Original Article
Evaluation of cerebral-cardiac syndrome using echocardiography in a canine model of acute traumatic brain injury

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Abstract: Previous studies have confirmed that traumatic brain injury (TBI) can induce general adaptation syndrome (GAS), which subsequently results in myocardial dysfunction and damage in some patients with acute TBI; this condition is also termed as cerebral-cardiac syndrome. However, most clinicians ignore the detection and treatment of myocardial dysfunction, and instead concentrate only on the serious neural damage that is observed in acute TBI, which is one of the most important fatal factors. Therefore, clarification is urgently needed regarding the relationship between TBI and myocardial dysfunction. In the present study, we evaluated 18 canine models of acute TBI, by using real-time myocardial contrast echocardiography and strain rate imaging to accurately evaluate myocardial function and regional microcirculation, including the strain rate of the different myocardial segments, time-amplitude curves, mean ascending slope of the curve, and local myocardial blood flow. Our results suggest that acute TBI often results in cerebral-cardiac syndrome, which rapidly progresses to the serious stage within 3 days. This study is the first to provide comprehensive ultrasonic characteristics of cerebral-cardiac syndrome in an animal model of TBI.

Keywords: Traumatic brain injury, real-time myocardial contrast echocardiography, strain rate imaging, myocardial ischemia, cerebral-cardiac syndrome

Introduction

Acute traumatic brain injury (TBI) often leads to neurohormonal disorders that induce cerebral-cardiac syndrome, which is characterized by acute myocardial damage [1], myocardial ischemia, and heart failure [2, 3]. Because neural damage is usually an urgent and serious condition, abnormal cardiac function is easily ignored in clinical practice, and tends to be one of the most important fatal factors in cases of acute TBI. However, the cardiac symptoms are occasionally mild in TBI patients, or may only manifest as slight palpitations and chest discomfort, which is not always identified in the patients’ complaints. Moreover, abnormalities are not always observed during clinical examinations in the early stage [4]. Therefore, it is necessary to further clarify the relationship between TBI and cardiac dysfunction.

To date, only a few studies have quantifiably evaluated cerebral-cardiac syndrome by ultrasonography in animal TBI cases, because of the variable injury standards and difficulty involved in the emergency treatment of TBI. To attain consistent and reliable data, the current study used real-time myocardial contrast echocardiography (RTMCE) and strain rate imaging (SRI) to accurately evaluate the extent of cerebral-cardiac syndrome in a canine model of TBI.

Materials and methods

Animal samples

Twenty healthy male and female mongrel dogs were used in this study. The body weight range was 14-20 kg (mean, 16.06 ± 2.08 kg).

Imaging methods

We used a GE Vivid 7 color ultrasound system (GE Company, USA) that was equipped with a 2.5-MHz probe and a system for contrast echocardiography and strain measurements. The
Echocardiographic features of cerebral-cardiac syndrome

Table 1. Myocardial contrast echocardiography results for the injured mongrel dogs before and after injury

<table>
<thead>
<tr>
<th>Detection time</th>
<th>A</th>
<th>β</th>
<th>A·β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injury</td>
<td>31.55 ± 6.56</td>
<td>1.20 ± 0.60</td>
<td>37.17 ± 10.36</td>
</tr>
<tr>
<td>6 h after injury</td>
<td>29.35 ± 5.82</td>
<td>1.11 ± 0.70</td>
<td>35.65 ± 9.22</td>
</tr>
<tr>
<td>1 day after injury</td>
<td>19.23 ± 8.76*</td>
<td>0.83 ± 0.23*</td>
<td>18.56 ± 6.68*</td>
</tr>
<tr>
<td>3 days after injury</td>
<td>13.87±6.46*</td>
<td>0.73 ± 0.35*</td>
<td>13.78 ± 5.33*</td>
</tr>
</tbody>
</table>

*Compared to results before and 3 h after the injury, P < 0.05. Data are presented as mean ± standard deviation.

Results

Establishing animal models

Based on the standard dog model of acute TBI, we successfully created 18 models in this study. Among these animals, 1 died at 10 h after the injury, 2 died after 1 day, and 15 survived until 3 days after the injury.

RTMCE results before and after the injury

A total of 50-70 images that were recorded after ultrasonic destruction of the microbubble were selected, and 2-5 regions of interest (their size was consistent with inner end-diastolic wall thickness) were selected based on the extent of the lesion. Compared to those before the injury, the post-injury levels of A, β, and A·β decreased significantly in 4 myocardial segments of the anterior and inferior left ventricle wall in 3 mongrel dogs at 6 h. At 1 and 3 days after the injury, the levels of A, β, and A·β decreased significantly in 29 myocardial segments, compared to the pre-injury values (P < 0.05; Table 1, Figure 1).

Myocardial strain rate for each segment before and after the injury

Before the injury, the systolic longitudinal strain rates were negative along the long axis, and the color coding revealed that the tone transitioned from yellow to red for increasingly negative strain rates. In the same direction, the diastolic strain rates were positive, and the tone transitioned from cyan to blue for increasingly positive strain rates. The 3 major peaks in the strain rate-time curve (i.e., the S, E, and A peaks) had clear outlines. The color of each injured myocardial segment gradually decreased from 6 h to 3 days after the injury, and exhibited irregular variations. The color in a few segments was pure green, and the strain rate-time curve lost its normal shape and exhibited an irregular outline (Figure 2).

The crests of the S, E, and A peaks were very small and subsequently disappeared, and the peak values were significantly lower than those obtained before the injury (P < 0.05, Table 2).

Discussion

Acute brain injury is followed by different levels of cerebral edema, which suppress and displace brain circulation; consequently, the increased intracranial pressure can directly or indirectly affect the hypothalamus and brain stem. Unfortunately, hypothalamic dysfunction-induced autonomic dysfunction can result in sympathetic-adrenal medulla abnormalities and increased catecholamine release. The excess catecholamine can then travel from the adrenergic nerve endings in the heart to the myocardia, and cause focal dissolution, cardiomyocyte necrosis, and changes in the contrac-
tion device. Furthermore, the excess catechol-
amine can lead to increased contractions or 
spasms of the small coronary vessels, which 
can subsequently cause myocardial ischemia 
and hypoxia [6-8]. In contrast, in cases with 
acute brain lesions, the body is in a state of 
stress, while the sympathetic-adrenal system is 
in an excited state, thus leading to an increased 
secretion of catecholamine, epinephrine, and 
neuropeptides. This increased secretion subse-
quently increases the autonomic dysfunction 
that is characterized by sympathetic nerve hy-
peractivity and parasympathetic nerve hypoac-
tivity, which subsequently result in strengthen-
ed cardiovascular activity, spasm, coronary 
artery contraction, and ultimately induced isch-
emic heart damage [9, 10].

The findings of the current study revealed that 
myocardial ischemic injury occurred 6 h after 
the acute brain injury, and that significant 
changes occurred in the myocardial microcircu-
lation and regional activities after 3 days. 
Therefore, patients with brain injury should 
receive comprehensive care, and close moni-
toring of their cardiac function should be per-
formed. When brain disease is being treated, 
active treatments should be used to protect the 
myocardial function and prevent excessive 
dehydration or over-hydration, thereby ensuring 
that the patients survive the acute stage and 
maximizing their chances of recovery [11, 12].

RTMCE is a newly developed approach that 
involves the non-invasive monitoring of myocar-

Figure 1. Short-axis imaging of the left ventricle: anterior myocardial perfusion was significantly reduced at 3 days after the injury, compared to that before the injury. (A) Ultrasonic image recorded before TBI, (B) Images of 3 days after TBI.

Figure 2. Long-axis imaging of the left ventricle at 1 day after the injury: no variations are observed in the color of the regional myocardium, and the strain rate-time curve is disordered (A) strain rate recorded before TBI, (B) images of 1 day after TBI.
Table 2. Comparison of the strain rates in each myocardial segment along the long axis of the left ventricle before and after injury

<table>
<thead>
<tr>
<th>Detection time</th>
<th>S (s⁻¹)</th>
<th>E (s⁻¹)</th>
<th>A (s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injury</td>
<td>1.98 ± 0.51</td>
<td>2.87 ± 0.60</td>
<td>2.22 ± 0.46</td>
</tr>
<tr>
<td>6 h after injury</td>
<td>1.88 ± 0.49</td>
<td>2.33 ± 0.58</td>
<td>1.96 ± 0.49</td>
</tr>
<tr>
<td>1 day after injury</td>
<td>0.87 ± 0.49*</td>
<td>1.08 ± 0.51*</td>
<td>1.02 ± 0.46*</td>
</tr>
<tr>
<td>3 days after injury</td>
<td>0.78 ± 0.49*</td>
<td>1.12 ± 0.41*</td>
<td>0.98 ± 0.56*</td>
</tr>
</tbody>
</table>

*Compared to results before and 3 h after the injury, P < 0.05. Data are presented as mean ± standard deviation.

SRI is a new technique that is based on tissue Doppler technology, and is used to analyze regional myocardial activities. The SRI technique detects the regional myocardial activities throughout the cardiac cycle, and clarifies the small differences between the myocardial deformation of the different segments in various periods. In this context, the strain rate of the regional myocardium is less likely to be influenced by the overall movement of the heart or the dragging force from adjacent segments, thereby increasing its accuracy for quantitative analysis of the segment movements in the regional myocardium [7, 16, 17]. Injury to the longitudinal myocardial fibers of the subendocardium in the early stage of ischemia does not cause a change in the movement of the entire myocardium layer, although the shortened systolic and extended diastolic cycle lengths does affect the periodic change in the wall thickness. Therefore, SRI can identify ischemic myocardium at an earlier stage and provide a more reliable evaluation of the regional heart functions [18-20]. In the present study, both the brain function and the time had corresponding effects on the systolic and diastolic movement of the regional myocardium between 6 h and 3 days after the injury. Furthermore, the crests of the S, E, and A peaks decreased or disappeared, and the peak values decreased significantly, compared to the pre-injury values (P < 0.05). These findings indicate that regional myocardial dysfunction is caused by early stage myocardial ischemia.

The findings of the current study suggest that myocardial ischemic injury and regional functional changes can occur in the early stage of acute brain injury. The RTMCE and the SRI techniques provide real-time, non-invasive, and accurate measures of microcirculation perfusion in the impaired myocardium, as well as regional myocardial function, in patients with acute TBI. Therefore, we suggest that microcirculation perfusion is a new clinical indicator for the early and rapid diagnosis of brain-heart syndrome in acute TBI, and that it can facilitate timely clinical decision-making to protect myocardial function.

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Disclosure of conflict of interest

None.

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References

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