

## **Circadian Index, as a Additional Parameter for Assessment of the Heart Rhythm in Patients With Heart Failure**

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The 24-hour heart rate variability (HRV) by results of Holter monitoring (HM) is the most informative method for assessment of the condition and prognosis for patients with heart failure (HF). This mention also suggest numerous materials of the World-web symposium ISHNE for Heart Failure. However specific methods for assessment of the circadian changes of heart rate during 24 hours of the HM are not yet in standard use. Several years above we proposed the Circadian Index (CI), calculated as the ratio of the average HR during day time (bpm) to average night time HR, as additional method for assessment of the circadian HR and defined normative parameters of the CI for healthy persons ( $1,32 \pm 0,06$ , range 1,24-1,44, without significant sex and age differences /1-5/). We had founde that CI is a stable steady value, irrespective of sex, age and average level of heart beats (sinus bradycardia or tachycardia). At the present moment it is one of the standard index for final protocol of HM in Russia, calculated in numerous commercial systems of HM in Russia and some other countries /6-9/. The aim of this study was to present of the possible values of the CI as additional specific parameter in patients with HF.

We had been calculated of the CI from 20 works published previously /10-22/ where the values of the average HR during day and night in healthy subjects and patients with different kinds of disease from 2 /15/ to 99 /10/ years old were presented (Table).

**Table**

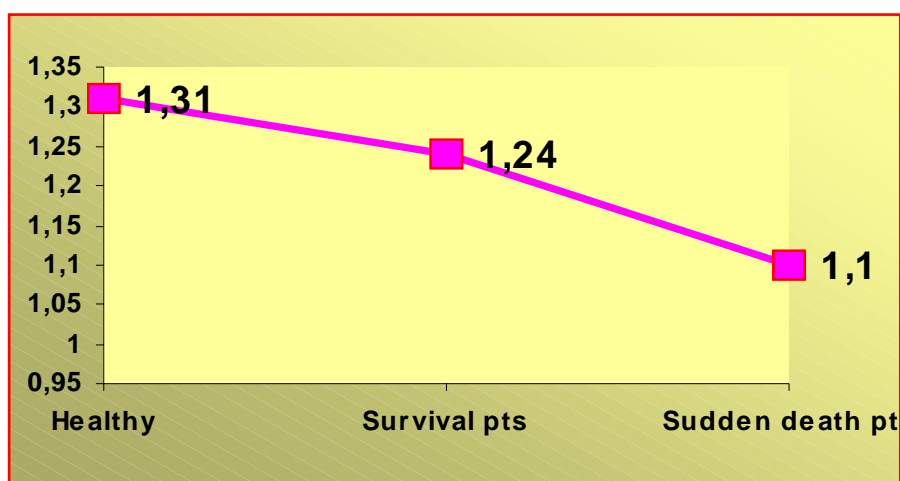
***Circadian Index (CI) in healthy subjects calculated from a series of published works***

<b>N</b>	<b>Author/Reference</b>	<b>n</b>	<b>Age (y.o.)</b>	<b>Sex</b>	<b>CI</b>	<b>Day Period</b>	<b>Night period</b>
1	Staessen J et al./9/	6974	10- 99	F/M	1,26	Awake Period	Sleeping Period
2	Sapoznikov D et al./11/	50	17-70	F/M	1,27	Awake Period	Sleeping Period
3	Fauchier L. et al /12/	63	48 ± 11	F/M	1,31	9 a.m. – 9 p.m.	0 a.m. – 6 a.m.
4	Casolo G et al./13/	20	54 ± 7	F/M	1,31	7 a.m. – 11 p.m.	12 p.m. – 6 a.m.
5	Molnar G et al./14/	20	56 ± 13	F/M	1,31	10 a.m. – 4 p.m.	12 p.m. – 6 a.m.
6	Ardura J et al./15/	10	10 ± 4	F/M	1,31	Awake Period	Sleeping Period
7	Vitasalo G et al./16/	35	15 ± 0,7	M	1,38	7 a.m. - 9 p.m.	10 p.m. - 6 a.m.
8	N.Neyroud et al./17/	25	31 ± 17	F/M	1,37	8 hrs shortest RR	4 hrs longest RR
9	Broadhurst P. et al./18/	30	18-74	M	1,39	Awake Period	Sleeping Period
10	Broadhurst P. et al./18/	20	18-74	F	1,37	Awake Period	Sleeping Period
11	Brodsky M et al./19/	50	22 ± 0,7	M	1,39	Awake Period	Sleeping Period
12	V.Rasmussen et al./20/	60	20 – 79	F/M	1,3	10 a.m. - 6 p.m.	10 p.m. - 6. A.m.
13	F.Extramiana et al /20/	60	20-50	F/M	1,34	8 hrs shortest RR	4 hrs longest RR
14	F.Extramiana et al /20/	30	20-50	F	1,32	8 hrs shortest RR	4 hrs longest RR
15	F.Extramiana et al /20/	30	20-50	M	1,36	8 hrs shortest RR	4 hrs longest RR
17	Ewing D et al./22/	25	20-65	M	1,41	Awake Period	Sleeping Period

In one study authors use ratio of heart rate day to night (CI by our approach) /12/. Values of the CI in healthy persons calculated by us from those papers were identical of our results that we have been obtained before ( $1,32 \pm 0,06$ ) /1-5/. We had selected from those papers the values of the average day and night HR (bpm) in patient with HF for calculation of CI /12-14/.

In all cases we have found the progressive smoothing of the circadian rhythm profile according to progressive of the heart failure. Molnar et al. /14/ analyzed circadian changes of the dispersion of QT interval (QTd) in survivors of sudden cardiac death patients with HF in comparison with analogous sex and age-dependent groups of patients with analogous pathology

(dilated cardiomyopathy, arterial hypertension, myocardial infarction with HF and other) and healthy volunteers. The calculation of the CI of examined groups revealed that progressive smoothing of circadian rhythm occurred together with a worsening prognosis of the disease and HF. The values of CI were 1,31, 1,24 and 1,1 respectively in healthy, survived and sudden death patients /14/. Fig. 1.

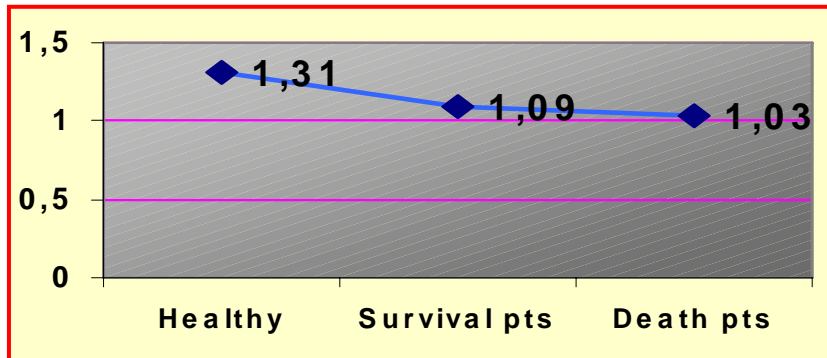


*Fig. 1 Decreasing of the circadian Index (CI) in healthy persons, survivors and sudden death patients with HF. (Calculated by us from Molnar et al. /14/)*

It is important to note that the authors' results of QTd evaluation did not demonstrate so a logical sequence (QTd parameters of healthy individuals were higher than those in the groups of patients with cardiac pathology). Calculation of the CI from in study

Fig. 2 Decreasing of the circadian Index (CI) in healthy persons survivors patients and death patients with HF. (Calculated by us from Casolo G. et al. /13/)

Casolo et al. /13/ in patients with hypertrophic cardiomyopathy and HF we received the similar sequence: CI in control healthy persons – 1,31, in survived patients - 1, 09 and in died patients - 1,03. Fig. 2.



L. Fauchier et al /12/ using ratio of HR to night as the part of assesment of heart rate (circadian index by our approaches) in patient with idiopathic dilated cardiomyopathy (IDC) received values CI as  $1,31 \pm 0,13$  in control group,  $1,26 \pm 0,09$  in patients with IDC without HF (NYHA class 1) and  $1,18 \pm 0,1$  in patients with IDC with HF (NYHA class II-IV),  $p < 0,05$  versus control and NYHA class 1 groups. Fig. 3.

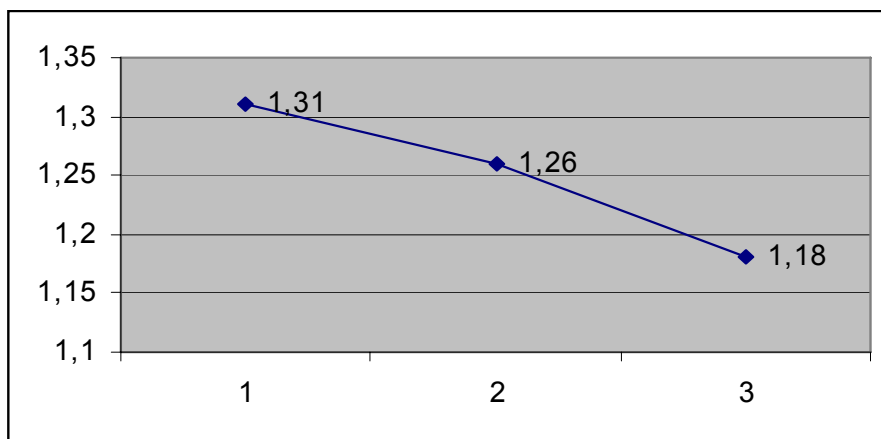
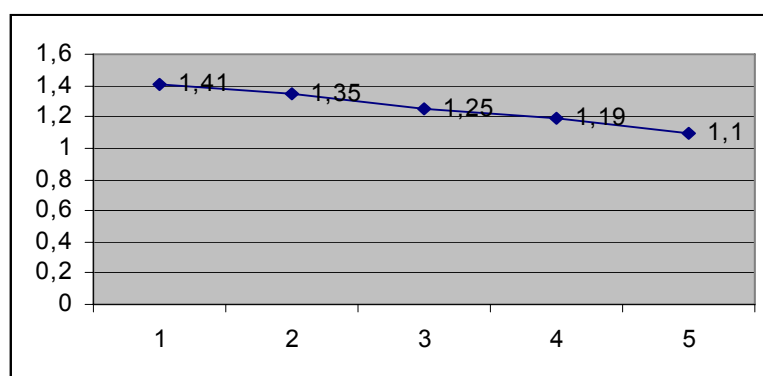


Fig. 3 Decreasing of the day HR/night (CI) in healthy persons survivors patients and death patients with HF. (Fauchier L., et al. /12/)

Very important that authors did not found correlation between standard HRV parameters (SDNN, rMSSD) and CI in patients with ICD.

It is speculated that the mechanisms for the circadian HR regulation reflected in CI changes lies in the autonomic system. Evaluation of the CI in patients with specific autonomic abnormalities may be useful in explanation of the CI changes. The diabetes is typical models of cardiac autonomic abnormality. By the same approaches we had calculated CI from research of D.Ewing et al. /22/. Values of CI in healthy control and diabetics who had normal cardiovascular reflexes did not differ from our normal value (CI = 1,41 and 1,35), while patients with abnormal only parasympathetic cardiovascular reflexes had considerable lowering



*Fig. 4 Decreasing of the CI in healthy persons (1) diabetics patients: with normal cardiovascular reflex (2), with parasympathetic cardiovascular reflexes (3), total autonomic blockade (4) and cardiac transplant patients (5). (Calculated by us from D.Ewing et al. /22/) of the given value of CI (1,25) and especially in diabetic patients with total autonomic blockade (CI=1,19) and cardiac transplant patients have extreme “smooth” of the circadian heart rate (CI=1,1). Fig. 4.*

#### Conclusions:

1. The Circadian Index is a specific for Holter monitoring parameter indicating a stable structure of the circadian heart rate. The normal value of this parameter is 1,24 -1,44 (Mean  $1,32 \pm 0,06$ ).
2. A reduction of the Circadian Index to less than 1,2 is found in diseases connected with a decrease of autonomic control of heart rate. In patients with HF it is associated with a higher risk of life threatening arrhythmias, sudden death, and a poor prognosis in heart failure.
3. Evaluation of the Circadian Index may be useful additional criteria for assessment patients with heart failure.

## References

1. Makarov L., Shkolnikova M. Circadian ECG and regulation of cardiac rhythm in healthy children by 24 Hour Holter monitoring. In: *Electrocardiology 96: "From cell to the body surface"*. World Scientific Publ.Co. J.Liebman (ed). 1997 USA p.357-360.
2. Makarov L. Specific features of heart rhythm variability under condition of free activity. *Human Physiology*. (Moscow. Engl.)-1998.- Vol. 24 № 2.- p.180-185
3. Makarov L. Method of assessment of cardiovascular and autonomic systems condition (Circadian Index). Patent of Russia Federation # 2151545 C1 Bul. # 18 27/06/2000. Priority # 99120985 from 08/10/1999.
4. Makarov L. Holter monitoring in children: what is normal? *Annals of Noninvasive Electrocardiology* Vol 3 (3) Part 2, July.- 1998.- p. 35, N 139. Abstr. of the 8<sup>th</sup> Congress ISHNE 1998 Ulm, Germany
5. Makarov LM. Circadian index as indicator of stable organization of heart circadian rhythm. *Klin Med (Mosk)*. 2000;78(1):24-7. Review. Russian. Res. Engl. PMID: 10697369 [PubMed - indexed for MEDLINE]
6. Makarov L. Holter monitoring. 2 th edit. Moscow. "Medpractica-M" Publ. House. 2003 – 340 p (Rus)
7. Riabykina G., Sobolev A. Monitoring of ECG with analysis of heart rate variability. Moscow. "Medpractica-M" Publ. House. 2005 – 224 p (Rus)
8. Shubik Y. Circadian ECG monitoring in the cardiac arrhythmias. S.Petersburg. Inkart, 2001, 216 p (Rus).
9. Medilog Darwin Clinical Application Guide. Issue 1.0 © 2005 VIASYS Healthcare, p.7.
10. Staessen., L. Bieniaszewski., O'Brien E., Gosse Ph., Hayashi H., Imai Y., Kawasaki T., Otsuka K., P.Palatini., Lutgarde Th., Thijs L., Fagard R. Nosturnal blood pressure fall on ambulatory monitoring in a large international database.*Hypertension* 1997 vol 29 N1 part1 p.30-39.
11. Sapoznikov D., Luria M., Mahler Y., Gotsman M. Day vs night ECG and heart rate variability patterns in patients whithout obvious heart diseases.*J Electrocardiology* 1992; 25:175-184.
12. Fauchier L., Babuty D., Cosnay P., Laurence Autret M., Fauchier P.Heart rate variability in idiopathic dilated cardiomyopathy: characteristics and prognosis value. *JACC* 1997;30(4);1009-1014.
13. Casolo G., Balli E., Taddei T. et al.: Decreased spontaneous heart rate variability in congestive heart failure. *Am J Cardiology* 1989;15:p.1162-1167.
14. Molnar J, Rosenthal J, Weiss S, Somberg C.: QT interval dispersion in healthy subjects and survivors of sudden cardiac death: Circadian variation and twenty four-hour assesment. *Am J Cardiol* 1997; 79 (1) : p.1190-1193

15. Ardura J., Silva J., Khatib A., P.Aragon. Electrocardiogramma continuo de Holter en ninos. Ann Esp Pediatr:19:1983p.88-99 (Res.Engl.)
16. Vitasalo M., Kala R., Eisalo A.: Ambulatory electrocardiographic findigs in young athletes between 14 and 16 years of age. European Heart J 1984;5:p.2-6.
17. Neyrod N., Maison-Blanche, I.Denjoi et al.:Diagnostic perfomance of QT variables from 24-hour electrocardiography in the long QT syndrome. European Heart J: 19:1998,158-165.
18. Broadhurst P., Brigden G., Daspupta P., Lahini A., Raftery E. :Ambulatory intra-arterial blood pressure in normal subjects. Am Heart J :120 ; 1990 p.160-166.
19. Brodsky M., Wu D., Penes P. et al: Arrhythmias documented by 24 hour continuous electrocardiographic monitoring in 50 male medical students without apparent heart diseases. Am J Cardiology:39;1997, p.390-395.
20. Rasmussen V, Jensen J, Hansen J. QT interval in 24-hour ambulatory ECG recordings from 60 healthy adult subjects. J Electrocardiol 1991;24:p.91-95.
21. Extramiana F., P.Maison-Blanche, F.Badilini, J.Pinoteau, T.Deseo, P.Coumel:Circadian Modulation of QT Rate Dependence in healthy Volunteers. J Electrocardiology 32:1;1999, p.33-43
22. Ewing D., Nelson J., Travis P: New method for assessing cardiac parasympathetic using 24-hour electrocardiogram.// Brit. Heart J. 1984 52 p.396-402.