Original Article

Both decreased and increased grey-to-white matter attenuation ratio in the putamen and caudate on early head computed tomography differentiate patients with favorable and unfavorable outcomes after prolonged cardiac arrest—secondary analysis of the Prague OHCA study

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Background: Neurological damage remains the leading cause of death in cardiac arrest victims with early neuroprognostication being the cornerstone of the decision-making process to continue or discontinue advanced treatments. In this study, we aimed to find markers of favorable and unfavorable outcome on early brain computed tomography (CT) in patients after prolonged out-of-hospital cardiac arrest (OHCA) treated both by conventional and extracorporeal cardiopulmonary resuscitation (ECPR).

Methods: In a secondary analysis of the Prague OHCA study, patients who underwent brain CT within 36 hours after cardiac arrest were identified. Qualitative findings (brain edema, hemorrhage) and quantitative measurements [attenuation of grey matter structures and grey-to-white matter attenuation ratio (GWR)] between patients with cerebral performance category (CPC) of 1–2 (favorable outcome) and 3–5 (unfavorable outcome) within 180 days after the event were compared.

Results: In 45 eligible patients, intracranial edema (n=16, 50%) was present in patients with CPC 3–5 only (n=32, 71%). Attenuation of brain structures and GWR did not differ between patients with favorable and unfavorable outcomes. However, the GWR in the caudate and putamen of most CPC 1–2 patients was within a narrow range of values (1.18 to 1.30 and 1.20 to 1.33) that separated patients with CPC 1–2 from CPC 3–5 with a sensitivity of 78% and 66% a specificity of 85% and 100%, and area under the curve (AUC) of 0.86 (P=0.0001) and 0.77 (P=0.0053), respectively. Patients treated by ECPR had lower attenuation in the centrum semiovale (28.3±2.7) compared to those who were not (31.0±2.8, P=0.003). The most common causes of death in CPC 3–5 patients were brain death in 13 (41%) patients, multiorgan failure in 12 (38%), and cardiac rearrest in 4 (13%).

Conclusions: Both decreased and increased grey-to-white matter differentiation in the putamen and caudate on early non-contrast brain CT after prolonged OHCA indicate poor neurological outcome within 180 days after cardiac arrest.

Keywords: Cardiac arrest; computed tomography (CT); brain edema; prognosis

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Introduction

Refractory out-of-hospital cardiac arrest (OHCA) is burdened with high mortality and poor neurological outcome (1). Two recent randomized controlled trials, ARREST and Prague OHCA study suggested reasonable neurologically favorable survival using an invasive approach including extracorporeal cardiopulmonary resuscitation (ECPR) despite prolonged periods of CPR (2,3). Still, neurological damage remains the leading cause of death in cardiac arrest victims with early neuroprognostication being the cornerstone of the decision-making process to continue or discontinue advanced treatments (4,5).

Brain computed tomography (CT) is an integral part of neuroprognostication after cardiac arrest, however, is not routinely recommended in all patients after OHCA. European Resuscitation Council and European Society of Intensive Care Medicine guidelines suggest brain imaging for an unknown cause of cardiac arrest and prognostication in centers with specific experience (6). Acute findings in OHCA patients are present in 40% and brain imaging provides information leading to changes in patients' management in 16% within the first 2 days (7). The morphological hallmark of adverse neurological outcome is loss of cortical grey-white matter differentiation due to global cerebral edema, decreased attenuation of deep grey matter, and less frequently hemorrhage (7). Loss of grey-white matter differentiation on early brain CT is a reliable predictor of poor neurological outcome, in addition to predictors based on pre-hospital circumstances and in-hospital parameters (8,9). Brain CT imaging may be affected by previous contrast agent administration in patients managed with invasive assessment and therapy (i.e., coronary angiography/percutaneous coronary intervention) influencing grey matter attenuation in hypoxic-ischemic injury (10). All these predictors have already been evaluated in OHCA patients with sustained return of spontaneous circulation (7-10). Whether the same criteria may also be applied to refractory OHCA patients treated with ECPR has not been extensively studied yet (11-13).

Therefore, we analyzed a randomized population derived from the Prague OHCA trial to identify the signs of an adverse neurological outcome within 180 days in patients with refractory OHCA using brain CT in the first 36 hours after cardiac arrest.

Methods

Population and study design

This study is a secondary analysis of the Prague OHCA study, a randomized clinical trial conducted at a single center in Prague, Czech Republic, from March 1, 2013, to October 25, 2020. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The original study as well as secondary analyses were approved by the Ethics Committee of the General University Hospital in Prague (No. 192/11 S-IV) and informed consent was taken from all individual participants or their relatives.

Adult patients resuscitated for witnessed OHCA of presumed cardiac etiology after at least 5 minutes of advanced cardiovascular life support (ACLS) were eligible for enrollment in the trial. A web-based secured randomization system was used to assign patient number and intervention group during ongoing CPR in the field. The methodology and results of the intention to treat analysis were published in detail elsewhere (2,14). The Prague OHCA study database provided clinical and laboratory data (2).

In the current analysis, out of 256 patients included in the Prague OHCA study, we identified patients, who underwent brain CT within 36 hours after cardiac arrest (15,16). As a non-contrast brain CT was not part of the protocol, reasons for performing the examination have also been identified.

Brain CT acquisition and evaluation

Non-contrast brain CT was performed in a spiral mode on either a 256-slice (Brilliance iCT, Philips, Best, Netherlands) or 64-slice scanner (Somatom Definition, Siemens, Forchheim, Germany) with a peak voltage of 120 kV, tube time-current product between 189–349 mAs from the vertex to C1 vertebra. The images were reconstructed in 5 mm contiguous axial sections and analyzed. Briefly, CT images were assessed for the presence of intracranial hemorrhage, edema, and traces of contrast material

following eventual previous contrast agent administration [attenuation in venous sinuses ≥70 Hounsfield unit (HU)] by two radiologists with clinical experience of 4 and 13 years in consensus, who were blinded to the clinical outcome. The quantitative analysis of the images involved measurement of attenuation of deep grey matter (caudate, putamen, thalamus), medial frontal and occipital cortex, and semioval center as a reference attenuation of the white matter (17). Attenuation was measured on a clinical workstation (Intellispace Portal, Philips, Best, The Netherlands) on 5 mm axial sections in a manually drawn spline area of interest (≥30 mm^2, Figure S1). The measurements were repeated in ten randomly selected patients to quantify interobserver agreement. The measurements from bilateral structures were averaged and grey-to-white matter attenuation ratio (GWR) was calculated.

Outcomes

The primary outcome of the current analysis was the best neurological outcome achieved within 180 days after cardiac arrest. A cerebral performance category (CPC) of 1–2 was considered a good neurological outcome and a CPC of 3–5 was a poor neurological outcome (18).

Statistical analysis

Statistical analysis was performed in Prism (GraphPad Software, La Jolla, CA, USA) and R (R foundation for statistical computing, Vienna, Austria). The normality of the continuous data was tested using the D'Agostino & Pearson omnibus normality test. To test for statistical significance, we used the *t*-test, Mann-Whitney test, Fischer test, or χ^2 test as appropriate. Two-sided attenuation thresholds were proposed to separate patients with CPC 1–2 and CPC 3–5 after inspection of the distribution of the data in a plot. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated. Receiver operator characteristic (ROC) curves were created and areas under the ROC curve (AUCs) were calculated using absolute difference from the average of the two proposed thresholds. Association between attenuation or GWR in grey matter structures and mean attenuation in the superior and inferior sagittal sinuses was calculated using Spearman's rank correlation coefficient (rho). Interobserver agreement was expressed as an intraclass correlation coefficient (ICC). A P value <0.05 was considered significant.

Results

The Prague OHCA study database provided clinical data including the CPC shown in *Table 1*. Out of 256 patients enrolled in the main study, 101 (39%) had a CT of the brain performed during their hospital stay, and 45 of them within the first 36 hours after initial collapse, representing the current study population. There were 32 (71%) patients with unfavorable neurological outcomes (CPC 3 in a single patient, CPC 4 in 9 patients, CPC 5 in 22 patients) and 13 (29%) with favorable neurological outcomes (CPC 1 in 12 patients; CPC 2 in a single patient), see *Figure 1*. In patients with CPC 3–5, following causes of death were recorded: brain death in 13 (41%) patients, multiorgan failure in 12 (38%), cardiac rearrest in 4 (13%), hemorrhage in 2 (6%), and unknown cause in 1 (3%).

ECPR was performed in 24 (75%) patients with CPC 3–5 and 7 (54%) patients with CPC 1–2 (P=0.29). Patients with CPC 3–5 had lower pH (P=0.005), higher lactate (P=0.002), and longer duration of cardiac arrest (P=0.021). All but three patients (93%) had undergone coronary angiography before head CT.

CT examination was requested for adverse neurological status (n=22), unknown cause of cardiac arrest (n=15), craniocerebral trauma (n=5), or performed alongside CT of the thorax (n=3), see *Table 2* for details. CT examinations were performed 4.3 [interquartile range (IQR), 2.5–14.4] hours after an emergency call.

High attenuation of dural venous sinuses attributable to residual contrast material after a previous angiography was present in 22 (49%) patients. A normal finding was reported in 14 (44%) patients with CPC 3–5 and all 13 patients with CPC 1–2 (P=0.0004). Intracranial edema (n=16) and hemorrhage (n=6) were present in patients with CPC 3–5 only.

Attenuation of brain structures and GWR were not different between patients with favorable and unfavorable outcomes (Table S1, Figure S2). However, the GWR in the caudate and putamen of most CPC 1–2 patients was within a narrow range of values (1.18 to 1.30, n=11, 85% and 1.20 to 1.33, n=13, 100%, respectively) that separated CPC 1–2 and CPC 3–5 with a sensitivity of 78% and 66% a specificity of 85% and 100%, and AUC of 0.86 (P=0.0001) and 0.77 (P=0.0053), respectively (*Table 3*, *Figures 2*,*3*). These thresholds, however, did not differentiate patients treated by conventional *vs.* extracorporeal CPR (AUC =0.64, P=0.13 and AUC =0.66, P=0.082, respectively) (Table S1). Patients treated with ECPR had lower attenuation in the

Table 1 Patients' data

Characteristics	CPC 3–5 (n=32)	CPC 1–2 (n=13)	P
Gender (male)	24 [75]	8 [62]	0.47
Age (years)	59.0±1.9	55.3±3.6	0.33
Arterial hypertension	17 [65]	6 [46]	0.31
Diabetes	7 [28]	0	0.07
Coronary artery disease	5 [20]	1 [8]	0.64
Shockable rhythm	11 [34]	13 [100]	<0.001*
pH on admission	6.959±0.027	7.107±0.041	0.005*
Lactate on admission (mmol/L)	12.72±0.76	8.25±0.95	0.002*
Duration of cardiac arrest (min)	49±3	36±5	0.021*
ECPR	24 [75]	7 [54]	0.29
CPC (best CPC within 180 days)			–
CPC 1		12 [92]	
CPC 2		1 [8]	
CPC 3	1 [3]		
CPC 4	9 [28]		
CPC 5	22 [69]		
Coronary angiography before head CT			
Number of patients	31 [97]	11 [85]	0.20
Time before CT (hours)	3.4 (1.4 to 19.5)	2.8 (1.0 to 9.8)	0.51

Values are expressed as number [%], mean ± standard deviation, or median (IQR). *, significant P values. CPC, cerebral performance category; ECPR, extracorporeal cardiopulmonary resuscitation; CT, computed tomography; IQR, interquartile range.

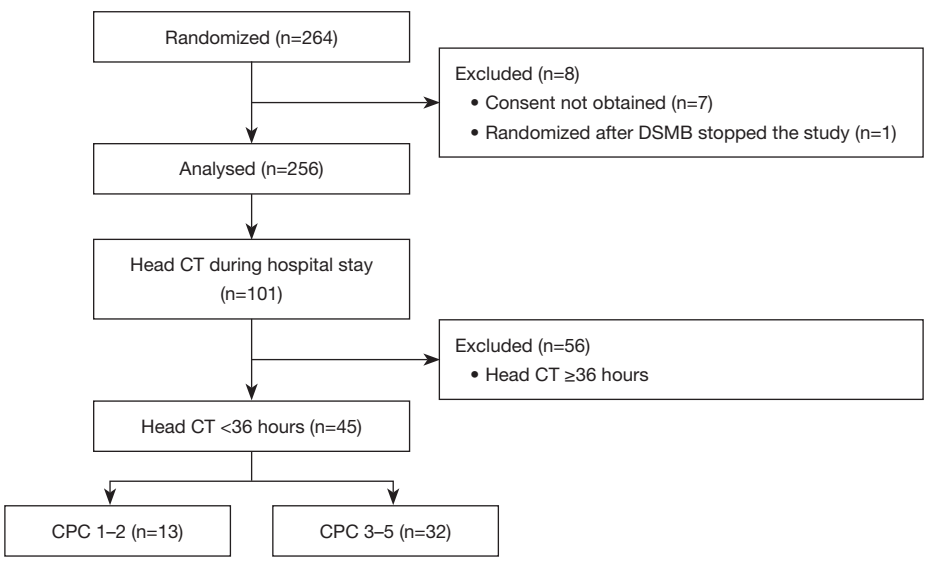

Figure 1 Flow chart of the study. DSMB, Data and Safety Monitoring Board; CT, computed tomography; CPC, cerebral performance category.

Table 2 Clinical reasons for brain CT imaging requests, timing, and major findings

CT	CPC 3–5 (n=32)	CPC 1–2 (n=13)	P
CT requested for			0.012
Adverse neurological status	19 [59]	3 [23]	
Unknown cause of cardiac arrest	9 [28]	6 [46]	
Craniocerebral trauma	1 [3]	4 [31]	
At the occasion of CT of the thorax or abdomen	3 [9]	0 [0]	
The time between cardiac arrest and CT (hours)	4.8 (2.6 to 20.0)	2.8 (2.2 to 10.4)	0.37
CT findings			
Intracranial hemorrhage	6 [19]	0 [0]	0.16
Edema or conus	16 [50]	0 [0]	0.0014*
Normal appearance	14 [44]	13 [100]	0.0004*
Attenuation in sinus rectus ≥70 HU	16 [50]	6 [46]	1.0

Values are expressed as number [%] or median (IQR). *, significant P values. CT, computed tomography; CPC, cerebral performance category; HU, Hounsfield unit; IQR, interquartile range.

Table 3 Comparison of attenuation of grey and white matter structures and GWRs between patients with favorable (CPC 1–2) and unfavorable (CPC 3–5) outcomes

Brain structure	Patients with CPC 3–5 (n=32)	Patients with CPC 1–2 (n=13)	P (CPC 3–5 *vs.* CPC 1–2)	Selected threshold		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	P
				Lower	Upper						
Panel A: attenuation (HU)											
Caudate	36.83±5.67	36.50±3.08	0.85	33	40	41	92	93	39	0.67	0.073
Putamen	37.05±4.60	37.42±2.81	0.79	33	39	41	69	76	32	0.57	0.48
Thalamus	35.0 (4.1)	36.5 (3.0)	0.15	33	40	22	85	78	31	0.58	0.42
Medial cortex	33.3 (4.9)	32.5 (4.8)	0.88	30	39	25	100	100	35	0.54	0.66
CS	28.8 (3.9)	29.0 (4.0)	0.99	27	33	28	62	64	26	0.51	0.95
Panel B: attenuation ratio (GWR)											
Caudate: CS	1.27±0.20	1.25±0.04	0.81	1.18	1.30	78	85	93	61	0.86	0.0001*
Putamen: CS	1.28±0.17	1.29±0.05	0.92	1.20	1.33	66	100	100	54	0.77	0.0053*
Thalamus: CS	1.25 (0.16)	1.28 (0.11)	0.22	1.21	1.40	59	100	100	50	0.73	0.015*
Medial cortex: CS	1.15 (0.12)	1.16 (0.04)	0.94	1.10	1.20	47	100	100	43	0.82	0.0008*

Data are expressed as mean ± standard deviation or median (IQR). In this table, IQRs are expressed Q75 minus Q25. *, significant P values. GWR, grey-to-white matter attenuation ratio; CPC, cerebral performance category; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the ROC curve; ROC, receiver operator characteristic; HU, Hounsfield unit; CS, centrum semiovale; IQR, interquartile range; Q25, 25th percentile; Q75, 75th percentile.

centrum semiovale (28.3±2.7 HU) compared to those without (31.0±2.8 HU, P=0.003) and marginally higher GWR in the thalamus [1.30 (IQR, 0.15) *vs.* 1.22 (IQR, 0.11), P=0.024] and medial cortex [1.16 (IQR, 0.09) *vs.* 1.13, (IQR, 0.10), P=0.021]. There was a positive association between mean attenuation in the superior and inferior sagittal sinus and attenuation in the putamen and the thalamus (Table S2). No significant correlation was found between time from

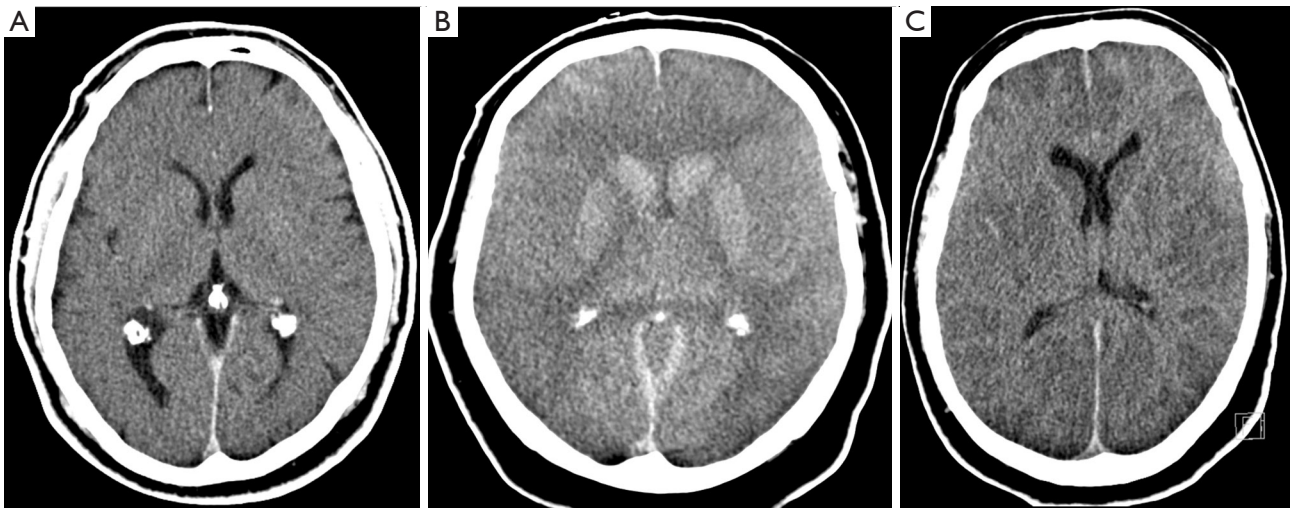

Figure 2 Example of head CT in three patients with CPC 5: (A) effacement of grey-white matter differentiation in a 65-year-old male; (B) loss of cortico-subcortical differentiation with sparing of deep grey matter that shows increased differentiation in a 66-year-old-female; (C) reversal sign with inverted grey-white matter differentiation in a 51-year-old-male. CT, computed tomography; CPC, cerebral performance category.

the event and attenuation or attenuation ratios in the parenchymal brain structures, although attenuation of the venous sinuses was negatively correlated (–0.51, P=0.0003). The reliability of attenuation measurements was excellent (ICC was between 0.905 and 0.982).

Discussion

In this secondary analysis of the randomized Prague OHCA study, where patients were treated by both conventional and ECPR, we analyzed a potential prognostic value of non-contrast brain CT performed within 36 hours after prolonged cardiac arrest. We have identified lower and upper thresholds of GWR as a quantitative marker of hypoxic-ischemic brain injury that differentiated patients with favorable and unfavorable neurological outcomes. These thresholds did not distinguish patients with and without ECPR. Still, patients treated with ECPR demonstrated lower white matter attenuation. Nearly half of brain CTs showed residual contrast material contamination from previous coronary angiography. The attenuation in the venous sinuses correlated with attenuation in the putamen and the thalamus.

Despite the fact, that morphological examination of the brain by CT or magnetic resonance imaging (MRI) is an integral part of routine multimodal neuroprognostication approach (19), the actual patient's management is rarely influenced (16%) and thus has a questionable impact on the patient's outcome (7). Routine early post-resuscitation brain CT is not recommended despite being performed in a similar manner in prospective trials (20,21). In the Prague OHCA study, brain CT was requested in only 101 (39%) patients. The examinations were performed based on clinical indications, most frequently to elaborate on adverse neurological status, in patients with concomitant craniocerebral trauma, and in cases where the cause of cardiac arrest was unknown and a primary neurological origin had to be excluded.

The morphological hallmark of a hypoxic-ischemic brain injury on CT is diminished grey-to-white matter differentiation due to cytotoxic edema (19). This appearance has a high specificity (0.97) but low sensitivity (0.44) for poor neurological outcome (19,22). In our study, apparent cerebral edema equaled an unfavorable outcome, which has also been observed by others (22).

Previously reported methods for the quantification of cerebral edema on CT used absolute numbers of grey matter attenuation or more frequently GWRs (19). A GWR below 1.1 in OHCA patients is highly specific for the poor neurological outcome and the GWR cut-offs previously reported with a 100% specificity for non-survival ranged between 1.1 and 1.2 (11,23,24). In our study, we showed that these lower thresholds are acceptable, but vary across the grey matter structures measured. We additionally identified

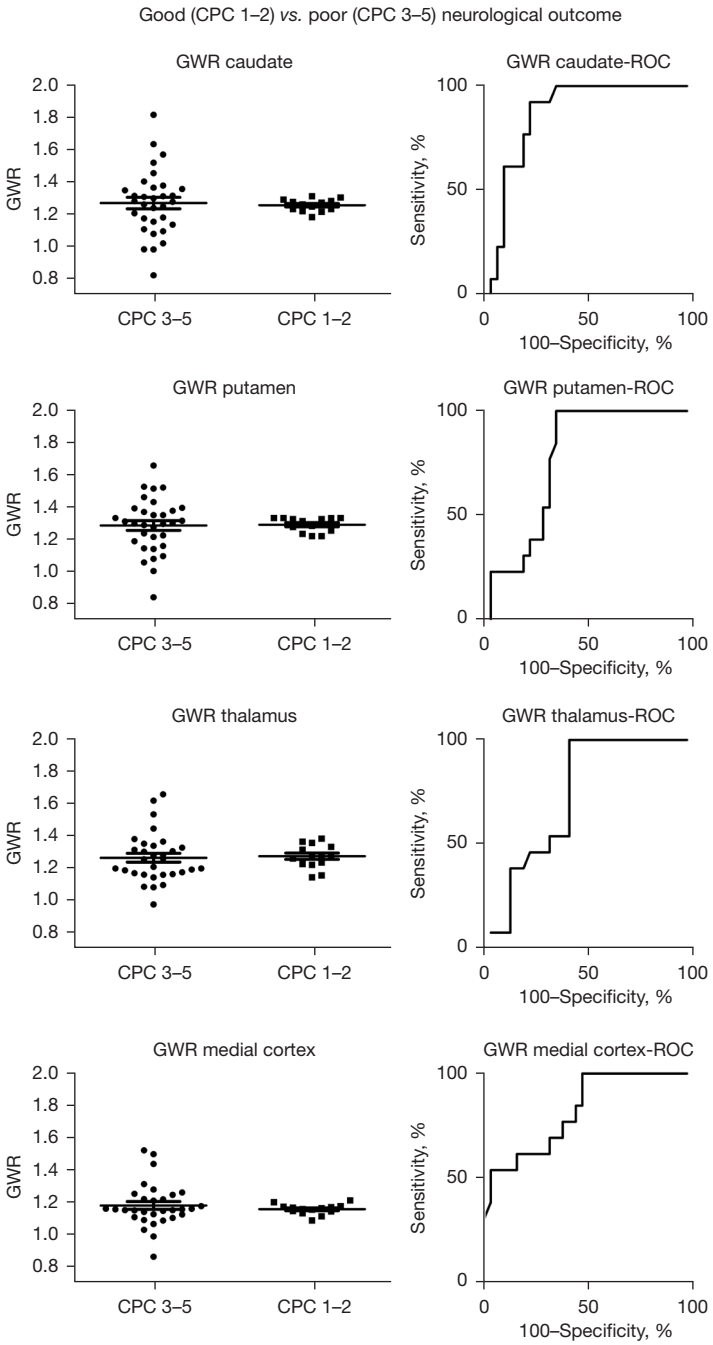

Figure 3 Comparison of GWRs in deep grey matter structures (caudate, putamen, thalamus) and cerebral cortex in a dot plot (left column) between patients with good (CPC 1–2) and poor (CPC 3–5) neurological outcomes. Corresponding ROC curves are shown in the right column. GWR especially in the caudate and putamen in CPC 1–2 patients is in a narrow interval. CPC, cerebral performance category; GWR, grey-to-white matter attenuation ratio; ROC, receiver operator characteristic.

an upper threshold between 1.3 and 1.4 for GWR in deep grey matter structures. We showed that in prolonged OHCAs treated by both ECPR or conventional CPR, the GWR within a narrow range of values (1.25 to 1.35) may help to separate favorable and unfavorable outcome groups and significantly contribute to neuroprognostication within the first 36 hours after admission. Previous two studies that analyzed OHCAs treated by ECPR reported decreased GWR in patients with poor neurological outcomes with cut-off values between 1.21 and 1.24, but neither reported patients with increased GWR (11,12). Although early neuroprognostication using head CT in patients after cardiac arrest has been well documented, delaying CT may improve its predictive power (25).

Additionally, we found that patients treated with ECPR had lower attenuation of the white matter measured in the centrum semiovale. Decreased white matter attenuation in an acute setting is considered to be caused by vasogenic edema, probably due to altered cerebral autoregulation, reperfusion, hyperoxia, and non-pulsatile blood flow (26). As a denominator in the GWR equation, decreased white matter attenuation also increases the GWR.

For the quantification of the GWR, we measured attenuation in structures, that have been reported previously (17). For practical purposes, we used caudate, putamen, and thalamus that can be well detected even in patients with brain edema. The medial cortex was chosen, because there is a lower risk of partial volume bias (cortex and subarachnoid space). Centrum semiovale is a larger structure compared to the internal capsule and therefore it was preferred. In contrast to previous studies (16,17), we used oval (not circular) regions of interest of larger size to cover a greater part of the structures.

GWR has excellent specificity and PPV, but so does CT evaluation by experienced radiologists. All our patients with favorable outcome had a normal finding. This raises a question of the practical applicability and usefulness of the measurement of brain structures attenuation.

Contrast material contamination of brain CT was noted in half of the patients. All but three patients had initial coronary angiography. This is a frequent scenario in OHCAs of presumed cardiac origin as admission to cardiac centers and early invasive investigation in selected patients may bring a survival benefit (27). Because deep grey matter structures are more susceptible to hypoxic-ischemic injury, they also suffer early disruption of the blood-brain barrier. This is supported by our observation that attenuation in the thalamus and putamen correlated with attenuation in the dural sinuses probably as a result of leakage and retention of contrast material during the initial angiography, making the use of attenuation values or GWR for prognostication difficult (10).

Consequently, brain CT remains just a part of the multimodal neuroprognostication approach with numerous other predictors of patients' outcomes combined in prognostic prediction models (28). These include patients' demographics, prehospital circumstances, duration of cardiac arrest, cardiac rhythm, neurological criteria, laboratory values and proteomics, EEG, evoked potentials, and others (8).

Study limitations

This study has the following limitations. Firstly, brain CT was not protocolized and within the first 36 hours after cardiac arrest was performed in only 18% of all patients in the Prague OHCA study based on the clinician's decision. Secondly, brain CT was contaminated with contrast material from the previous coronary angiography in half of the patients, again as a consequence of routine clinical triage and management of the most frequent cause of refractory OHCA.

Conclusions

Lower and upper thresholds of GWR in the putamen and caudate on early non-contrast brain CT after prolonged OHCA treated both by conventional or ECPR differentiate patients with favorable and unfavorable neurological outcomes regardless of type of CPR.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-430/coif). LL serves as an unpaid editorial team member of *Quantitative Imaging in Medicine and Surgery*. LL and AB

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The original study as well as secondary analyses were approved by the Ethics Committee of the General University Hospital in Prague (No. 192/11 S-IV) and informed consent was taken from all individual participants or their relatives.

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Supplementary

Table S1 Attenuation of grey and white matter structures, GWRs in patients with and without ECPR

Brain structure	Patients with ECPR (n=31)	Patients without ECPR (n=14)	P (with *vs.* without ECPR)	Selected threshold		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	P
				Lower	Upper						
Panel A: attenuation (HU)											
Caudate	36.3±5.6	37.6±3.6	0.44	33	40	30	67	71	26	0.62	0.22
Putamen	36.8±4.6	37.9±2.9	0.45	33	39	36	58	71	25	0.57	0.44
Thalamus	35.5 (4.0)	37.0 (4.4)	0.18	33	40	18	79	67	29	0.52	0.80
Medial cortex	32.8 (4.5)	34.6 (4.6)	0.29	30	39	15	79	63	28	0.50	0.98
CS	28.3±2.7	31.0±2.8	0.003*	27	33	36	86	86	36	0.63	0.16
Panel B: attenuation ratio (GWR)											
Caudate: CS	1.28±0.19	1.22±0.08	0.22	1.18	1.30	64	57	78	40	0.64	0.13
Putamen: CS	1.32 (0.11)	1.22 (0.11)	0.090	1.20	1.33	52	71	81	38	0.66	0.082
Thalamus: CS	1.30 (0.15)	1.22 (0.11)	0.024*	1.21	1.40	39	57	68	29	0.53	0.78
Medial cortex: CS	1.16 (0.09)	1.13 (0.10)	0.021*	1.10	1.20	39	64	72	31	0.53	0.78

Lower and upper thresholds are obtained from *Table 3*. Data are expressed as mean ± standard deviation or median (IQR). In this table, IQRs are expressed Q75 minus Q25. *, significant P values. GWR, grey-to-white matter attenuation ratio; ECPR, extracorporeal cardiopulmonary resuscitation; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the ROC curve; ROC, receiver operator characteristic; HU, Hounsfield unit; CS, centrum semiovale; IQR, interquartile range; Q25, 25th percentile; Q75, 75th percentile.

Table S2 Correlation (rho) between attenuation in brain structures (and GWRs) with mean attenuation in the superior and inferior sagittal sinus (residual contrast material opacification)

Brain structure	Correlation	
	Rho	P value
Attenuation (HU)		
Caudate	0.22	0.14
Putamen	0.32	0.033*
Thalamus	0.38	0.011*
Medial cortex	0.24	0.12
CS	0.26	0.087
Attenuation ratio (GWR)		
Caudate: CS	0.036	0.82
Putamen: CS	–0.029	0.85
Thalamus: CS	0.150	0.32
Medial cortex: CS	0.055	0.72

*, significant P values. GWR, grey-to-white matter attenuation ratio; HU, Hounsfield unit; CS, centrum semiovale.

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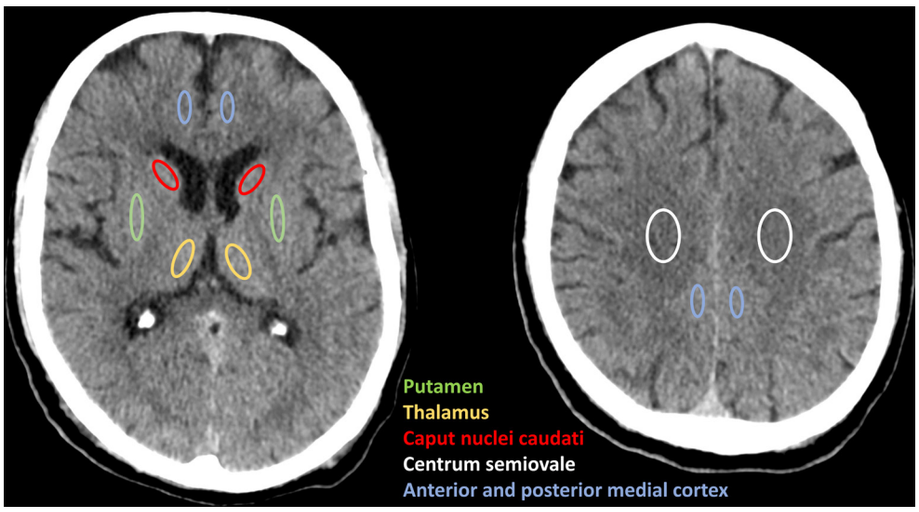

Figure S1 Measurement of attenuation of grey and white matter on axial 5 mm CT scan at the level of basal ganglia and centrum semiovale. CT, computed tomography.

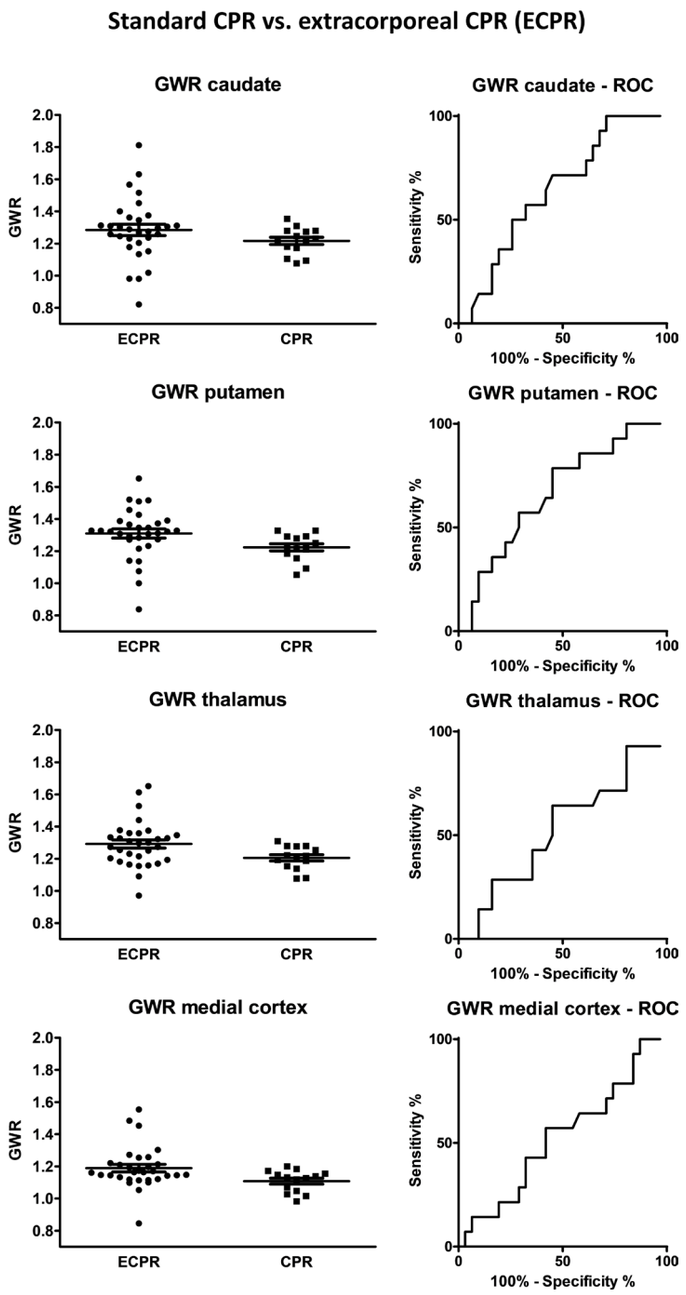

Figure S2 Comparison of GWRs in deep grey matter structures (caudate, putamen, thalamus) and cerebral cortex in a dot plot (left column) between patients treated with standard CPR and ECPR in a dot plot (left column). Corresponding ROC curves are shown in the right column. CPR, cardiopulmonary resuscitation; ECPR, extracorporeal cardiopulmonary resuscitation; GWR, grey-to-white matter attenuation ratio; ROC, receiver operator characteristic.

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