5 at 90-day follow-up. As well as differences in timing to CT scan and definitions of outcome, this difference can be partially explained by differences in the qualitative assessment of an abnormal GWR. Certain thresholds can be used in quantitative measurements, but this is not possible if an abnormal GWR is only assessed by visual inspection. If a standardised description were used, sensitivity and specificity of the CT scan might increase to an optimal ratio. CT scan of the brain could then play a more prominent role in neurological prognostication and may possibly assist EEG in neurological prognostication in comatose patients. Currently, in the real-life situation, where qualitative reporting is the standard no conclusions on neurological prognostication can be drawn based on a sole CT scan report, and therefore it can be considered as obsolete if used on its own. However, as part of a multimodal approach, where it is combined with clinical examination, neurophysiology, and biomarkers it might just add some extra information to strengthen the standpoint on a patient's situation.

This study has several limitations. First, CT scans were not conducted in every patient, but only if indicated, therefore resulting in selection bias. Second, as time to CT is mainly within 12 hours after ROSC changes in GWR may not yet be visible. Third, as this was a post-hoc analysis of the COACT trial,[9] more CT scans of the brain may have been performed than is usual in standard care, as a non-coronary cause of the arrest had to be excluded in the COACT trial and in some cases, brain injury had to be ruled out. Finally, since only 79.4% of the COACT patients were included, this may have resulted in less statistical power for comparison between the GWR groups.

In conclusion, the current value of early brain CT scan and GWR in neuroprognostication is limited. Over 50% of OHCA patients underwent a brain CT scan within 24 hours after ROSC. In the reports of these CT scans the GWR is identified in 83.3% of cases, and always expressed qualitatively. An abnormal GWR was not a predictor of outcome and neurological prognosis. More research is needed to examine if a more standardised and quantitative description or identification of ischaemic injury by machine learning could increase CT performance, the rate and quality of GWR reporting, and the correlation with outcome.

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CRediT authorship contribution statement

K.O. Adriaansens: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Project administration. **L.S.D. Jewbali:** Conceptualization, Methodology, Validation, Resources, Writing – original draft, Writing – review & editing, Supervision, Project administration. **J.S. Lemkes:** Resources, Writing – review & editing. **E.M. Spoormans:** Resources, Writing – review & editing. **M. Meuwissen:** Resources, Writing – review & editing. **M.J. Blans:** Resources, Writing – review & editing. **P. van der Harst:** Resources, Writing – review & editing. **B.J.W. Eikemans:** Resources, Writing – review & editing. **G.B. Bleeker:** Resources, Writing – review & editing. **A. Beishuizen:** Resources, Writing – review & editing. **J.P. Henriques:** Resources, Writing – review & editing. **A. van der Lugt:** Resources, Writing – review & editing. **N. van Royen:** Resources, Writing – review & editing. **C.A. den Uil:** Conceptualization, Methodology, Validation, Resources, Writing – original draft, Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Prof. Van Royen received grant support from Philips, Biotronik, and Abbott and honoraria from Medtronic. No other potential conflict of interest relevant to this article was reported.]

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REFERENCES

1. Patel N, Patel N, Macon C, et al. Trends and outcomes of coronary angiography and percutaneous coronary intervention after out-of-hospital cardiac arrest associated with ventricular fibrillation or pulseless ventricular tachycardia. JAMA Cardiol 2016;1:890–9.
2. Dragancea I, Rundgren M, Englund E, Friberg H, Cronberg T. The influence of induced hypothermia and delayed prognostication on the mode of death after cardiac arrest. Resuscitation 2013;84:337–42.
3. Laver S, Farrow C, Turner D, Nolan J. Mode of death after admission to an intensive care unit following cardiac arrest. Intensive Care Med 2004;30:2126–8.
4. Xiao F. Bench to Bedside: Brain Edema and Cerebral Resuscitation: The Present and Future. Acad Emerg Med 2002;9:933–46.
5. Sandroni C, D'Arrigo S, Nolan J. Prognostication after cardiac arrest. Crit Care 2018;22:150–8.
6. Kjos B, Brant-Zawadzki M, Young R. Early CT findings of global central nervous system hypoperfusion. AJR Am J Roentgenol 1983;141:1227–32.
7. Chakraborty S, Symons S, Chapman M, Aviv R, Fox A. Diffuse ischemia in noncontrast computed tomography predicts outcome in patients in intensive care unit. Can Assoc Radiol J 2012;63:129–34.
8. Sandroni C, Cariou A, Cavallaro F, et al. Prognostication in comatose survivors of cardiac arrest: An advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine. Resuscitation 2014;85:1779–89.
9. Lemkes J, Janssens G, Van der Hoeven N, et al. Coronary angiography after cardiac arrest without ST-segment elevation. N Engl J Med 2019;380:1397–407.
10. Nolan J, Sandroni C, Böttiger B, et al. European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care. Resuscitation 2021;161:220–69.
11. Salat D, Lee S, Van der Kouwe A, Greve D, Fischl B, Rosas H. Age-associated alterations in cortical gray and white matter signal intensity and gray to white matter contrast. Neuroimage 2009;48:21–8.
12. Keijzer H, Hoedemaekers C, Meijer F, Tonino B, Klijn C, Hofmeijer J. Brain imaging in comatose survivors of cardiac arrest: Pathophysiological correlates and prognostic properties. Resuscitation 2018;133:124–36.
13. Caraganis A, Mulder M, Kempainen R, et al. Interobserver Variability in the Recognition of Hypoxic-Ischemic Brain Injury on Computed Tomography Soon After Out-of-Hospital Cardiac Arrest. Neurocrit Care 2020;33:414–21.
14. Na M, Kim W, Lim T, et al. Gray matter to white matter ratio for predicting neurological outcomes in patients treated with target temperature management after cardiac arrest: A systematic review and meta-analysis. Resuscitation 2018;132:21–8.
15. Barber P, Demchuk A, Zhang J, Buchan A. Aspects Study Group. Validity and reliability of a quantative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. Lancet 2000;355:1670–4.
16. Hong J, Lee D, Oh J, et al. Grey-white matter ratio measured using early unenhanced brain computed tomography shows no correlation with neurological outcomes in patients undergoing targeted temperature management after cardiac arrest. Resuscitation 2019;140:161–9.
17. Hannawi Y, Muschelli J, Mulder M, et al. Postcardiac arrest neurological prognostication with quantitative regional cerebral densitometry. Resuscitation 2020;154:101–9.
18. Horn J, Hoedemaekers C, Hofmeijer J, Jewbali L, Koelman J, Ruijter D. Prognose van postanoxisch coma 2019; (Accessed at 28 February 2020, at https://richtlijnendatabase.nl/richtlijn/prognose_van_postanoxisch_coma/startpagina.html#tab-content-accountability).
19. Ruijter B, Tjepkema-Cloostermans M, Tromp S, et al. Early Electroencephalography for Outcome Prediction of Postanoxic Coma: A prospective Cohort Study. Ann Neurol 2019;86:203–14.
20. Inamasu J, Miyatake S, Suzuki M, et al. Early CT signs in out-of-hospital cardiac arrest survivors: Temporal profile and prognostic significance. Resuscitation 2010;81:534–8.