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PAPER

Abnormal breathing patterns in stroke: relationship with location of acute stroke lesion and prior cerebrovascular disease

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Objective: To determine whether central periodic breathing (CPB) is associated with acute involvement of any particular part of the brain, or the extent of total damage in patients with acute stroke.
Methods: CPB was identified using portable monitoring equipment in patients with stroke on admission. A neuroradiologist classified acute stroke lesions and prior cerebrovascular disease on brain images.
Results: Among 134 patients with acute stroke, those with CPB were more likely to have a large acute stroke lesion in a cerebral hemisphere ($p = 0.01$) and more mass effect ($p = 0.03$). There was no association between CPB and severe prior cerebrovascular disease on imaging ($p = 0.76$).
Conclusion: CPB is related to the acute (not old) lesions, particularly large acute cerebral hemispheric lesions with mass effect. A relationship between lesions in any discrete brain location (unilateral or bilateral) and CPB could not be shown.

Central periodic breathing (CPB), including Cheynes–Stokes respiration, during wakefulness has been reported to occur in 53% of patients with acute stroke.[1] Limited information suggests a possible relationship between the site and size of the stroke lesion and the presence of CPB. Previous studies suggested that the presence of bilateral hemispheric or brain stem stroke lesions might be crucial for the presence of CPB after stroke.[2 3] However, these were small studies (n = 28, n = 49) predating computed tomography, which found that hospitalised patients with intermittent CPB during wakefulness had bilateral hemispheric or brain stem lesions on autopsy. More recent studies have failed to find any association between the location of brain lesion on imaging and CPB while patients were awake[1] (n = 32) or asleep[4 5] (n = 93, n = 39).

We reported previously that CPB was associated with a poor functional outcome at 3 months after stroke, even after accounting for clinical stroke severity, but the mechanism linking CPB with poor outcome was unclear.[6] Therefore, we aimed to determine, using data from the same cohort, whether CPB was related to features of the acute stroke lesion on brain imaging or to prior cerebrovascular disease (ie, previous infarcts, haemorrhages and/or periventricular white matter lesions (PVWML)/leucoaraiosis).

PATIENTS AND METHODS

Patient recruitment and respiratory monitoring

We included patients within 24 h of a suspected first or recurrent ischaemic or haemorrhagic stroke, admitted within working hours (09:00–17:00) on weekdays. Resources limited inclusion of patients (who had similar characteristics as those included in the study) arriving out of hours. Patients were connected to validated portable continuous monitoring equipment (Embletta PDS, Medcare Flaga, Reykjavik, Iceland)[7] to record breathing patterns in the emergency room, during transfer around the hospital, during imaging and for 2 h on the stroke ward (median recording duration 4 h).

CPB was defined as cyclical increases in the rate and depth of breathing (hyperpnoea) alternating with either a reduction by >50% (hypopnoea) or complete cessation (apnoea) of nasal air flow and respiratory effort lasting ⩾10 s.[7] The monitoring equipment and respiratory analyses have been described in detail previously.[6]

Image acquisition and analysis

Patients underwent either computed tomography scanning (GE spiral) and/or magnetic resonance imaging (GE 1.5 Signa Horizon LX). A consultant neuroradiologist reviewed the brain images (blind to the breathing results and clinical details) to identify any acute stroke lesions (including type, location, side, size and swelling) and prior cerebrovascular disease. We used a validated scale to classify the appearance of the acute stroke lesions.[8] We collapsed the eight original codes for middle cerebral artery territory lesions and/or anterior or posterior cerebral lesions into small (original score 1; collapsed score = 0), medium (original score 2–5; collapsed score = 1) or large (original score 6–8; collapsed score = 2) acute stroke lesions according to the proportion of brain territory affected. We coded the mass effect on a six-point scale,[8] collapsed into "mild" (score 0–1 = no swelling or only effacement of cortical sulci) or "severe" (score ⩾2 = any effacement of the adjacent ventricles or more mass effect). The presence of old stroke lesions (none = 0, one = 1, two or more = ⩾2), atrophy (mild, none or localised = 1; severe, diffuse, affecting the sulci—cortical and ventricals—central areas of brain = 2) or PVWML (mild, none or multiple focal lesions = 1; severe, multiple lesions in the anterior and posterior perventricular white matter = 2) was also coded.[9] The overall burden of prior cerebrovascular disease was obtained from the sum of the scores for old lesions, PVWML and atrophy, which was then

Abbreviations: CPB, central periodic breathing; ICH, intracerebral haemorrhage; IQR, interquartile range; PVWML, periventricular white matter lesions

Table 1 Relationship between central periodic breathing and the appearance of acute stroke lesions and prior cerebrovascular disease on brain imaging

Brain imaging findings	CPB n = 31 (23%)		Without CPB n = 103 (77%)		
	n	%	n	%	p Value*
Median delay to scanning from stroke onset, hours (IQR)	7 (3–26)		8 (4–23)		0.72
Acute stroke lesions					0.88†
Visible	29	94	83	81	
Not visible	2	6	20	19	
Type of acute lesion					0.24‡
Infarct	24	77	70	68	
ICH	5	16	13	13	
None	2	6	20	19	
Topography of acute lesion					0.05‡
Cerebral					
Cortical	22	71	60	58	
Lacunar	3	10	19	18	
Posterior fossa	3	10	3	3	
Cerebellum					
Brain stem	1	3	1	1	
None	2	6	20	19	
Size of acute lesion					0.01‡
Large	14	45	17	17	
Medium	9	29	31	30	
Small	6	19	35	34	
None	2	6	20	19	
Mass-effect					0.03‡
None/mild	22	71	91	88	
Severe	9	29	12	12	
Side of acute lesion					0.09‡
Left	10	32	44	43	
Right	18	58	36	35	
Bilateral	1	3%	3	3	
None	2	6	20	19	
Visible old stroke lesions					0.76‡
None evident (score = 0)	19	61	70	68	
One lesion (score = 1)	9	29	25	24	
Two or more lesions (score ⩾2)					
The total number of old stroke lesions in 45 patients	3	10	8	8	1.00‡
Topography of any old stroke lesions					
Cerebral: cortical	15	73	41	73	
Subcortical/lacunar	11/15	20	30/41	20	
Posterior fossa (all in the cerebellum)	3/15	7	8/41	7	
Side of any stroke lesion (including old, recent and acute stroke lesions)					0.09‡
Left	7	23	44	43	
Right	16	52	36	35	
Bilateral	7	23	14	14	
None	1	3	9	9	
PVWML					0.47†
None/mild	27	87	84	82	
Severe	4	13	19	18	
Atrophy					0.20†
None/mild	14	45	60	58	
Severe	17	54	43	42	
Total prior cerebrovascular disease					0.76‡
None/mild	9	29	38	37	
Moderate	12	39	36	35	
Severe	10	32	29	28	

CPB, central periodic breathing; ICH, intracerebral haemorrhage; IQR, interquartile range; PVWML, periventricular white matter lesions.
*p value based on statistical tests.
†χ^2 test.
‡Fisher's exact test for nominal data and Mann-Whitney U test for continuous data.

collapsed into the following simple scale: none/mild (score = 0), moderate (score = 1) or severe (score ≥2).[10]

Statistical analysis

Differences between nominal variables were compared by χ^2 and Fisher's exact tests using SPSS V.11.0.0.

Ethics and consent

The local research ethics committee approved the study. Consent was sought from the patient, or care giver if the patient was unable to communicate.

RESULTS

Comparison of characteristics between patients with stroke with and without CBP have been described in detail previously.[6] Of the 138 patients with stroke recruited, 105 (76%) underwent a computed tomography scan, 23 (17%) underwent magnetic resonance imaging, 6 (4%) underwent both, and 4 (3%) did not undergo a scan as they died before it could be performed. Brain imaging was performed at a median of 7.8 (interquartile range (IQR), 4–25) h after stroke onset and at a median of 2.5 (IQR, 2–5) h after arrival at the hospital.

Of the 112 (84%) patients with a visible acute lesion, 94 (84%) had an infarct and 18 (16%) had intracerebral haemorrhage. Most lesions were in the cerebral hemispheres (82/112, 73%), of which 63 were located in the middle cerebral artery territory, 22 (20%), were lacunar and 8 (7%) were in the posterior fossa (six in the cerebellum and two in the brain stem). Visible old lesions were seen in 45 of 134 (34%) patients, of whom 12 did not have a visible acute lesion. Severe PVWML and atrophy were present in 23 of 134 (17%) and 60 of 134 (45%) patients, respectively.

Relationship between CPB (n = 31, 23%) and brain imaging appearance

There was no significant association between the presence of a visible acute lesion and CPB ($\chi^2 = 2.92$, $p = 0.88$; table 1). There were more patients with CPB and acute lesions involving the cerebral cortex than other parts of the brain, but the association between acute lesion site and CPB only reached borderline statistical significance (Fisher's exact test, $p = 0.05$). Only 4 of 31 patients with CPB had a posterior fossa lesion. CPB was associated with large (all of which were in the cerebral hemispheres) rather than small/medium-sized acute lesions (Fisher's exact test, $p = 0.01$), and severe rather than no/mild mass effect (Fisher's exact test, $p = 0.03$). There was no significant association with CPB and the side of visible acute lesions (Fisher's exact test, $p = 0.09$). There were no significant differences between patients with and without CPB in the number, type and side of visible old lesions, PVWML and/or atrophy, regardless of the severity of the disease. Overall, prior mild, moderate or severe cerebrovascular disease occurred in similar numbers of patients with and without CPB.

DISCUSSION

CPB on admission to hospital was more common in patients who had large acute stroke lesions in the cerebral hemispheres and severe mass effect on brain imaging than among those with smaller lesions or less mass effect. This is consistent with our findings reported previously, that CPB is clinically associated with a total anterior circulation syndrome.[6] There were too few patients with posterior-fossa lesions to confirm whether they are associated with CPB. Our findings also do not suggest an association between CPB and bilateral acute stroke lesions or the severity of prior stroke disease (old strokes, PVMWL or atrophy).

The lack of a clear association between CPB and one specific area of brain could be because respiratory control may be distributed across diverse areas of brain above the brain stem (eg, midbrain nuclei and fronto-orbital, cingulate, insular, anterior temporal and sensorimotor cortices) rather than being localised just to respiratory centres in the brain stem.[1] Alternatively, one could speculate that larger volumes of ischaemic tissue may release more ''humoral agents'' into the cerebrospinal fluid and blood, which could affect respiratory centres, whereas small lesions may not produce enough ''substances'' to do this.

We may have underestimated brain stem lesions because they are often not visible on computed tomography early after stroke onset.[11] Indeed, brain imaging in the present study was not specifically designed to look in detail at small brain areas that may subserve the respiratory system. Certainly, many patients with acute stroke would not have been able to co-operate with the scanning required and this would have reduced our sample size considerably. However, future studies should consider using more detailed brain-imaging techniques to define the relationship between the site of the acute lesion and CPB.

CPB in acute stroke is associated with a poor outcome independently of stroke severity.[6] Rather than monitoring all patients with acute stroke for CPB, identifying those with large cerebral hemispheric lesions on imaging might help to focus the use of respiratory monitoring equipment on patients with a high risk of CPB. Future studies need to determine why large lesions are associated with CPB (eg, knock-out respiratory control, or release of some humoral agent that affects respiratory centres) and need to identify interventions to reduce the adverse effects of CPB.

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