Původní sdělení | Original research article

Characteristics of hippocampus, cognitive functions, lipid profile, and severity of chronic heart failure in patients with coronary heart disease

Natalya S. Akimova, Oksana V. Bugaeva, Diana G. Persashvili, Larisa E. Konshina, Yury G. Shvarts

V.I. Razumovsky Saratov State Medical University, Saratov, Russia

ARTICLE INFO

Article history:
Submitted: 10. 9. 2019
Accepted: 8. 11. 2019
Available online: 10. 2. 2020

Klíčová slova:
Centrální nervový systém
Chronické srdeční selhání
Hipokampus
Lipidový profil
Kognitivní dysfunkce

SOUHRN

Souvislosti a cíle: V současné době není jednoznačně pochopen vztah mezi závažností chronického srdečního selhání a hlavními kvantitativními charakteristikami hipokampu, kognitivních funkcí a složek lipidového profilu u pacientů s ischemickou chorobou srdeční (ICHS).
Materiály a metody: Bylo vyšetřeno 50 pacientů s ICHS a funkční třídou II–IV chronického srdečního selhání. Studie nezahrnovala pacienty, kteří měli závažné zdravotní stavy, které by mohly vyvolat morfologické změny v mozku. Kromě rutinních klinických testů byla provedena dopplerovská echokardiografie a magnetická rezonance mozku; byly vypočteny pravé a levé hipokampální objemy a délky, jakož i tloušťka kortikální šedé hmoty. Byly měřeny hodnoty N-terminálních fragmentů natriuretického propeptidu typu B (NT-proBNP) a lipidové panely. Kognitivní funkce byly hodnoceny pomocí Wechslerovy verbální a neverbální stupnice schopností (subtesty V a VII) a Bourdonova testu (Dot Cancellation Test).
Výsledek: Kanonická korelační analýza odhalila významné vztahy mezi skupinami příznaků charakterizujících závažnost ICHS, parametry hipokampu, složek lipidového profilu a kognitivních skóre.
Párová korelační analýza stanovila, že pokles Wechslerova VII skóre a čas strávený nad Bourdonovým testem byly spojeny se zvětšenými srdečními komorami, zvýšenou funkční třídou, sníženým objemem pravého hipokampu a zvýšenými koncentracemi cholesterolu a lipoproteinů o nízké hustotě. Wechslerovo V skóre bylo nižší u pacientů s vyšší funkční třídou, nižší ejekční frakcí levé komory (EF LK), zkrácením pravé hipokampální délky a vyššími hodnotami lipoproteinů s nízkou hustotou. Pokles Bourdonových testovacích parametrů byl spojen s vyšší funkční třídou, nižší EF LK a menším objemem pravého a levého hipokampu.
Závěr: Dyslipidemie, jakož i vývoj a progrese chronického srdečního selhání u pacientů s ICHS mohou být prediktory hipokampální atrofie, která může být zase jednou z přímých příčin kognitivní dysfunkce v této populaci.

SUMMARY

Background: Currently, the relationship between the severity of chronic heart failure (CHF) and the main quantitative characteristics of the hippocampus, cognitive functions, and lipid profile components in patients with coronary heart disease (CHD) is not clearly understood.
Materials and methods. Fifty patients with CHD and functional class (FC) II–IV CHF were examined. The study did not include patients who had severe medical conditions which could develop the morphological changes in the brain. In addition to the routine clinical tests, Doppler echocardiography and nuclear magnetic resonance imaging (MRI) of the brain were performed; the right and left hippocampal volumes and lengths as well as the cortical gray matter thickness were calculated; N-terminal pro-B-type natriuretic peptide (NT-proBNP) and lipid panel components were measured. The cognitive functions were assessed via Wechsler Verbal and Nonverbal Scale of Ability (V and VII subtests) and Bourdon test (Dot Cancellation Test).
Results: The canonical correlation analysis revealed significant relationships between the groups of signs characterizing the severity of chronic heart failure parameters of the hippocampus, lipid profile components, and cognitive scores.

Address: Natalya S. Akimova, MD, DSc, V.I. Razumovsky Saratov State Medical University, 112, Bolshaya Kazachya str., Saratov, 410012, Russia,
e-mail: astraveritas@yandex.ru
DOI: 10.33678/cor.2019.074

Please cite this article as: Akimova NS, Bugaeva OV, Persashvili DG, et al. Characteristics of hippocampus, cognitive functions, lipid profile, and severity of chronic heart failure in patients with coronary heart disease. Cor Vasa 2020;62:29–32.

Keywords:
Central nervous system
Chronic heart failure
Cognitive dysfunction
Hippocampus
Lipid profile

The pairwise correlation analysis determined that the decrease in the Wechsler VII scores and time spent for the Bourdon test were associated with enlarged cardiac chambers, increased functional class, decreased right hippocampal volume and elevated cholesterol and low-density lipoprotein (LDL) levels. The Wechsler V scores were lower in patients with higher functional class, lower left ventricular ejection fraction (LVEF), shorten right hippocampal length, and higher LDL levels. The decline of Bourdon test parameters was associated with higher functional class, lower LVEF, and smaller right and left hippocampal volumes.
Conclusion: The dyslipidemia, as well as development and progression of chronic heart failure in patients with coronary heart disease may be predictors for hippocampal atrophy which, in turn, may be one of the direct causes of cognitive dysfunction in this population.

Introduction

Chronic heart failure (CHF) is a complex clinical syndrome that develops when the heart is unable to provide normal blood supply to the organs and tissues.[1] Decreased cardiac output and ventricular contractile dysfunction cause deterioration of the cerebral blood flow contributing to development and/or progression of cognitive disorders (loss of memory, poor attention, and mental deficiency and stagnation) which can subsequently result in dementia.[2,3] Generally, the patients with chronic cerebral ischemia adhere to the assigned treatment regimen to a lesser extent which, in turn, may deteriorate the outcome and survival of patients with CHF. Atherosclerosis is one of the most common causes of CHF and cerebrovascular disorders.[4–6]

The changes observed in the hippocampus may be early markers of moderate cognitive dysfunction. The number of studies evaluating the relationship between the hippocampal parameters and cognitive functions in patients with CHF is sufficiently small; so far, this problem has not been adequately investigated.[4–8] Particularly, the relationships between the cognitive functions, hippocampal morphology, and signs attributed to severity of CHF (namely, of ischemic origin) were not evaluated with maximum exclusion of all diseases and conditions that can independently cause central nervous system (CNS) disorders.

The objective of the study

To evaluate the relationships between the cognitive functions and primary quantitative parameters of the hippocampus, lipid profile components, and severity of CHF in patients with coronary heart disease (CHD).

Materials and methods

The main criterion for patients with CHD to be included in our study was functional class (FC) II–IV ischemic CHF. The patients who had severe medical conditions which could develop the morphological changes in the brain were not included in the study. Additionally, the exclusion criteria were as follows: hemodynamically significant stenoses and atherosclerotic plaques in the arteries of the head and neck and substance use. The main clinical characteristics of the study population are presented in Table 1.

The inclusion and exclusion criteria were selected based on the most common causes of CHF in the Russian Federation: hypertension (95.5%), CHD (69.7%), previous myocardial infarction (15.3%), and diabetes (15.9%). The most patients with CHF have CHD combined with hypertension. Among all causes of CHF, the portions of the chronic and paroxysmal atrial fibrillation, previous acute

Table 1 – The main clinical characteristics of the study population (median and quartiles)

Parameter	Patients with CHF (n = 50)
Age, years	63.2 (41; 75)
Males, n (%)	23 (46)
Higher education, n (%)	30 (60)
Height, cm	168 (155; 190)
Body weight, kg	88 (52.5; 120)
Ejection fraction, %	62 (33; 78)
NT-proBNP level, pg/mL	385.5 (40; 1979)
Left ventricular end diastolic dimension (LVEDD), cm	5.2 (3.8-6.6)
Left atrial end systolic dimension (LAESD), cm	4.0 (3,2; 5,8)
Right ventricular end diastolic dimension (RVEDD), cm	3.0 (2.4; 3,7)
Right atrial end systolic dimension (RAESD), cm	3.75 (3.2; 6.0)
Left ventricular end systolic dimension (LVESD), cm	3.2 (2.5; 5.4)
Previous myocardial infarction, n (%)	13 (26)
Arterial hypertension, n (%)	48 (96)
Wechsler V, scores	10 (7; 14)
Wechsler VII, scores	32 (14; 54)
Bourdon test (accuracy)	2 (0,357; 20)
Bourdon test (vigilance)	0.81 (0.07; 1)
Bourdon test (time spent)	97 (57.7; 154)
Right hippocampal length	0.3 (0.24; 0.4)
Right hippocampal volume	4.695 (2.03; 8.09)
Left hippocampal length	0.305 (0.24; 0.37)
Left hippocampal volume	4.65 (2.34; 8.03)
Atherosclerosis, n (%)	37 (74)
Total cholesterol, mmol/L	4.885 (2.4; 9.66)
Triglycerides, mmol/L	1.675 (0.6; 5.3)
LDL, mmol/L	3.445 (1.4; 7.97)
HDL, mmol/L	0.97 (0.46; 2.7)

cerebrovascular accident, and chronic obstructive pulmonary disease (COPD) are 12.8%, 10.3%, and 13% of cases, respectively. In this study, COPD as an extracardiac cause of CHF was the exclusion criterion. The patients with CHF caused by the rare causes (previous myocarditis [3.6%], cardiomyopathies, toxic myocardial diseases of various origin, including iatrogenic ones, anemia [12.3%]) are largely incomparable with the patients with CHD, hypertension, diabetes mellitus, and, obviously, should be investigated in a separate study.[6]

As a result, the study population included 50 patients with CHF aged from 41 to 75 years old (mean age – 63.2 years old), including 23 men and 27 women. Cerebral MRI was performed using PHILIPS ACHIEVE 1.5T with analysis of the hippocampus, a part of the limbic system involved in the formation of emotions and memory consolidation. Moreover, the cortical gray matter thickness was measured. The cognitive functions were assessed via Wechsler Verbal and Nonverbal Scale of Ability (V and VII subtests) and Bourdon test (Dot Cancellation Test). Echocardiography was used to measure the parameters of the right and left cardiac chambers, such as left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left atrial end-systolic dimension (LAESD), right ventricular end-diastolic dimension (RVEDD), right atrial end-systolic dimension (RAESD) and left ventricular ejection fraction (LVEF). N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and lipid profile components were measured.

The canonical statistical analysis was used to evaluate the relationships between the cognitive functions, lipid profile components, parameters characterizing the severity of CHF and quantitative characteristics of the hippocampus (Table 2). The non-parametric correlation analysis (Kendall test for rank variables and Spearmen test for quantitative variables) was applied to investigate the relationships of the abovementioned parameters among themselves. Only statistically significant correlations are shown (p<0.5). STATISTICA 8 software was used.

Results and discussion

The canonical correlation analysis revealed statistically significant relationship (R = 0.66, p <0.05) between the parameters characterizing CHF (LVEDD, LVESD, LAESD, RAEDD, RAESD, FC, NT-proBNP) and cognitive scores.

The weak statistically significant relationships determined using the pairwise correlation analysis, were as follows: larger RAESD and higher FC corresponded to lower Wechsler VII scores (R = –0.31, –0.4 respectively). Larger LVESD, LAESD and RAESD and higher FC corresponded to shorten time spent for the Bourdon test (R = –0.34, –0.45, 0.39, respectively); lower LVEF corresponded to lower Wechsler V scores (R = 0.56); higher FC corresponded to lower vigilance in the Bourdon test (Kendall R = –0.37); higher FC corresponded to lower accuracy in the Bourdon test (R = –0.32).

The canonical correlation analysis revealed nonsignificant relationship (R =0.62, p = 0.16) between the hippocampal parameters and cognitive scores.

The weak statistically significant relationships determined using the pairwise correlation analysis, were as follows: smaller right hippocampal volume corresponded to lower Wechsler V scores (R = 0.36); smaller right hippocampal volume corresponded to lower vigilance in the Bourdon test (R = 0.38,). Smaller left hippocampal volume corresponded to lower vigilance and accuracy in the Bourdon test (R = 0.33, and 0.33, respectively).

The pairwise correlation analysis revealed statistically significant relationships between the left hippocampal dimensions and lipid profile parameters. It was found that the higher LDL levels and lower HDL levels corresponded to smaller left hippocampal length (R = –0.34 and R = 0.33, respectively). Moreover, higher triglyceride levels corresponded to smaller left hippocampal volume and length (R = –0.46 and R = –0.46, respectively). Multivariate statistical analysis showed that these relationships were independent from the associations with the cortical gray matter thickness. No significant correlations between the total cholesterol levels and hippocampal parameters were determined.

The canonical statistical analysis of the parameters characterizing the severity of CHF and quantitative characteristics of the hippocampus revealed the significant relationship (R = 0.56, p <0.05). The pairwise correlation analysis showed that the right hippocampal length and volume were slightly smaller in patients with FC III–IV (R = 0.30) compared to patients with FC II (R = 0.33). The decreased LVEF was also associated with smaller right hippocampal length (R = 0.38). The left hippocampal volume had weak statistically significant (p <0.05) inverse correlation to the sizes of the left and right cardiac chambers: larger LVEDD, LVESD, LAESD, RVEDD corresponded

Table 2 – Relationships between the cognitive functions, lipid profile components, parameters characterizing the severity of CHF and quantitative characteristics of the hippocampus

	Lipid profile components	Quantitative parameters of the hippocampus	Cognitive scores
CHF parameters	R* = 0.61 p** = 0.09	R = 0.56 p < 0.05	R = 0.66 p < 0.05
Lipid profile components	–	R = 0.61 p < 0.05	R = 0.65 p = 0.06
Quantitative parameters of the hippocampus	–	–	R = 0.62 p = 0.16

* – canonical correlation factor, ** – significance level.

to smaller left hippocampal volume (R = –0.31, –0.32, -0.30, –0.31, respectively). The canonical statistical analysis of the lipid profile components and cognitive scores revealed the pretty significant relationship (R = 0.65, p = 0.06). The statistically significant relationships determined using the pairwise correlation analysis, were as follows: higher cholesterol and low density lipoproteins (LDL) levels corresponded to lower Wechsler VII scores and shorter time spent for the Bourdon test (R = 0.34, 0.37, 0.39, 0.35, respectively); higher LDL levels corresponded to lower Wechsler V scores (R = 0.33).

Discussion

It is evident that both CHF and atherosclerosis may be relevant causes of cerebral blood flow deterioration which, in turn, can contribute to development of both functional and organic changes in the central nervous system. It was previously found that increase in clinical severity and deterioration of clinical and laboratory characteristics of CHF in patients with CHD were associated with decrease in the cortical gray matter thickness and worse cognitive scores. Probably, CHF existing in patients with CHD causes microdamages in the brain and, consequently, gradual decrease in the cortical gray matter thickness, which, in turn, leads to cognitive disorders.[9] Considering these data, it is understandable that the severity of CHF and dyslipidemia may indirectly influence the structure of the hippocampus being a part of the gray matter responsible for cognitive function.

Overall, the results obtained in this study suggest that the dyslipidemia as well as development and progression of CHF in patients with CHD may be predictors for hippocampal atrophy which, in turn, may be one of the direct causes of cognitive impairment in this population.

Therefore, when the patients with ischemic CHF are diagnosed and treated, especially in case of dyslipidemia, the possible development of hippocampal atrophy in such patients should be considered, measures should be taken in timely manner to identify and manage cognitive dysfunction, which can have a positive effect on adherence to treatment in patients with CHF and CHD and reduce the frequency of hospitalization and disability of population. The consideration of CHF and alterations in lipid profile as predictors for hippocampal atrophy, their early detection and management can reduce the incidence of cognitive disorders in this population.

Conclusion

The patients with ischemic CHF have negative statistical significant relationship between the hippocampal dimensions and cognitive scores. In patients with CHD, the significant trend to reduction of the hippocampal dimensions is observed when the severity of CHF is increased. The deteriorated lipid profile is associated with worsened cognitive parameters and diminished hippocampal sizes.

Dyslipidemia and increased severity of CHF in patients with CHD may be markers of hippocampal atrophy which may be one of the direct causes of cognitive deficits in this population.

Conflict of interest
The authors declare no conflict of interest.

Funding
None.

Ethical statement
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent
The patient's consent has been obtained.

References

1. Storozhakov GI, Gorbachenkova AA. Textbook of Cardiology: 3-Volume Teaching Guide. 3d ed. Moscow: Geotar-media, 2009:512.
2. Shvarts YG, Akimova NS, Martynovich TV. Analysis of changes in the white matter and cognitive disorders in patients with chronic heart failure and coronary heart disease. Saratov Journal of Medical Scientific Research 2013;9:78–82.
3. Azarenko VE, Potabashy VA, Fesenko VI, et al. Cognitive disorders in patients with ischemic chronic heart failure. Medical Perspective 2018;2:7–9.
4. Niizeki T, Iwayama T, Ikeno E, et al. Prognostic Importance of Hippocampal Atrophy in Patients With Chronic Heart Failure. Am J Cardiol 2019;123:1109–1113.
5. Suzuki H, Matsumoto Y, Ota H, et al. Hippocampal Blood Flow Abnormality Associated With Depressive Symptoms and Cognitive Impairment in Patients With Chronic Heart Failure. Circ J 2016;8:1773–1780.
6. Woo MA, Ogren JA, Abouzeid CM, et al. Regional hippocampal damage in heart failure. Eur J Heart Fail 2015;5:494–500.
7. Suzuki H, Matsumoto Y, Ota H, et al. Interactions between the heart and the brain in heart failure patients assessed by magnetic resonance imaging – interim results from Brain assessment and investigation in Heart Failure Trial (B-HeFT). Eur Heart J 2013;34:2732.
8. Goette A, Braun-Dullaeus RC. Atrial fibrillation is associated with impaired cognitive function and hippocampal atrophy: silent cerebral ischaemia vs. Alzheimer's disease. Eur Heart J 2008;17:2067–2069.
9. Akimova NS, Persashvili DG, Martynovich TV, et al. The relationship between the severity of chronic heart failure and status of the central nervous system in coronary heart disease. Fundamental Researches 2011;11:467–471.