Diagnostic and Prognostic Contribution of Cerebrospinal Fluid Analysis After Cardiac Arrest

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Abstract

Background: Lumbar puncture is among the investigations used to determine the aetiology and prognosis of cardiac arrest, despite a dearth of data on its performance. We aimed to assess the diagnostic and prognostic performance of lumbar puncture after cardiac arrest.

Methods: We retrospectively studied data from prospectively established databases of consecutive patients who were admitted to two French ICUs in 2007-2016 with sustained return of spontaneous circulation (ROSC) after cardiac arrest and who underwent lumbar puncture as an aetiological investigation.

Results: Of 1984 patients with sustained ROSC, 65 (3.3%) underwent lumbar puncture and were included. Lumbar puncture identified a neurological cause of cardiac arrest in 6/65 (9%) patients, including 5 with neurologic prodromal symptoms before cardiac arrest and 4 with the lumbar puncture done post-mortem. Lumbar puncture performed before death showed nonspecific cerebrospinal fluid abnormalities in 37/53 (69.8%) patients. By univariate analysis, factors significantly associated with cerebrospinal fluid abnormalities were shorter no-flow time (0 min [0-3] versus 4 min [2-10], p=0.004) and post-resuscitation shock (26 [70%] versus 5 [31%], p<0.01). Presence of cerebrospinal fluid abnormalities was non significantly associated with poorer outcomes (CPC 3-4-5) (p=0.06).

Conclusions: Lumbar puncture, although rarely performed, can contribute to the aetiological diagnosis of cardiac arrest. As a second-line investigation, it identified the cause in 9% of our patients. Nonspecific cerebrospinal fluid abnormalities are common after cardiac arrest, perhaps due to blood-brain barrier disruption, and may carry prognostic significance.

Background

Cardiac arrest (CA) is among the most common causes of death in Europe and the United States despite advances in resuscitation and intensive care [1]. During the early phase after the return of spontaneous circulation (ROSC), identifying the cause is crucial to allow specific treatments that may improve patient outcomes and to lower the risk of recurrent CA. Recent guidelines recommend considering coronary angiography and cerebral and/or chest computed tomography (CT), depending on the CA circumstances and the electrocardiographic findings after ROSC, [2]. Unfortunately, even when these guidelines are applied, over 40% of patients receive no definitive aetiologic diagnosis and may therefore be at higher risk for delayed or inappropriate treatments and for poorer outcomes [3].

According to recent data, neurological causes explain 7% of CA cases [4]. CT of the brain should be the first-line investigation when a neurological cause is suspected. However, analysis of cerebrospinal fluid (CSF) obtained by lumbar puncture may be useful also. Surprisingly, whereas several studies have assessed the usefulness of various CSF biomarkers for neuroprognostication [5,6], the possible contribution of CSF analysis to the aetiological diagnosis has not been investigated. Apart from a neurological cause, another source of potential CSF abnormalities is blood-brain barrier (BBB) disruption

due to CA [7]. Better knowledge of such abnormalities would help to interpret CSF findings after CA and might also assist in establishing the prognosis [5,8].

We therefore designed a retrospective study of prospectively established databases to evaluate the diagnostic and prognostic contribution of CSF findings in patients admitted to the ICU with ROSC after CA.

Methods

We used two prospectively collected databases established at the Cochin hospital and Versailles hospital (#NCT03594318), two reference CA centres serving the southern and southwest areas of the Paris metropolis (France), respectively. Data collection was approved by the ethics committee of the French Intensive Care Society (#CESRLF_12-384 and 20-41) and the data were collected in compliance with French data protection legislation (French Data Protection Authority #MR004_2209691).

Study setting and early patient management

In France, when the emergency services receive a call reporting a suspected case of OHCA, the fire department and mobile emergency unit system despatch a team to the scene. The staff in each mobile emergency unit includes at least one physician trained in emergency medicine in compliance with international guidelines [9], who performs resuscitation. Patients with in-hospital CA are initially managed by the nurses and/or bedside physician until the arrival of an emergency physician, intensivist, or anaesthesiologist, who performs resuscitation. Patients with a stable return of spontaneous circulation (ROSC) are then admitted to the intensive care unit (ICU).

Post-resuscitation diagnostic evaluation

As recommended in current guidelines [2], a standardized diagnostic workup is started immediately to allow the prompt identification and treatment of the cause of CA. In patients with clinical and/or electrocardiographic evidence of myocardial ischemia and in those with no obvious non-cardiac cause of CA, coronary angiography is performed at hospital arrival, before ICU admission. If prodromal symptoms or the clinical findings suggest a respiratory or neurological cause of CA, CT of the chest or brain, respectively, may be chosen as the best first-line investigation. When the first-line investigation fails to detect a cause, further tests are considered [10]. Additionally, after ICU admission, laboratory tests are performed routinely to look for metabolic abnormalities or toxic substances according to the clinical history. A lumbar puncture for CSF collection is performed in patients with meningeal syndrome and when deemed appropriate by the physician in charge. All these investigations were available in both participating centres 24 h a day and 7 days a week. No post-mortem examination was performed.

Study population

All eligible patients entered into the Cochin and Versailles CA databases between January 2007 and December 2016 were included if they were older than 18 years, had stable ROSC at hospital admission,

and underwent lumbar puncture as part of the aetiological CA work-up. We did not include patients who underwent lumbar puncture for other reasons or who had a traumatic lumbar puncture defined as a CSF white cell count/red cell count <1/1000.

Study objectives

The primary objective was to assess the potential contribution of CSF analysis to the aetiological evaluation of CA. The secondary objectives were to identify factors associated with CSF abnormalities (defined as protein >0.45 g/L and/or white cell count >5/mm^3) and factors associated with survival and functional outcome at ICU discharge in those patients whose CSF analysis did not contribute to the aetiological diagnosis [11].

Data collection

Demographic data and data related to the CA were collected prospectively in the two electronic databases according to the Utstein style[12]. These data included age and sex, location at CA occurrence and initial rhythm, no-flow and low-flow times, presence of a witness, bystander CPR, number of defibrillations, and epinephrine use. We also recorded comorbidities, initial ECG ST-segment elevation, coronary angiography and/or CT findings, and definitive cause of CA. The following were collected in the ICU: use of targeted temperature management, presence of post-resuscitation shock, post-anoxic status epilepticus, and/or awakening defined as a response to commands with a motor Glasgow Coma Scale score of 6.

To further investigate the value of CSF analysis after CA, we used standardized forms to retrospectively collect the following from the pre-hospital and ICU records: symptoms preceding CA (e.g., headache, focal signs, confusion, coma, and seizures), CSF characteristics (biochemistry, cytology, and culture results), time to CSF collection, blood sample findings on the day of CSF collection, and CSF/serum protein quotient.

The functional outcome was assessed using the Cerebral Performance Category (CPC) at ICU discharge, and causes of death were recorded [13–15]. We defined a favourable outcome as a CPC score of 1 or 2 at ICU discharge.

Statistical analysis

Quantitative parameters were described as median (interquartile range [IQR]) and qualitative parameters as number (percentage). We compared categorical variables using Fisher's exact test and continuous variables using the Wilcoxon rank-sum test.

We first tested univariate associations between CA characteristics and whether CSF analysis contributed to the aetiological diagnosis of CA. We then looked for associations linking CA features to specific CSF abnormalities and to survival and functional outcome at ICU discharge.

All tests were two-sided and *p* values <0.05 were considered significant. Analyses were performed using R statistical software version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org. accessed September 12, 2019).

Results

Figure 1 is the patient flow chart. Of the 1984 patients admitted with stable ROSC after CA, 65 (3.3%) had a lumbar puncture and were included in the study.

Characteristics and diagnostic workup

Table 1 and Table S1 report the patient characteristics and the diagnostic investigations performed to identify the cause of CA**.** Figure 2 shows the first-line, second-line, and third-line investigations. Overall, cerebral CT was done in 52 (80%) patients, cerebral MRI in 5 (8%) patients, coronary angiography in 31 (48%) patients, and chest CT in 33 (51%) patients. The cause of CA was identified in 52 (80%) of the 65 patients and was respiratory in 18 (27%) patients, neurologic in 16 (25%) patients, cardiac in 7 (11%) patients, metabolic in 7 (11%) patients, and septic in 4 (6%) patients.

Contribution of cerebrospinal fluid analysis to the aetiologic diagnosis

LP were assessed in cases of suspicion of a neurological cause for cardiac arrestin 69% of cases. CSF analysis identified a neurological cause of CA in 6/65 (9%) patients, including 3 with subarachnoid haemorrhage, 2 with non-specific encephalitis, and 1 with bacterial meningitis. In 4 of these 6 patients, the lumbar puncture was performed post-mortem.

Table 1 reports the results of the univariate analysis of factors associated with the CSF analysis contributing to the aetiological diagnosis of CA. In the patients with a contributory CSF analysis, lumbar puncture was mostly the second-line investigation, with a median time of 1.5 days (IQR, 1-2) after ICU admission. Neurologic prodromal symptoms before CA were more common in the patients whose CSF analysis was contributory compared to the other patients (83% vs. 68%), although the difference was not significant (p=0.66).

Patients with nonspecific cerebrospinal fluid abnormalities

We excluded the 6 patients whose CSF analysis was contributory (including 4 with post-mortem lumbar puncture) and the additional 6 patients with post-mortem lumbar puncture. Of the remaining 53 patients, 37 (70%) had abnormal CSF findings, which are reported in Table 2. Table 3 compares the patients with versus without nonspecific CSF abnormalities. Two factors were significantly associated with having nonspecific CSF abnormalities, namely, shorter no-flow time (0 min [0-3] versus 4 min [2-10], p=0.004) and having post-resuscitation shock (26 [70%] versus 5 [31%], p<0.01). All 5 patients with oedema by cerebral CT had CSF abnormalities.

Patient outcomes

Overall ICU mortality was 70% (46/65). Table 1 shows the causes of death. All 6 patients whose CSF analysis contributed to the aetiological diagnosis died. Nonspecific CSF abnormalities were more common in patients with poor outcomes defined as CPC 3, 4, or 5 (73% versus 27% of those with CPC 1 or 2), although the difference was not statistically significant (p=0.06). Table S2 reports the CSF features in patients with favourable versus unfavourable outcomes. The only factor significantly associated with outcome was the CSF/serum protein quotient (p=0.017), with higher values in patients with worse outcomes.

Discussion

To our knowledge, this study provides the first detailed information on the diagnostic and prognostic contribution of CSF analysis to the aetiological diagnosis of CA. Only 3.3% of all patients admitted to the ICU with stable ROSC after CA underwent CSF analysis, which contributed to the aetiological diagnosis in 6 (9.2%) patients, although in 4 this contribution was obtained only post-mortem. Of the patients alive at the time of lumbar puncture, many (69.8%) had nonspecific CSF abnormalities, among which the CSF/serum protein quotient was significantly associated with the outcome.

Our study design provides a pragmatic view of the contribution of CSF analysis to the aetiological diagnosis of CA in patients with sustained ROSC at hospital admission. Lumbar puncture was performed only very rarely in our study. Few previously published data are available with which to compare our results. Most studies of CSF analysis after CA focused on the neuroprognostication accuracy of CSF biomarkers reflecting neuronal damage [5,6,8]. We are not aware of previous studies investigating CSF analysis for the aetiological diagnosis or the presence of CSF abnormalities unrelated to the aetiology. In previous studies, CSF analysis was performed in 5.3% of patients with neurological causes of CA and stable ROSC at hospital admission, chiefly as part of the aetiological workup [4], and in 40% of patients with CA complicating convulsive status epilepticus [4,16].

Given, the low incidence of noncardiac causes of CA, recent guidelines focus on the indications of coronary angiography, cerebral CT, and chest CT. Important factors are the patient's medical history; the presence of cardiac, respiratory, or neurologic prodromal symptoms, the circumstances of CA onset, and the physical findings on the scene. In practice, lumbar puncture is not a first-line investigation, unless there is evidence of a neurological cause whose identification may be helped by CSF analysis. Obstacles to lumbar puncture include anticoagulant and/or antiplatelet treatments, and concern about inducing cerebral herniation. Thus, cerebral CT may be required before lumbar puncture is performed. As expected, lumbar puncture was mainly performed as a second- or third-line investigation in our study, predominantly in patients with neurological prodromal symptoms before CA. Interestingly, 10 (15%) lumbar punctures were post-mortem and contributed to the diagnosis in 4 patients. This finding suggests that the situations in which CSF analysis may be helpful may not be recognised sufficiently early. Work is clearly needed to determine the indications of lumbar puncture after CA. An optimal aetiological workup is crucial to determine when specific aetiological treatments are appropriate, thus improving patient outcomes. In previous studies, ICU survival was higher when the aetiology was identified [3,17]. In

addition, identifying the cause may allow measures to minimise the risk of recurrent CA. Finally, knowledge of the causes of CA is important from a public health perspective. Lumbar puncture identified the cause of CA in 9% of our patients, although this proportion dropped to 3% when only patients alive at the time of lumbar puncture were considered.

Over two-thirds of our patients without neurological causes of CA had nonspecific CSF abnormalities, of which the most common was an increase in protein (73%), followed by an increase in white cells (27%). Several hypotheses can be raised to explain these findings. First, we retrospectively identified neurological prodromal symptoms in 28 of the 59 patients whose CSF analysis did not contribute to the aetiological diagnosis, and many of these patients did not undergo a comprehensive neurological workup. For instance, cerebral MRI was performed in only 5 of these patients. Moreover, new tools for diagnosing auto-immune and/or infectious encephalitis were not available during the study recruitment period [18,19]. Thus, some of the patients whose CSF abnormalities were considered nonspecific may have had undiagnosed neurological conditions. Another hypothesis is that BBB disruption after CA may result in CSF abnormalities. In healthy individuals, most of the proteins found in the CSF are derived from the serum, although some are synthesized by the choroid plexus or within the brain. The passage of serum protein into the CSF varies with the condition of the BBB [20,21]. Normal BBB permeability is defined as a CSF/serum albumin quotient <0.007 [22,23]. BBB disruption may allow the passage of greater amounts of protein from the serum to the CSF. CSF findings may be difficult to interpret in patients with brain injury, as reported in a study of status epilepticus [24].

We identified post-resuscitation shock as factor associated with having nonspecific CSF abnormalities. The systemic inflammation seen in post-resuscitation shock may cause BBB alterations, as described in acute sepsis and cirrhosis, [25,26]. Moreover, patients presenting with confusion to coma before CA and who demonstrated oedema on cerebral CT Scan were more likely to have nonspecific CSF abnormalities. In the setting of primary brain injury, brain inflammation could cause BBB alteration as described in stroke and status epilepticus [24,27,28].

CSF changes may also occur in response to anoxic neuronal damage. Thus, elevated levels of pro-inflammatory cytokines in CSF have been reported after CA [29,30]. HMGB1 (high–mobility group box 1), released or secreted by necrotic brain cells, may act as an early inflammation trigger inducing the local recruitment of pro-inflammatory cytokines, independently of BBB alterations. [6] An increase in the levels of neuronal specific enolase, protein S100B, T-tau protein, neurofilament were also reported[6,31].Finally, CSF abnormalities can be induced by many factors including drugs, spinal cord compression, diabetes, and polyradiculoneuritis [32]. Influence of systemic and neuro inflammation after CA on CSF protein level could not be further explored because of the non-availability of albumin CSF/blood ratio or specific MRI exploration to assess the BBB function [33,34].

ICU mortality was 70% in the overall population of patients with lumbar puncture after CA. Of the 6 patients whose CSF analysis contributed to the diagnosis, 2 had the lumbar puncture done while alive but died subsequently and 4 had the lumbar puncture done post-mortem. Identifying a neurological cause of

CA has been reported to carry a very poor prognosis [4,35]. In our study, ICU mortality in the patients whose CSF analysis did not contribute to the diagnosis but showed nonspecific abnormalities was 73%. A higher CSF/serum protein quotient was the only variable significantly associated with a poor outcome. Similarly, a prospective study in 21 patients found that the CSF/serum albumin quotient was higher in the subgroup of 10 patients with poor outcomes than in the other patients[36]. These findings support the existence of BBB disruption after CA. Finally, in our cohort, 56% of deaths in case of nonspecific CSF abnormalities were ascribed to withdrawal of life-sustaining treatments due to severe post-anoxic encephalopathy.

Our study has several limitations. First, given the retrospective nature of this study design and our sample size, the extent to which our findings apply to the full spectrum of patients with CA is unclear. We included consecutive patients with lumbar puncture after ICU admission with stable ROSC after CA, but lumbar puncture was not performed according to predefined criteria, either in the ICU or post-mortem. Moreover, the two participating ICUs were in high-volume centres, and their recruitment may not reflect that of ICUs overall. However, one of the centres was a referring university hospital and the other a tertiary referral hospital. Second, we considered only CSF analysis performed at the early phase after CA, as part of the emergent aetiological workup. Delayed CSF analysis may provide important information. One study found that the CSF/serum albumin quotient increased between 24 h and 72 h after ROCS, and others reported an increase in protein levels after 2-3 weeks [7]. However, our focus was on the potential usefulness of CSF analysis for the aetiological diagnosis and the prognosis. Finally, CSF albumin values were not available, and we did not adjust the CSF protein values on age [37].

Conclusion

In conclusion, although rarely performed after CA, lumbar puncture may contribute to the diagnosis of a neurological cause. In our study, CSF analysis as a second-line investigation identified a neurological cause in 9% of patients. Nonspecific CSF abnormalities are common after CA, perhaps due to BBB disruption, and may have prognostic significance. Further studies are warranted to further assess these hypotheses.

Abbreviations

BBB: blood-brain barrier

CA: cardiac arrest

CPC: Cerebral Performance Category

CPR: cardiopulmonary resuscitation

CSF: cerebrospinal fluid

CT: computed tomography

EEG: electroencephalogram

ICU: intensive care unit

IQR: interquartile range

ROSC: return of spontaneous circulation

Declarations

Ethics approval and consent to participate

CESRLF 12-384 and 20-41

Consent for publication

Not applicable

Availability of data and material

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

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Authors' contributions

MP and SL wrote the first draft of the paper. All authors approved the final version of the manuscript.

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Tables

Table 1.
Diagnostic workup, identified causes, and outcomes in 65 patients who underwent lumbar puncture after cardiac arrest

	N (%) or Median (Interquartile Range)			
	All patients n=65 (100%)	**LP contributed to aetiologic diagnosis** n = 6/65 (9.2%)	**LP did not contribute to aetiologic diagnosis** n = 59/65 (90.8%)	***p* value**
Prodromal signs				
Neurological signs/symptoms before CA	45 (69.2)	5 (83.3)	40 (67.8)	0.66
Confusion to coma	20 (30.8)	3 (50.0)	17 (28.8)	0.36
Seizure	20 (30.8)	1 (16.7)	19 (32.2)	0.66
Neurological focal signs	6 (9.2)	1 (16.7)	5 (8.5)	0.45
Headache	2 (3.1)	1 (16.7)	1 (1.7)	0.18
Tests to identify cause of cardiac arrest				
Electrocardiographic ST-segment elevation	6 (9.5)	0	6 (10.5)	-
Coronary angiography	31 (47.7)	3 (50.0)	28 (47.5)	1.00
Cerebral CT	52 (80.0)	4 (66.7)	48 (81.4)	0.59
Cerebral MRI	5 (7.7)	1 (16.6)	4 (6.8)	0.39
Chest CT	33 (50.8)	1 (16.7)	32 (54.2)	0.10
Lumbar puncture				
First-line test	10 (15.4)	0	10 (17.0)	0.15
Second-line test	29 (44.6)	5 (83.3)	24 (40.7)	
Third-line test	26 (40.0)	1 (16.7)	25 (42.4)	
Post mortem	10 (15.4)	4 (66.7)	6 (10.2)	0.004
Time from cardiac arrest to LP, days	1 (1-2)	1.5 (1-2)	1 (1-2)	1
Cause of CA				0.009
Respiratory	18 (27.7)	0	18 (30.5)	
Neurologic	16 (24.6)	5 (83.3)	11 (18.6)	

Cardiac	7 (10.8)	0	7 (11.9)	
Metabolic	7 (10.8)	0	7 (11.9)	
Septic shock	4 (6.2)	1 (16.7)	3 (5.1)	
Undetermined	13 (20.0)	0	13 (22.0)	
Outcomes				
ICU length of stay, days	6 (2-8)	2.5 (1.3-3)	6 (3-8.5)	0.06
Awakening during ICU stay	20 (30.8)	0	20 (33.9)	0.17
CPC score at ICU discharge				0.48
1-2	19 (29.2)	0	19 (32.2)	
3-4	0	0	0	
5	46 (70.8)	6 (100)	40 (67.8)	
Reason for ICU death				0.006
Multiorgan failure	18 (39.1)	3 (50.0)	15 (37.5)	
Anoxic encephalopathy	20 (43.5)	0	20 (50.0)	
Brain death	7 (15.2)	3 (50.0)	3 (7.5)	
Other	1 (2.2)	0	1 (2.5)	

CA: cardiac arrest; CPC: Cerebral Performance Category; CSF: cerebrospinal fluid ; CT: computed tomography; ICU: intensive care unit ;IQR: interquartile range; LP: lumbar puncture; MRI: magnetic resonance imaging.

Table 2.

Cerebrospinal fluid characteristics in patients whose lumbar puncture did not contribute to the aetiological diagnosis

	n (%) or Median (interquartile range) / mean [range]				
	All Patients n = 65 (100%)	CSF analysis contributed to the aetiological diagnosis n = 6/65 (9.2%)	CSF analysis did not contribute to the aetiological diagnosis n = 59/65 (90.8%)	Postmortem CSF analysis did not contribute to the aetiological diagnosis n=6/59 (10.2%)	Abnormal CSF† in patients who were alive at the time of LP and whose CSF analysis did not contribute to the aetiological diagnosis n =37/53 (69.8%)
CSF white-cell count, per mm^3	1 (0-5) / 15.2 [0-297]	1 (0-4) / 131 [6-297]	111 (17-224) / 7 [0-144]	6 (1-12) / 7 [0-30]	2 (0-5) / 10 [0-144]
CSF neutrophil count, per mm^3*	1 (1-9)	18 (14-23)	1 (1-3)	2 (1-3)	1 (1-5)
CSF lymphocyte count, per mm^3*	0 (0-4)	170 (87-229)	0 (0-3)	2 (1-3)	0 (0-3)
CSF protein, g/L	0.56 (0.40-0.70) / 0.79[0.20-5.55]	1.54 (1.30-2.60) / 2.30 [0.59-5.55]	0.55 (0.42-0.65) / 0.68 [0.20-3.99]	0.60 (0.40-0.80) / 0.66 [0.30-1.35]	0.62 (0.54-0.76) / 0.83 [0.42-3.99]
CSF glucose, mmol//L	4.8 (4.2-6.0)	4.9 (4.8-5.3)	4.8 (4.1-6.0)	5.4 (3.7-6.1)	4.8 (4.0-6.0)
CSF red-cell count, per mm^3	28 (1-322)	9500 (4100-20000)	15 (1-229)	208 (14-1142)	20 (1-221)
CSF lactate, mmol/L	4.6 (4.1-8.0)	5.4 (4.8-6.1)	4.6 (4.1-8.7)	7.9 (6.0-9.7)	4.7 (4.3-7.7)
Blood protein, g/l	62 (53-68)	41 (41-57)	63 (54-68)	60 (60-60)	60 (52-68)
Blood glucose, mmol/L	7.3 (6.0-9.4)	10.3 (8.2-16.6)	7.1 (6.0-9.3)	6.9 (5.7-8.1)	7.3 (5.9-11.8)

Protein CSF/blood ratio	0.009 (0.007-0.01)	0.02 (0.01-0.02)	0.009 (0.007-0.01)	0.009 (0.009-0.009)	0.01 (0.009-0.01)
Glucose CSF/blood ratio	0.6 (0.5-0.8)	0.5 (0.5-0.95)	0.65 (0.5-0.8)	0.8 (0.6-0.8)	0.7 (0.5-0.8)
Positive CSF culture	1 (1.5)	1 (16.7)	0	0	0
Abnormal cells	0	0	0	0	0

CSF: cerebrospinal fluid; IQR: interquartile range; LP: lumbar puncture.

*in patients with CSF white cell count >4/mm^3

† Abnormal CSF was defined as CSF white-cell count >4/mm^3 and/or CSF protein >0.45 g/L.

Table 3:

Demographic and cardiac arrest characteristics in patients alive at lumbar puncture whose cerebrospinal fluid analysis did not contribute to the aetiological diagnosis of cardiac arrest (n=53)

	N (%) or Median (interquartile range)		
	Normal LP	**Abnormal LP†**	
	n=16 (30.2%)	**n=37 (69.8%)**	***p* value**
Demographic characteristics and comorbidities			
Age, years	49 (39-65)	56 (40-74)	0.24
Male sex	9 (56.3)	26 (70.3)	0.36
Diabetes mellitus	17 (18.7)	6 (16.2)	1.00
Spinal cord compression	1 (6.3)	1 (2.7)	0.52
Haematological malignancy	0	2 (5.4)	-
Epilepsy	4 (25.0)	5 (13.5)	0.43
Cardiac arrest characteristics			
Neurological signs/symptoms before CA	10 (62.5)	28 (75.7)	0.34
Confusion to coma	2 (12.5)	13 (35.1)	0.11
Seizure	8 (50.0)	10 (27.0)	0.13
Neurological focal signs	1 (6.3)	3 (8.1)	1.00
Headache	0	1 (2.7)	-
Cardiac arrest in a public place	3 (18.7)	5 (13.5)	0.69
Arrest witnessed/monitored	13 (81.2)	32 (86.5)	0.69
Bystander CPR	12 (75.0)	31 (83.8)	0.47
Shockable first recorded rhythm	5 (31.2)	6 (16.2)	0.27
Total number of defibrillations before ROSC	0 (0-2)	0 (0-1)	0.16
Use of epinephrine	11 (68.8)	30 (81.1)	0.48
Total epinephrine dose before ROSC, mg	1 (0-3)	2 (1-4)	0.081
Time from collapse to CPR (no-flow), min	4 (2-10)	0 (0-3)	0.004
Time from collapse to ROSC (low-flow), min	16 (9-21)	10 (6-20)	0.41
Lactate concentration on ICU admission, mmol/L	3.9 (2.5-7.4)	6.5 (2.3-11.0)	0.40

Oedema on cerebral CT	0	5 (16.1)	-
Targeted temperature management (32-36°C) on day 1	14 (87.5)	31(83.8)	1.00
Sepsis before LP	1 (6.3)	9 (24.3)	0.25
Post-resuscitation shock	5 (31.2)	26 (70.3)	0.01
Renal replacement therapy	4 (25.0)	9 (24.3)	1.00
Status epilepticus as a cause of CA (before LP)	2 (66.7)	3 (42.9)	1.00
Outcomes			
ICU length of stay, days	7 (5-9)	6 (3-9)	0.55
Awakening during ICU stay	10 (62.5)	10 (27.0)	0.029
CPC score at discharge			0.044
1-2	9 (56.3)	10 (27.0)	
3-4	0	0	
5	7 (43.7)	27 (73)	
Reason for ICU death			0.09
Multiorgan failure	1(14.3)	8 (29.6)	
Anoxic encephalopathy	5 (71.4)	15 (55.6)	
Brain death	1 (14.3)	3 (11.1)	
Other	0	1 (3.7)	

CPC: Cerebral Performance Category; CPR: cardiopulmonary resuscitation; CT: computed tomography; ICU, intensive care unit; LP: lumbar puncture; ROSC: return of spontaneous circulation.

† Abnormal CSF was defined as CSF white-cell count >4/mm^3 and/or CSF protein >0.45 g/L.

Figures

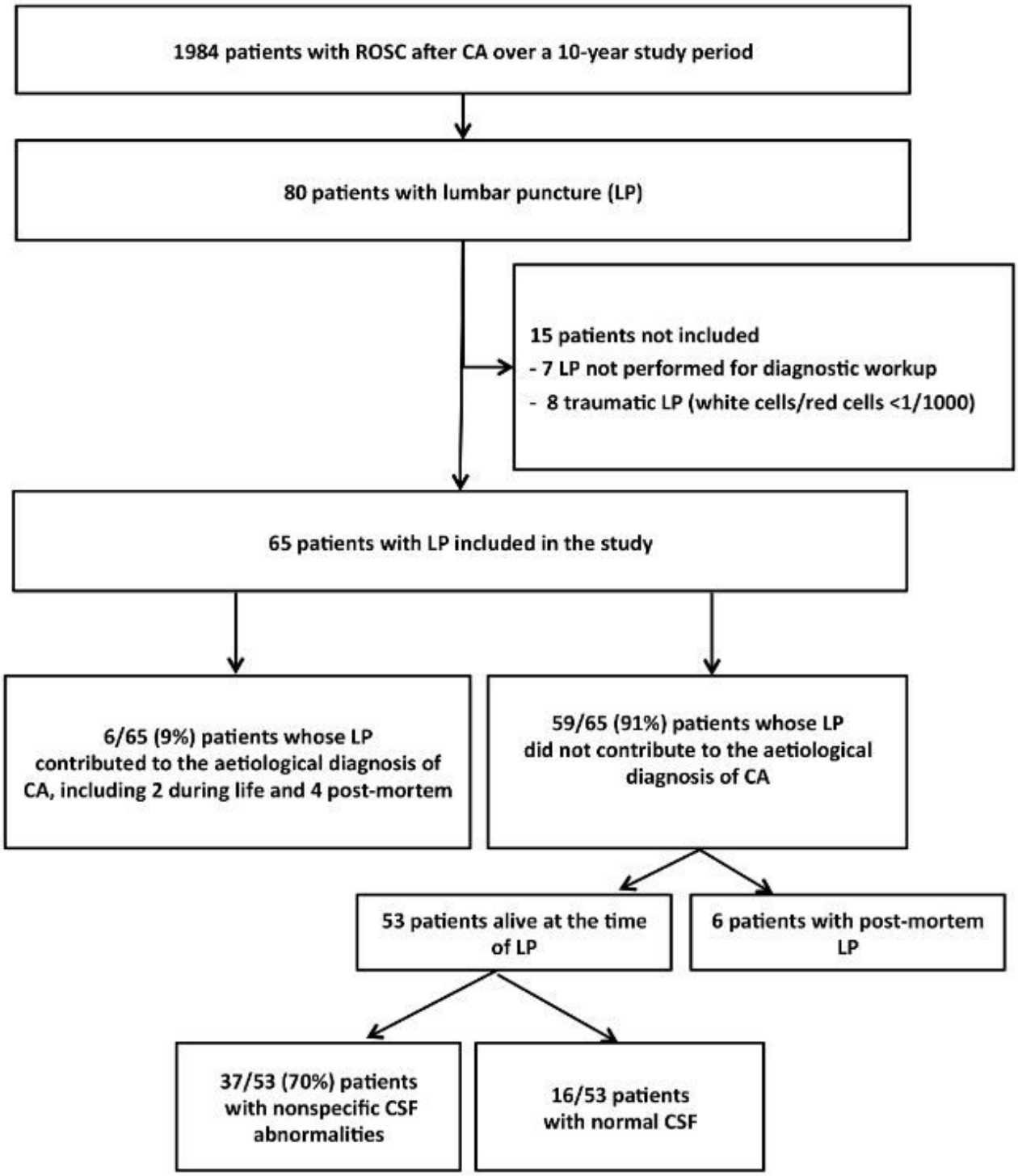

Figure 1

Patient flow diagram ROSC denotes return of spontaneous circulation and CA cardiac arrest.

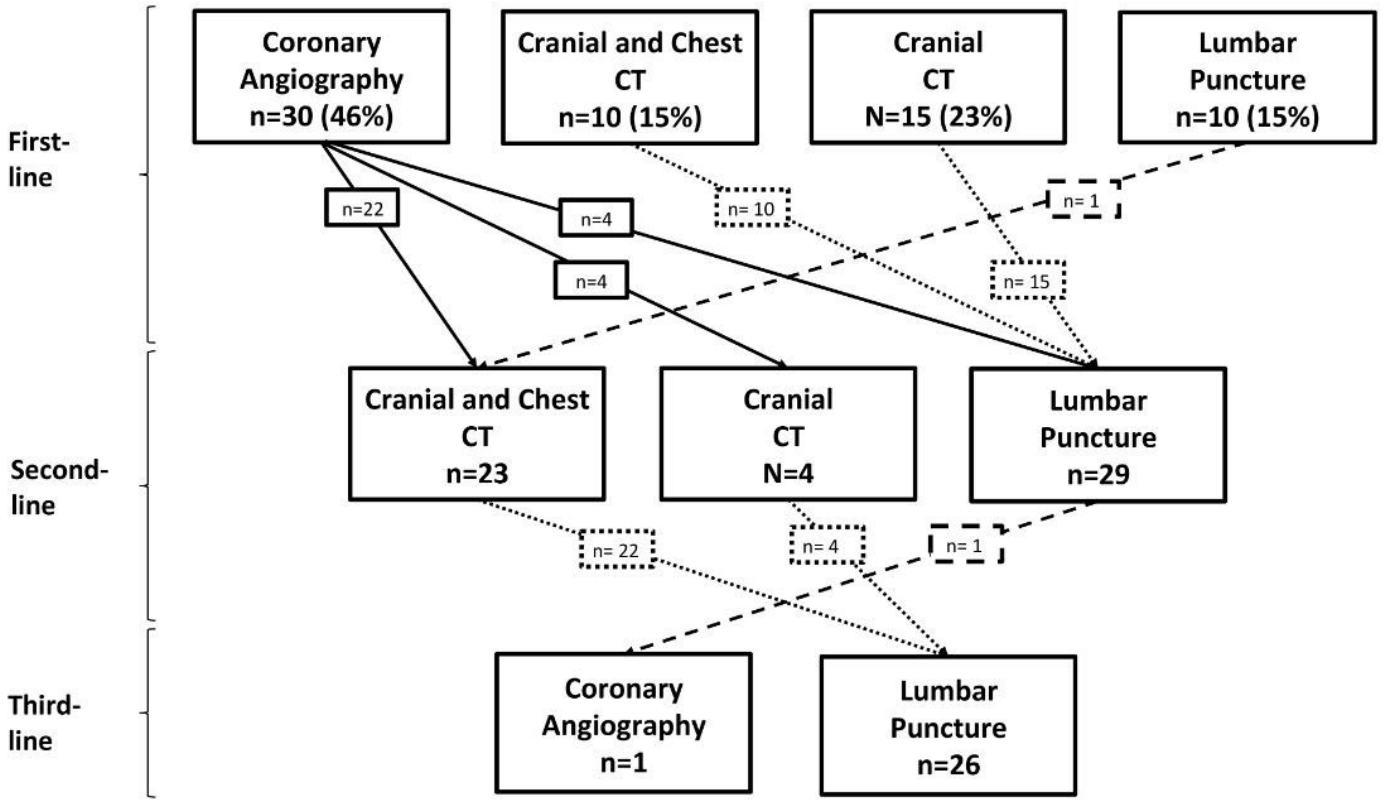

Figure 2

Diagnostic work-up in 65 patients with a lumbar puncture after cardiac arrest CT denotes computed tomography.

Supplementary Files

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- ESM0308.docx