Global Impairment of Cerebral Perfusion Measured using Dynamic Susceptibility Contrast Perfusion-Weighted Imaging in Out-of-Hospital Cardiac Arrest Survivors: A Prospectively Preliminary Study

Changshin Kang
Chungnam National University Hospital https://orcid.org/0000-0001-8848-5062
In Ho Lee
Chungnam National University School of Medicine
Jung Soo Park (cpcr@cnu.ac.kr)
Chungnam National University Hospital https://orcid.org/0000-0002-4283-5423
Yeonho You
Chungnam National University Hospital
Insool Yoo
Chungnam National University School of Medicine
Yong Chul Cho
Chungnam National University Hospital
Wonjoon Jeong
Chungnam National University Hospital
Hong Joon Ahn
Chungnam National University School of Medicine
Chan Kang
Chungnam National University School of Medicine

Research

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Abstract

Background: Dynamic susceptibility contrast perfusion weighted imaging (DSC-PWI) is useful for measuring cerebral perfusion (CP). This study aimed to assess global impairment and the prognostic performance of CP parameters measured by DSC-PWI in out-of-hospital cardiac arrest (OHCA) survivors.

Methods: This is a single-centre, prospective observational study. OHCA survivors who underwent DSC-PWI within 6 h after restoration of spontaneous circulation were enrolled. CP parameters (cerebral blood volume [CBV], cerebral blood flow [CBF], mean transit time [MTT], time to peak [TTP], and time to the maximum of the residue function [Tmax]) were quantified by normalisation + leakage correction (LC) or by arterial input function (AIF) + LC. The primary outcome was survival to discharge; subjects who died due to withdrawal of life-sustaining therapy or who were diagnosed with brain death (BD) were included in non-survival. The secondary outcome was 6-months neurological outcome. CP parameters were compared across groups, and receiver operating characteristic (ROC) curves were constructed to assess prognostic performances.

Results: Thirty-one subjects (male, 20; 64.5%) participated. Relative CBV (rCBV) and CBF (rCBF) quantified by normalisation + LC were significantly higher in the non-survival group (p=0.02 and p=0.03, respectively). The area under the ROC curves (AUROCs) and 100% specific sensitivities for non-survival were 0.75/31.3% and 0.73/25.0%, respectively. MTT and Tmax quantified by AIF + LC were significantly higher in non-survival (p=0.01 and p=0.01, respectively). Their AUROCs and 100% specific sensitivities were 0.77/56.3% and 0.76/43.8%, respectively. rCBV and rCBF quantified by normalisation + LC were significantly higher in the poor neurological outcome group (p<0.01 and p=0.02, respectively). The AUROCs and 100% specific sensitivities for poor neurological outcome were 0.81/23.8% and 0.77/19.1%, respectively. Tmax quantified by AIF + LC was significantly higher in poor neurological outcome (p=0.04). Its AUROC and 100% specific sensitivity were 0.74/33.3%.

Conclusion: Hyperaemia and delayed CP were present in the non-survival and poor neurological outcome groups. MTT quantified by AIF + LC could be the most powerful parameter for predicting mortality or BD in OHCA survivors at an early stage of post cardiac arrest care. AIF may be more appropriate as quantifying method for CP in OHCA survivors than normalisation.

Introduction

Although significant improvements have been achieved in the cardiac arrest (CA) and post-cardiac arrest (PCA) care bundles, rates of death and poor neurological outcome remain high [1]. Brain death (BD) may occur in a sixth to a half of successful resuscitations after CA [2, 3]. To assess BD, whether for withdrawal of life-sustaining therapy (WLST) or for organ donation by CA survivors in whom early death is strongly anticipated, an earlier prediction of outcome is desirable for the process of care and for the provision of information to the patient's relatives [4]. Currently, however, neurological assessment of BD in patients remaining unconscious is not recommended earlier than 72 h after CA.

The current high rates of mortality and poor neurological outcome after CA are mainly due to hypoxic-ischemic brain injury (HIBI), which is a complex pathophysiological mechanism accompanying the impairment of cerebral perfusion [5]. The current gold standard for the assessment of cerebral perfusion is dynamic susceptibility contrast perfusion-weighted imaging (DSC-PWI), which is a proven diagnostic tool for BD and has 100% sensitivity and specificity [6, 7]. Cerebral perfusion measures that can be derived from this technique include: cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT), time to peak (TTP), and time to the maximum of the residue function (Tmax) [8, 9]. Furthermore, several methods are available for the optimal quantification of the cerebral perfusion parameters, such as normalisation, calculation of the arterial input function (AIF), and leakage correction (LC) [10, 11].

To the best of our knowledge, the association between the impairment of cerebral perfusion measured by DSC-PWI and clinical outcomes has not been assessed at early stages of PCA care in survivors of out-of-hospital cardiac arrest (OHCA). Therefore, we aimed to explore in a preliminary way the usefulness of various cerebral perfusion parameters derived from DSC-PWI in the prediction of mortality including BD and neurological outcome at early stages of PCA care.

Methods

Study design and population

This single-centre, prospective observational study included OHCA patients admitted to Chungnam National University Hospital (CNUH) in Daejeon, between August 1, 2018 and April 30, 2019, and was approved by the CNUH Institutional Review Board (CNUH-2017-10-027). Informed consent was obtained from their substitute decision-makers prior to enrolment.

We enrolled OHCA survivors who had undergone DSC-PWI within 6 h after restoration of spontaneous circulation (ROSC). Patients were subsequently excluded if they had (1) younger age than 18 y, (2) CA due to trauma, (3) ineligibility for targeted temperature management (e.g., brain haemorrhage, active bleeding, known terminal illness, poor pre-arrest neurological status), (4) no responsible relative able to approve magnetic resonance imaging (MRI), contraindication for MRI (e.g., indwelling metal device), or (5) opposition to further patient treatment by the next of kin.

Post-CA care

All comatose, non-traumatic OHCA survivors received PCA care based on the 2015 international guidelines [12]. We used an Arctic Sun^{TM} system (Bard Medical, Louisville, CO, USA) to administer targeted temperature management. Patients were sedated using midazolam and paralysed using cisatracurium. Physicians expert in emergency medicine and intensive care optimized cerebral perfusion by maintaining arterial blood gas levels and blood pressure as follows: oxygen saturation, 94–96%; partial pressure of carbon dioxide, 35–45 mmHg; and mean arterial pressure (MAP), >70 mmHg. If evidence of seizure was found by electroencephalography or clinical observation, anti-epileptics were

administered. BD was determined based on the guidelines of the Korea Medical Association [13]. These include documentation of the following symptoms: absence of brain stem reflexes—including bilateral absence of pupillary response to light, pupils equal to or greater than mid-size, bilateral absence of corneal responses, bilateral absence of vestibulo-ocular responses, and absent gag and cough reflexes—all confirmed by two qualified physicians, and demonstration of electrical inactivity by electroencephalography. BD was confirmed by ancillary testing when documentation of the minimum clinical criteria could not be completed, or when confounding factors that could not be corrected were present.

MRI protocol

DSC-PWI was performed with a 3-T scanner (Achieva; Philips Medical Systems, The Netherlands) within 6 h after ROSC. DSC-PWI using T2 fast field echo planar imaging sequence was acquired with 24 sections. For each section, we obtained 50 images at each repetition time. After 5 seconds of imaging, a bolus of gadobutrol (Gadovist, Bayer Healthcare, Berlin, Germany) at a dose of 0.1 mmol/kg of body weight and a rate of 2.5 ml/sec was injected intravenously.

Image processing

Fig. 1 shows the quantification methods for cerebral perfusion analysis used here. Post-processing of cerebral perfusion parameters was performed with a dedicated software package (nordicICE; Nordic Imaging Lab, Bergen, Norway). All maps of CBV, CBF, MTT, TTP, and Tmax were analysed after manually masking the whole-brain parenchyma using the DSC-PWI raw data. Masking and region-of-interest (ROI) placement were verified by an experienced, board-certified neuroradiologist. Normalisation or AIF with LC were performed to account for confounding effects. To compare the predictive performance of the two methods, we acquired the data as follows: first with application of normalisation with LC (Normalisation + LC), and second with application of AIF with LC (AIF + LC). Cerebral perfusion parameters calculated with the two methods represented the global average.

Outcomes

The primary outcome was survival to discharge. Since WLST is performed strictly in a conservative manner in Korea, WLST during PCA care can be performed only in patients who are strongly anticipated to be BD or expired within a few days, according to legal requirements. Therefore, patients with WLST or BD were included in the non-survival group. The secondary outcome was poor neurological outcome at 6 mo after the OHCA. Neurological outcome was measured using the Glasgow Pittsburgh Cerebral Performance Categories (CPC) scale, either through face-to-face interview or through a structured telephone interview [14]. The interviews were performed by an emergency physician well versed in our protocol and blinded to the patients' prognosis and clinical data. Patients were classified into 5 categories based on their Glasgow score: CPC 1 (good performance), CPC 2 (moderate disability), CPC 3 (severe disability), CPC 4 (vegetative state), and CPC 5 (brain death or death).

Statistical analysis

Categorical variables are presented as frequencies and percentages, and comparisons were by Fisher's exact test. Continuous variables are presented as median and interquartile range (IQR). The Mann-Whitney U test was used to compare median CBV, CBF, MTT, TTP, and Tmax. Receiver operating characteristic (ROC) curves were constructed for assessing the prognostic value of each perfusion parameter. The ROC curve plots sensitivity on the y-axis and specificity (one minus the type-1 error rate) on the x-axis, and measures the overall test accuracy. The most important summary index of the ROC curve is the area under the ROC curve (AUROC). The cut-off values were used to determine sensitivities at a specificity of 100%, because high specificity is the most critical metric with CA survivors, in whom false-positive predictions may lead to a patient who has a potentially good outcome dying by WLST or donation. Statistical analyses were performed using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA), and MedCalc version 15.2.2 (MedCalc Software; Mariakerke, Belgium). Results were considered significant at $p<0.05$.

Results

Patient characteristics

Overall, 35 patients comatose after OHCA were received with PCA care at our hospital during the study period, of whom 31 were finally enrolled (Fig. 2). Each analysis had 15 and 16 subjects in survival and non-survival groups, respectively, and 10 and 21 subjects with good and poor neurological outcomes, respectively (Fig. 2).

Table 1 shows the baseline data of all subjects. The median age was 54.5 (IQR, 19.0 – 78.0) y, and 64.5% were male. The number of witnessed arrests and shockable rhythms was significantly higher in the survival group. The durations of no and low flow time were significantly shorter in the survival and good-neurological-outcome groups. The numbers of shockable rhythms and cardiac aetiologies were significantly higher in the group with good neurological outcomes. The average MAP before and after MRI was not significantly different in any group.

Cerebral perfusion in survival versus non-survival groups

In the parameters quantified by normalisation + LC, the median relative cerebral blood volume (rCBV), relative cerebral blood flow (rCBF), and TTP were significantly greater in the non-survival group ($p=0.02$, $p=0.03$, and $p=0.02$, respectively). In the parameters quantified by AIF + LC, the median MTT and Tmax were significantly greater in the non-survival group ($p=0.01$ and $p=0.01$, respectively). No other comparisons reached significance (Table 2, Fig. 3).

Cerebral perfusion in groups with good versus poor neurological outcomes

In the parameters quantified by normalisation + LC, the median rCBV and rCBF were significantly greater in the poor-outcomes group ($p=0.01$ and $p=0.02$, respectively). In the parameters quantified by AIF + LC,

the median Tmax was significantly greater in the poor-outcomes group (p=0.04). No other comparisons reached significance (Table 2, Fig. 3).

ROC analysis of the significant outcome predictors

Table 3 shows the AUROC of cerebral perfusion parameters for predicting non-survival and poor neurological outcome. Cerebral perfusion parameters appear quantified by the two different methods.

The non-survival AUROCs for rCBV and rCBF quantified by normalisation + LC were 0.75 and 0.73, respectively. The 100% specific cut-off values and sensitivities were: rCBV, 4.50 ml/100 g and 31.3 %, respectively; and rCBF, 3.96 ml/100 g/min and 25.0 %, respectively. The non-survival AUROCs for MTT and Tmax quantified by AIF + LC were 0.77 and 0.76, respectively. The 100% specific cut-off values and sensitivities were: MTT, 8.23 s and 56.3 %, respectively; and Tmax, 4.50 s and 43.8%, respectively (Table 3).

The AUROCs for poor neurological outcome of rCBV and rCBF quantified by normalisation + LC were 0.81 and 0.77, respectively. The 100% specific cut-off values and sensitivities were: rCBV, 4.50 ml/100 g and 23.8 %; and rCBF, 3.96 ml/100 g/min and 19.1%, respectively. The AUROC for poor neurological outcome of Tmax quantified by AIF + LC was 0.74 and the 100% specific cut-off value and sensitivity were 4.5 s and 33.3 %, respectively.

Discussion

This study is the first to quantitatively analyse in OHCA survivors the various cerebral perfusion parameters that can be measured using DSC-PWI. We report the global impairment of cerebral perfusion in OHCA survivors and compare the prognostic performances of five cerebral perfusion parameters, each derived by two alternative quantification methods. Although a significant difference was shown in cerebral perfusion between outcomes with both quantification methods, the specific parameters among the five parameters that best predicted outcomes were completely inconsistent between quantification methods. rCBV and rCBF calculated by normalisation + LC were significantly higher in non-survival and poor neurological outcome groups. However, with AIF + LC, Tmax was significantly higher in both the non-survival and poor neurological outcome groups, and MTT was significantly more delayed in the non-survival group.

CBV and CBF showed completely different results according to which quantification method was used. Conventionally, the normalisation method quotes relative values of CBV and CBF (rCBV and rCBF) instead of absolute values. Relative values are obtained from the ratio of the maximum ROI between an affected and an unaffected hemisphere, and, thus, the normalisation method especially applies to cerebral infarction or brain tumour models [15]. In contrast, HIBI in CA model has completely different pathophysiological characteristics: global and diffuse whole-brain damage [16, 17]. Given the specific pathophysiologic characteristics of CA survivors and the calculation process of normalisation, we suggest that this method might be not appropriate for the assessment of CA survivors with HIBI. In

addition, this method can introduce bias from the inclusion of the contralateral reference ROI in white matter [18, 19]. Ann et al. have suggested that the absolute CBV and CBF of the whole brain can be quantitatively calculated by AIF measurement [8].

Our study found proof of cerebral hyperaemia in OHCA survivors, as demonstrated by a higher absolute CBV and CBF compared to the healthy brain, which has average values of 4 ml/100 g and 60 ml/100 g/min, respectively, with the AIF + LC method [10]. Reactive hyperaemia, which has been linked to a loss of vascular tone and a vasodilatation secondary to acidosis, has been reported to appear in the immediate phase (0 – 20 min) of post-resuscitation in CA survivors [20, 21]. However, our mean time from ROSC to MRI was 4.1 h (IQR, 2.4 – 5.9), which corresponds to the early phase of post-resuscitation, when cerebral hypoperfusion is generally reported suggesting secondary ischemic brain damage [21]. There are several possible explanations for this conflicting result between the present and previous studies. First, cerebral perfusion can vary according to the characteristics of CA: shockable versus non-shockable rhythm [22], and asphyxia CA versus potassium chloride-induced CA [23]. Second, cerebral perfusion during each stage is different in various brain regions: subcortex versus cortex, and grey versus white matter [24]. Third, cerebral perfusion is dependent on insult duration: hyperaemia is less frequently observed in prolonged insults [25]. Finally, the baseline characteristics of patients, such as age, sex, and race, also influence cerebral perfusion post-resuscitation [26]. Hence, even though we did not observe significantly different absolute CBV and CBF between survival and non-survival groups, we did find an increased CBV and CBF during the early phase (20 min to 12 h from ROSC) in OHCA survivors compared to the healthy brain. This cerebral hyperaemia can be caused by an intravascular stasis (known as the no-reflow phenomenon) [27] and by an imbalance between vasodilators and vasoconstrictors (e.g., nitrogen oxide and endothelin-1, respectively) [28].

In DSC-PWI, the time required for the change in signal intensity to reach the maximum can be demonstrated as TTP (the time to peak concentration of contrast), as MTT (the mean transit time of contrast through whole brain), and as Tmax (the time to the maximum of the residue function). However, without quantification of the AIF, these parameters can depend on tissue properties as well as on non-tissue-related characteristics (e.g. injection rate, cardiac output, arterial status, etc.), and thus their physiological interpretation could be very complex [29, 30]. To clarify these confounding effects, the AIF, which is defined as the function describing the time-dependent concentration input to the tissue, has been alternatively suggested as an important tool for quantifying the cerebral perfusion measured using DSC-PWI more accurately [10]. Hence, in a previous study, Lansberg et al. have suggested that MTT and Tmax with quantification by AIF are considered as an idealised bolus of contrast agent in cardiovascular disease [6].

In this study, MTT and Tmax calculated from the AIF with LC were significantly higher in the non-survival and poor neurological outcome groups. These results could theoretically be deduced from low MAP, high intra-cranial pressure (ICP), or increased blood capacity of the tissues, which can be conceived as pumpability, resistance, and the capacity of a tank or pipe, respectively [31]. MAP was not significantly different between groups, and we assumed that ICP was not significantly different between groups either

based on our previous study reporting that within the first 12 h after CA, ICP is not significantly different between good and poor neurological outcomes [32]. Patients with a poor outcome, whether mortality or neurological, reportedly showed an increased CBV due to coupled pathophysiological processes: vasodilatation mediated by adenosine, nitric oxide, or prostaglandin [33], mitochondrial injury resulting from anaerobic metabolism [34], increased lactate and acidity [35], and hyperglycolysis [36]. Based on these reports, we suggest that the increased MTT and Tmax we observed, indicating delayed cerebral perfusion, are caused by vasodilatation and increased permeability of cerebral vessels, resulting in an increased capacity for blood in the tissue. The coupled and sequential pathophysiological processes operating in severe HIBI can be demonstrated as prolongations of the MTT and Tmax. Consistent with this, MTT calculated from the AIF had the highest sensitivity in predicting non-survival observed here. Therefore, cerebral perfusion parameters obtained from DSC-PWI via determination of the AIF, especially MTT and Tmax, could be appropriate for prognostication in OHCA survivors.

In contrast to normalisation and AIF, LC was applied to all image quantifications in this study. LC reportedly leads to greater accuracy in measuring cerebral perfusion in CA patients, who are anticipated to suffer from blood-brain barrier (BBB) disruption and/or high cerebral capillary permeability, which, if LC is not applied, can produce underestimation of cerebral perfusion due to extravasation of the contrast agent from the intravascular compartment to the extravascular-extracellular space [37, 38]. Additionally, a study on an animal model of CA has reported that cerebral vasoparalysis and BBB disruption are observed at about the immediate period (30 min after ROSC) [39]. Hence, we suggest that LC is essential in quantifying cerebral perfusion in OHCA survivors.

This study had several limitations on generalisability. First, it was single-centre and with small sample size. Second, the inclusion of only patients undergoing evaluation by MRI may have led to selection bias. Third, the DSC-PWI data were variable within each ROI [24], which could lead to an additional bias. However, MTT and Tmax were approximately uniform across normal grey and white matter, which is beneficial for visual contrast and when maps are thresholded [40]. Finally, the pattern of cerebral perfusion derangement observed in CA survivors reportedly differs by CA aetiology and brain region. However, these variables were not considered here.

Conclusion

Hyperaemia and delayed cerebral perfusion were observed in non-survivor/BD and poor neurological outcome groups. MTT and Tmax quantified by AIF with LC and measured by DSC-PWI were useful in predicting mortality/BD at an early stage of PCA care. AIF may be more appropriate than normalisation in OHCA survivors. Further prospective multicentre studies are required to confirm our results.

Abbreviations

AIF, arterial input function; AUROC, area under the ROC curve; BD, brain death; CA, cardiac arrest; CBF, cerebral blood flow; CBV, cerebral blood volume; CP, cerebral perfusion; DSC-PWI, dynamic susceptibility

contrast, perfusion weighted imaging; HIBI, hypoxic-ischemic brain injury; ICP, intra-cranial pressure; IQR, interquartile range; LC, leakage correction; MAP, mean arterial pressure; MRI, magnetic resonance imaging; MTT, mean transit time; OHCA, out-of-hospital cardiac arrest; PCA, post-cardiac arrest; rCBF, relative cerebral blood flow; rCBV, relative cerebral blood volume; ROC, receiver operating characteristic; ROI, region of interest; ROSC, restoration of spontaneous circulation; Tmax, maximum of the residue function; TTP, time to peak; WLST, withdrawal of life-sustaining therapy

Declarations

Ethics approval and consent to participate

The study design and plan were approved by the institutional review boards (IRB) of Chungnam National University Hospital (Approval No. CNUH-2017-10-027). Written informed consent was waived by the IRB.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

JS Park contributed to study conception and design. C Kang and IH Lee contributed to data acquisition. YC Cho, W Jeong, and HJ Ahn contributed to data analysis and interpretation. I Yoo and C Kang contributed to statistical analysis and revision. Y You contributed to acquisition of funding. CKang, IH Lee and JS Park contributed to the drafting of the manuscript and its critical revision for important intellectual content. All authors have read and approved the final version of the manuscript.

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Tables

Table 1. Baseline demographics and clinical characteristics

	All patients	Survival to discharge		*p*	Neurological outcome		*p*
	(n=31)	Survival, (n = 15)	Non-survival, (n = 16)		Good, (n = 10)	Poor, (n = 21)	
Age, mean ± SD, years	52.5 ± 16.3	52.5 ± 15.7	52.7 ± 14.5	0.87	51.7 ± 13.9	53.1 ± 15.7	0.70
Male, n (%)	20 (64.5)	13	7	0.02*	9	11	0.06
Cardiac arrest characteristics							
Witness, n (%),	16 (51.6)	11	5	0.03*	8	8	0.05
Bystander CPR, n (%)	23 (74.2)	12	11	0.69	9	14	0.22
Shockable rhythm, n (%)	9 (29.0)	8	1	<0.01*	8	1	< 0.01*
Cardiac aetiology, n (%)	8 (25.8)	6	2	0.38	6	2	0.02*
No flow time, min, median (IQR)	2.0 (0.0 – 140.0)	1.0 (0.0 – 54.0)	15.0 (0.0 – 140.0)	0.02*	0.0 (0.0 – 23.0)	13.5 (0.0 – 140.0)	< 0.01*
Low flow time, min, median (IQR)	23.0 (2.0 – 53.0)	15.0 (2.0 – 30.0)	37.0 (7.0 – 52.0)	<0.01*	11.0 (2.0 – 30.0)	30.0 (7.0 – 52.0)	< 0.01*
GCS after ROSC, median (IQR)	3 (2 – 8)	3 (3 – 8)	3 (2 – 4)	0.06	3 (3 – 8)	3 (2 – 4)	0.05
Average of MAP measured before and after MRI, mmHg (IQR)	98.5 (66.0 – 154.0)	99.0 (66.0 – 154.0)	95.0 (74.0 – 115.0)	0.55	103.0 (73.0 – 154)	92.5 (66.0 – 118.0)	0.07
Time to perfom MRI, h (IQR)	4.1 (2.4 – 7.4)	4.5 (2.7 – 7.4)	4.0 (2.4 – 5.8)	0.10	4.3 (2.7 – 7.4)	4.2 (2.4 – 5.8)	0.52

BD, brain death; SD, standard deviation; CPR, cardiopulmonary resuscitation; IQR, interquartile range; GCS, Glasgow coma scale; ROSC, restoration of spontaneous circulation; MAP, mean arterial pressure; MRI, magnetic resonance image

* *p* values are significant at $p < 0.05$

Table 2. Cerebral perfusion parameters

ROI	Survival to discharge		*p*	Neurological outcome		*p*
	Survival, (n = 15)	Non-survival, (n = 16)		Good, (n = 10)	Poor, (n = 21)	
LC + Normalisation						
rCBV, mL/100g (IQR)	2.72 (2.02–4.50)	3.71 (0.66–8.18)	0.02*	2.57 (2.02-4.50)	3.41 (0.66-8.18)	<0.01*
rCBF, mL/100g/min (IQR)	2.64 (2.10–3.96)	3.28 (0.82–6.54)	0.03*	2.48 (2.10-3.96)	3.19 (0.82-6.54)	0.02*
MTT, s (IQR)	22.51 (15.61–26.19)	21.87 (12.94–30.86)	0.52	20.89 (15.61-26.19)	24.05 (12.94-30.86)	0.31
TTP, s (IQR)	19.47 (14.43-23.32)	22.80 (15.12-60.52)	0.02*	19.78 (15.82-23.32)	21.70 (14.43-40.52)	0.37
LC + AIF						
CBV, mL/100g (IQR)	17.69 (14.22-46.38)	20.31 (9.14-28.89)	0.55	16.67 (14.21-23.36)	19.74 (9.14-46.38)	0.19
CBF, mL/100g/min (IQR)	154.35 (135.14-223.72)	134.67 (29.39-247.55)	0.16	150.28 (135.14-197.68)	149.01 (29.39-247.55)	0.72
MTT, s (IQR)	6.63 (4.44-8.23)	8.63 (5.70-13.89)	0.01*	6.60 (4.44-8.23)	7.88 (5.39-13.89)	0.05
Tmax, s (IQR)	0.85 (0.37-4.50)	3.29 (0.20-17.82)	0.01*	0.56 (0.37-4.50)	1.60 (0.20-17.82)	0.04*

LC, leakage correction; rCBV, relative cerebral blood volume; IQR, interquartile range; rCBF, relative cerebral blood flow; MTT, mean transit time; TTP, time to peak; AIF, arterial input function; CBV, cerebral blood volume, CBF, cerebral blood flow; Tmax, time to maximum of the residue function

* *p* values are significant at $p < 0.05$

Table 3. Prognostic performances of cerebral perfusion parameters for non-survival and 6-months poor neurological outcomes

Variables	Cut off	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)	*p* value
For non-survival group							
LC + Normalisation							
rCBV	>4.50	31.3 (11.0 – 58.7)	100	100	57.7 (36.9 – 76.6)	0.75 (0.57 – 0.89)	0.02
rCBF	>3.96	25.0 (7.3 – 52.4)	100	100	55.6 (35.3 – 74.5)	0.73 (0.54 – 0.87)	0.03
LC + AIF							
MTT	>8.23	56.3 (29.9 – 80.2)	100	100	68.2 (45.1 – 86.1)	0.77 (0.58 – 0.90)	0.01
Tmax	>4.50	43.8 (19.8 – 70.1)	100	100	62.5 (40.6 – 81.2)	0.76 (0.58 – 0.90)	0.01
For poor neurological outcomes group							
LC + Normalisation							
rCBV	> 4.50	23.8 (8.2 – 47.2)	100	100	38.5 (20.2 – 59.4)	0.81 (0.63 – 0.93)	<0.01
rCBF	>3.96	19.1 (5.4 – 41.9)	100	100	37.0 (19.4 – 57.6)	0.77 (0.59 – 0.90)	0.02
LC + AIF							
Tmax	>4.50	33.3 (14.6 – 57.0)	100	100	41.7 (22.1 – 63.4)	0.74 (0.55 – 0.88)	0.04

CI, confidence interval; PPV, positive predict value; NPV, negative predict value; AUC, area under the curve; LC, leakage correction; rCBV, relative cerebral blood voluime; rCBF, relative cerebral blood flow; AIF, arterial input function; MTT, mean transit time; Tmax, time to maximum of the residue function

Figures

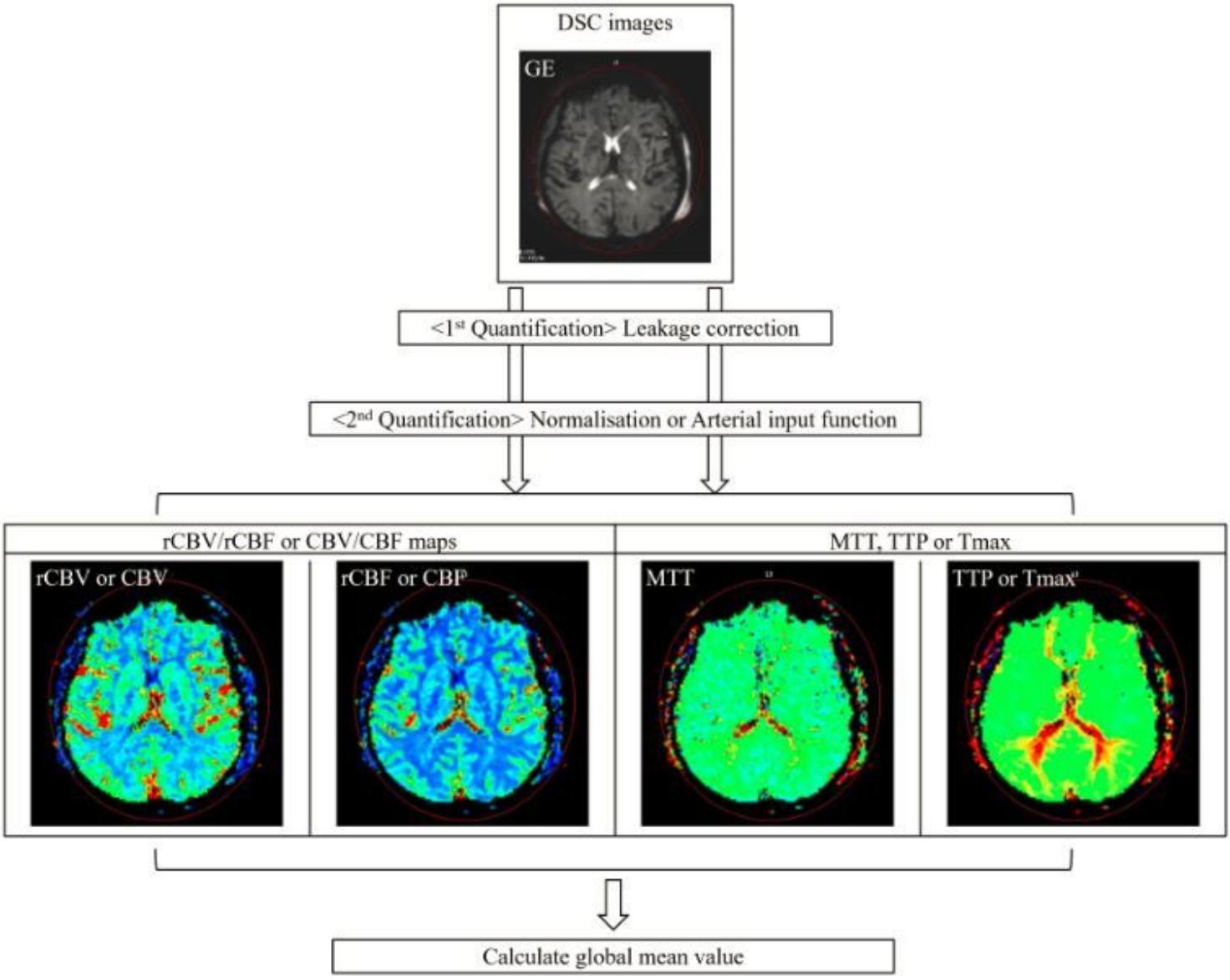

Figure 1

Flow chart summarizing the steps of analysis of cerebral perfusion for generation of haemodynamic images for two quantification methods. DSC, dynamic susceptibility contrast; rCBV, relative cerebral blood volume; rCBF, relative cerebral blood flow; MTT, mean transit time; TTP, time to peak; CBV, cerebral blood volume, CBF, cerebral blood flow; Tmax, time to maximum of the residue function.

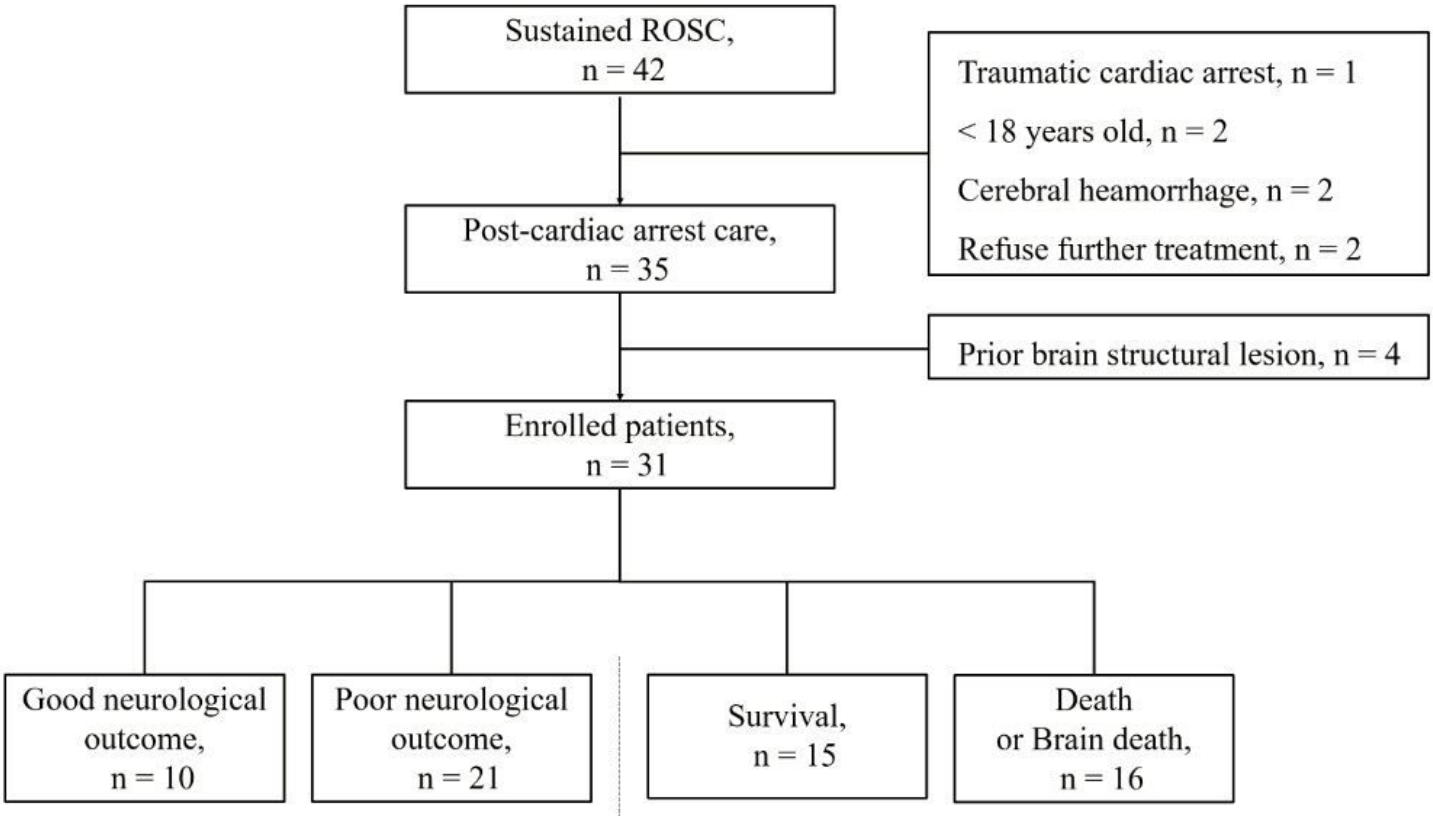

Figure 2

Flow diagram of patients included in the present study. ROSC, restoration of spontaneous circulation.

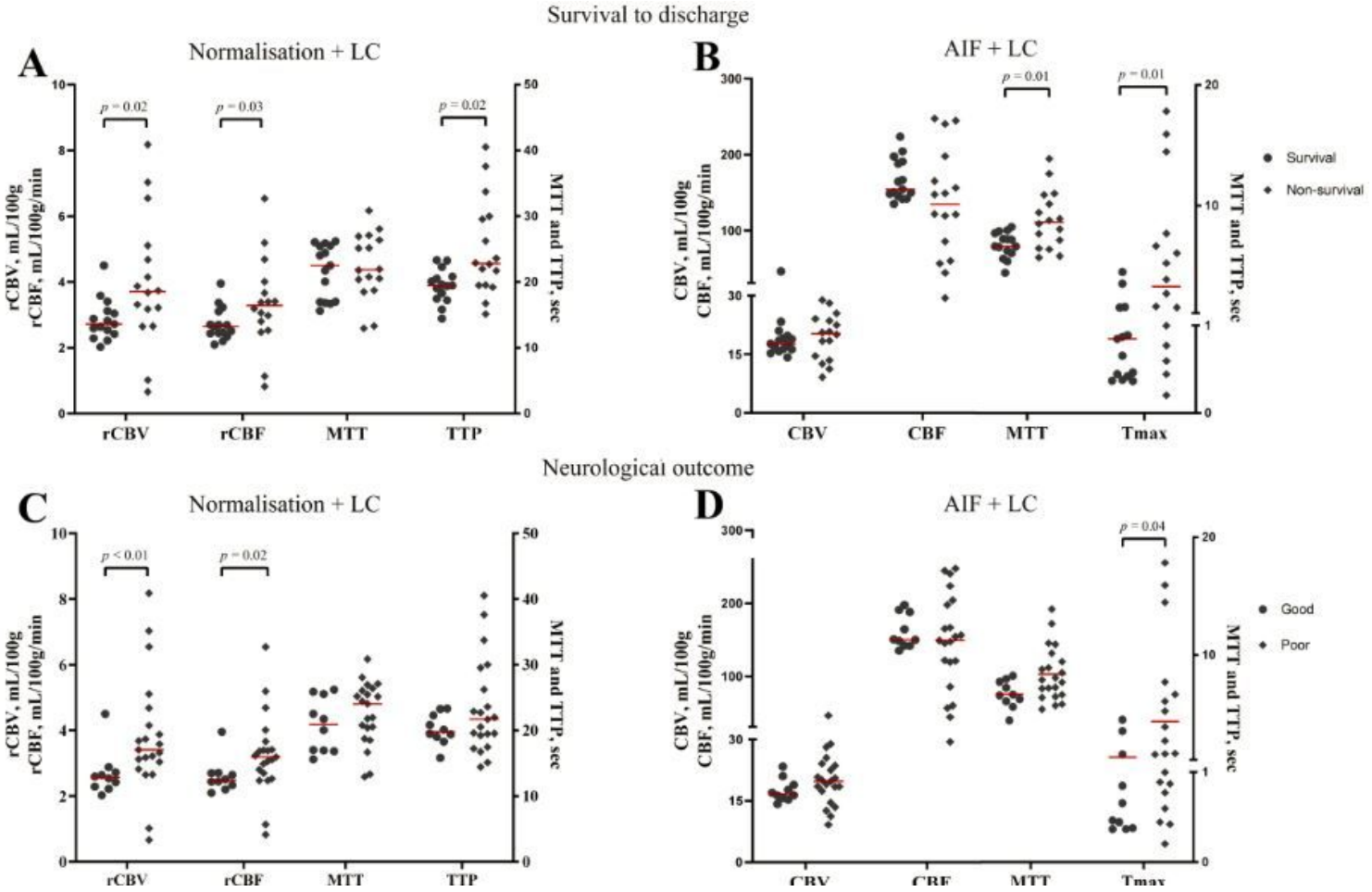

Figure 3

Survival to discharge versus non-survival/brain death: groupwise comparison of cerebral perfusion parameters quantified by (A) normalisation and leakage correction (LC) or by (B) calculation of the arterial input function (AIF) and LC. Good versus poor 6-mo neurological outcome: groupwise comparison of cerebral perfusion parameters quantified by (C) normalisation and LC or by (D) AIF and LC.