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Autonomic cardiac modulation in postmenopausal women with dry eye syndrome: a cross-sectional analytical study

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SUMMARY

OBJECTIVE: The aim of this study was to assess cardiac autonomic modulation in postmenopausal women with and without dry eye syndrome (DES) and to identify associations between clinical and socioeconomic factors.

METHODS: A cross-sectional study was carried out at the Institute of Ocular Surgery of the Northeast (ICONE), Brazil. Convenience sample of postmenopausal women, over 40 years old, who were divided into two groups: with and without DES. Clinical, sociodemographic, and ophthalmological characteristics of these women were assessed. Capture of RR intervals was performed using a cardio frequency meter. Differences between the groups were analyzed using the Chi-square test, the Student's t test, and the Mann-Whitney test.

RESULTS: Women with DES were present in 60.4% (n=58), highest median age (63.5 years, 95%CI 62.0–67.9; p<0.001), median length of time menopause (19 years old, 95%CI 10.4–24.0; p<0.001). There was a difference in the standard deviation of all normal-to-normal index between the groups. However, when the differences were adjusted to the clinical model, no association was found between DES and heart rate variability (HRV).

CONCLUSIONS: The analysis of cardiac autonomic modulation in postmenopausal women is similar in the presence or absence of DES. Clinical factors, time of menopause, and intensity of symptoms were not associated with HRV indices.

KEYWORDS: Heart rate. Autonomic nervous system. Postmenopausal. Climacteric. Dry eye syndromes.

INTRODUCTION

Dry eye syndrome (DES) affects 15% of the population aged over 45 years, showing a controversial and unexplained higher prevalence in postmenopausal women using estrogens and associated estrogen and progestogen[1]. It involves factors related to the tear and the ocular surface[2], which is associated with symptoms such as mild eye discomfort, burning, foreign body sensation, photophobia, blurred vision[3], increased risk of ulcerations, corneal infections, and impaired visual acuity[1-3].

Tear production by the lacrimal gland parenchyma and its ocular release are influenced by the autonomic nervous system (ANS) that also controls heart rhythm through sympathetic and parasympathetic endings[1,3-5]. Postmenopause, the

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hypoestrogenism characteristic of ovarian insufficiency, can cause changes in the cardiac autonomic behavior and in the glands involved in tear production[5,6].

Heart rate variability (HRV) is an effective; noninvasive method to evaluate ANS function; being used in different situations, such as postmenopause, vasomotor symptoms (VMS), and their endocrine, nervous, and morbidity relationships. HRV has been considered as a homeostasis imbalance marker in women[7-9].

Understanding autonomic changes in the postmenopausal period, as well as the influence of menopause time associated with DES, becomes relevant in promoting women's health. Thus, the objectives of this study are to evaluate cardiac autonomic modulation in postmenopausal women with and without DES and to identify associations between clinical and socioeconomic factors.

METHODS

Design and ethical aspects

This is an observational analytical study conducted with postmenopausal women in an Ophthalmology Outpatient Clinic at the Northeast Institute of Ocular Surgery (Instituto de Cirurgia Ocular do Nordeste, ICONE), in Recife (PE), Brazil, from December 2017 to December 2018. All procedures were approved by the Research Ethics Committee (2,407,176 and CAAE No. 80490717.4.0000.5200).

Population and eligibility criteria

Study was conducted with women having routine ophthalmological consultations and by nonprobabilistic sampling of convenience. It included women aged over 40 years with a clinical (absence of menstruation for a period longer than 12 months) or laboratory (FSH greater than 30 IU/Ml[5]) diagnosis of postmenopause, who agreed to participate in the study by signing the informed consent form.

Exclusion criteria were use of hormone therapy in the previous 3 months, hysterectomy, cardiovascular diseases, use of systemic or ophthalmological medications, and history of eye infection or surgery.

Sample power

Sample size was calculated using the sample studied and the differences found in the analyses. Thus, we have considered as main parameter the statistical significance found in model II for analyzing the association between DES and HRV indices, r^2 of 0.02 in the initial model, and r^2 of 0.01 in the final model for a sample size of 96 participants, the test power was 0.28.

Data collection instruments

Kupperman-Blatt menopausal index

The Kupperman-Blatt menopausal index (KBMI) analyzes and classifies the intensity of menopausal symptoms through evaluation scales[5,10].

Capture of RR intervals

The RR intervals were captured following the protocols described by Vanderlei et al.[4] and Catai et al.[11] Procedure for capturing RR intervals was performed individually, using a Polar RS800CX HR monitor (Polar Electro, Kempele, Finland) validated equipment for HR capturing beat by beat. Data stored in the Polar RS800CX were used for HRV analysis[12,13].

HRV analysis

HRV was analyzed using the HR recorded beat by beat in RR interval capture. Only series with more than 95% sinus beats were used for analysis[11-13]. RR intervals digitally filtered using the Polar Precision Performance SW software (version 4.01.029), and manually to eliminate ectopic beats and artifacts. After filtering, the last 256 RR intervals were selected to undergo HRV analyses based on nonlinear and linear methods regarding time and frequency[11].

In domain of time, study evaluated the mean RR, the root mean square of the successive differences (RMSSD) between successive normal RR intervals from the analysis of adjacent RR intervals, and the standard deviation of all normal-to-normal (SDNN) RR intervals. RMSSD index translates parasympathetic modulation[14]. SDNN represents global variability[4,12].

In the domain of frequency, low (LF, 0.04–0.15 Hz) and high frequency (HF 0.15–0.40 Hz) spectral components were used to analyze HRV in normalized units that represent the relative value of each component in relation to total power, minus very low frequency (VLF) components in milliseconds squared and the ratio between these components (LF/HF). The spectral analysis was calculated using the Fourier transform algorithm[11,13].

Ophthalmological examination

Biomicroscopy examination analyzes the eyelids and the presence or absence of blepharitis, blepharochalasis, ptosis, ectropion, and entropion. Tear film, the presence or absence of mucus, oiliness, and thickness of the tear meniscus between the eyelid margin and the bulbar conjunctiva are examined[1-3]. Patency, ectopy, and the presence or absence from reflux to expression are evaluated in lacrimal points. Eyelid and bulbar conjunctivae are evaluated for the presence of hyperemia, edema, papillae, follicles, scar areas, and conjunctivochalasis.

The presence or absence of keratitis, irregularities, and cicatricial signs secondary to recurrent erosion should be evaluated in the cornea[1-3].

Statistical analysis

Qualitative variables were described by absolute and relative frequencies. Quantitative variables were described using means and 95% confidence intervals for the variables with normal distribution (Shapiro-Wilk, $p \geq 0.05$), and medians and confidence intervals for those that had no normal distribution (Shapiro-Wilk, $p < 0.05$).

Differences between the groups with and without DES were analyzed using the Chi-square test for qualitative variables, the Student's t-test for quantitative variables with normal distribution, and by the Mann-Whitney test for quantitative variables with no normal distribution.

HRV index differences between groups were analyzed using linear or median regression to estimate adjusted mean differences and adjusted median differences, respectively. The models were created according to the inclusion of all significant variables in the univariate analyses and using clinical criteria. All analyses considered a 5% significance level. The Stata® software (Stata Corp., L.L.C.) version 15 was used in the statistical analysis.

RESULTS

The study included 107 women, of which 11 were excluded due to schizophrenia, hysterectomy, congenital heart disease, and RR interval tracing errors. Sociodemographic and clinical characteristics showed no statistically significant differences (Table 1).

In the comparison of linear HRV indices, there were no statistically significant differences between the groups (Table 2).

Table 3 shows multivariate analyses in three regression models created to estimate differences. There was a difference in the SDNN between groups in model II. However, in model III, there were no association between DES and HRV.

DISCUSSION

These results indicate no differences in cardiac autonomic modulation in postmenopausal women with or without DES. Clinical factors, time of menopause, and intensity of symptoms are not associated with HRV indices.

DES group had a lower BMI and a higher percentage of physical activity practitioners than the control group. Mean chronological age corroborated the studies[5-7] that analyzed hormonal relationships in postmenopausal women with DES. About age at menarche and age at menopause, both groups presented similar results to those found in the literature[5,9,10]. Socioeconomic differences observed have also been described in previous Brazilian studies[5,7,8,10].

Comparison of HRV indices between groups showed no significant differences. When this comparison was adjusted for the different socioeconomic characteristics between groups (ethnicity, marital status, and education), DES group had a lower SDNN. This index represents global variability[4,11,12] that could indicate that some socioeconomic factors associated with DES would decrease global variability. Previous studies presenting global HRV decrease situations in different populations reported worse cardiovascular prognosis[12,13,15].

Jones et al.[14] analyzed the intensity of menopausal symptoms and HRV and reported a decrease in all HRV indices in both groups of postmenopausal women. Studies with different objectives also reported decreased cardiac autonomic regulation in postmenopausal women[7,9,16-18].

However, we do not believe that this difference can have relevant clinical implications since the comparison adjusted by different clinical variables between groups showed no differences in the HRV indices. This indicates that the predominance of age, time since menopause, age at menopause, or menopause symptoms had no influence on cardiac autonomic modulation in the present sample groups.

HRV allows the quantitative evaluation of autonomic balance and describes interval fluctuations between consecutive RR intervals[4,11], which can be an additional resource in the evaluation of menopausal women[16-18] diagnosed with DES. Menopausal women are more likely to develop this condition, probably due to decreased androgens and estrogen production resulting in Meibomian gland dysfunction, and age-related factors[2,6,9,10].

Calio et al.[19] demonstrated that regular physical activity improves or reduces the intensity of menopausal symptoms and improves HRV levels in postmenopausal women. A study on postmenopausal women showed increased post-exercise HRV indices with moderate and high intensity physical exercises. These findings indicate increased parasympathetic tonus, with efficient adaptation of cardiac autonomic modulation and a consequent cardioprotective factor[20]. Rezende Barbosa et al.[18] evaluated women practicing functional training and demonstrated that HRV has greater variability in functional training postmenopausal practitioners.

Regular physical activity represents an important factor to reduce morbidity and mortality rates due to cardiovascular or other causes, being related to improved autonomic control, which has been widely studied through HRV analysis[4,11,16,17]. Different studies[7,16-18] suggest that physical exercise may have a positive relationship with HRV, sometimes reflected by

Table 1. Sociodemographic and clinical characteristics in postmenopausal women with and without dry eye syndrome, Recife (PE), Brazil, 2017–2018.

Variables	Dry eye syndrome				p*
	No (n=38; 39.6%)		Yes (n=58; 60.4%)		
	Median	95%CI	Median	95%CI	p†
Age (years)	54	53.0–55.6	63.5	62.0–67.9	<0.001
Age at menopause (years)	49	48.0–49.5	50.0	49.0–50.9	0.364
Menopause time (years)	5	4.1–9.0	19	10.4–24.0	<0.001
Diastolic blood pressure (mmHg)	80.0	80.0–80.0	80.0	70.0–80.0	0.013
Hot flashes	3	2.0–4.0	1	0.0–2.0	0.019
	n	%	n	%	
Ethnicity					
White	6	12.5	42	87.5	<0.001
No white	32	66.7	16	33.3	
Marital status					
Single/widow/divorced	26	54.2	22	45.8	0.003
Stable union	12	25.0	36	75.0	
Education					
≤8 years	30	90.9	3	9.1	<0.001
>8 years	8	12.7	55	87.5	
Smoking					
No	31	81.6	56	96.6	0.014
Yes	7	18.4	2	3.4	
Alcoholism					
No	35	92.1	30	51.7	<0.001
Yes	3	7.9	28	48.3	
Physical activity					
No	29	76.3	23	39.7	<0.001
Yes	9	23.7	35	60.3	
Comorbidities					
No	29	76.3	42	72.4	0.670
Yes	9	23.7	16	27.6	
Menopausal symptoms (IMKB)					
Mild (≤19)	15	45.5	18	54.5	<0.001
Moderate (20–34)	11	22.9	37	77.1	
Severe (≥35)	12	80.0	3	20.0	
	Mean	95%CI	Mean	95%CI	p‡
Age at menarche (years)	13.3	12.7–13.8	11.7	11.3–12.1	<0.001
Body mass index	28.3	26.7–28.9	26.4	25.4–27.5	0.041
Systolic blood pressure (mmHg)	124.0	119.2–128.8	121.2	118.0–124.5	0.320

95%CI: 95% confidence interval; KBMI: Kupperman-Blatt menopausal index; *Chi-square test; †Mann-Whitney U test; ‡Student's t-test.

Table 2. Linear heart rate variability indices in postmenopausal women with and without dry eye syndrome, Recife (PE), Brazil, 2017–2018.

Variable	Dry eye syndrome				p*
	No (n=38)		Yes (n=58)		
	Median	95%CI	Median	95%CI	
Mean RR	887.5	803.4–967.8	903.0	867.5–946.9	0.727
SDNN	20.1	15.6–24.2	23.3	19.2–26.8	0.121
RMSSD	21.1	14.7–27.6	21.3	19.7–27.4	0.308
NN50	16.0	2.8–43.3	40.0	15.1–65.0	0.264
pNN50	1.4	0.2–5.7	2.6	1.1–5.2	0.351
LFms^2	155.0	103.4–226.2	167.0	128.0–266.8	0.148
LFms^2	144.0	81.6–260.0	190.5	120.0–236.5	0.297
Total	355.5	213.7–596.9	466.0	318.3–638.7	0.179
LFHF	1.3	0.8–1.8	1.1	1.0–1.5	0.810
	Mean	95%CI	Mean	95%CI	p†
LFnu	53.6	47.4–59.8	52.6	47.7–57.6	0.803
HFnu	46.3	40.1–52.5	47.2	42.3–52.2	0.805

95%CI: 95% confidence interval; RR: RR intervals; SDNN: standard deviation of all normal-to-normal; RMSSD: root mean square of the successive differences; NN50: total number of adjacent RR intervals with a difference of duration greater than 50 ms; pNN50: pPercentage of the total number of adjacent RR intervals with a difference of duration greater than 50 ms; LF: low frequency; HF: high frequency; *Mann-Whitney U test; †Student's t-test.

Table 3. Dry eye syndrome and socioeconomic and clinical factors (age, time of menopause, and intensity of menopausal symptoms) associated with linear cardiac autonomic modulation indices in postmenopausal women, Recife (PE), Brazil, 2017–2018.

Variable	Model I	p*	Model II	p*	Model III	p*
	Median difference (95%CI)		Median difference (95%CI)		Median difference (95%CI)	
Mean RR	16.59 (-64.03–97.23)	0.684	-22.4 (-95.5–50.7)	0.544	2.5 (-106.8–111.8)	0.964
SDNN	3.2 (-2.8–9.3)	0.294	8.2 (0.5–15.9)	0.037	6.3 (-1.7–14.4)	0.122
RMSSD	-0.8 (-9.2–7.6)	0.850	-2.1 (-10.9–6.6)	0.630	2.3 (-8.7–13.3)	0.682
NN50	25.0 (-23.0–73.0)	0.304	-14.5 (-113.9–84.9)	0.773	16.1 (-44.8–77.1)	0.601
pNN50	1.2 (-3.8–6.3)	0.638	-2.4 (-11.3–6.4)	0.589	1.9 (-5.3–9.1)	0.604
LFms^2	12.0 (-99.0–123.0)	0.831	65.3 (-133.3–263.8)	0.515	35.5 (-98.2–169.2)	0.599
LFms^2	29.0 (-78.3–136.3)	0.593	-56.8 (-268.1–154.5)	0.594	63.3 (-90.0–225.6)	0.440
Total	112.0 (-128.0–352.0)	0.357	166.9 (-319.9–653.7)	0.497	337.0 (-23.3–697.2)	0.066
LFHF	-0.2 (-0.8–0.3)	0.420	0.004 (-1.1–1.1)	0.994	0.25 (-0.5–1.0)	0.500
	Model I	p*	Model II	p*	Model II	p*
	Mean difference (95%CI)		Mean difference (95%CI)		Mean difference (95%CI)	
LFnu	-0.98 (-8.8–6.8)	0.803	3.1 (-11.8–18.0)	0.682	-2.7 (-13.2–7.8)	0.609
HFnu	1.0 (-6.8–8.8)	0.805	-3.2 (-18.1–11.7)	0.671	2.7 (-7.8–13.2)	0.611

95%CI: 95% confidence interval. RR: RR intervals; SDNN: standard deviation of all normal-to-normal; RMSSD: root mean square of the successive differences; NN50: total number of adjacent RR intervals with a difference of duration greater than 50 ms; pNN50: percentage of the total number of adjacent RR intervals with a difference of duration greater than 50 ms; LF: low frequency; HF: high frequency; *Linear regression. Model I estimated unadjusted linear index differences in both groups. Model II estimated linear index differences adjusted by for all significant variables in Table 1. Model III (clinical model) estimated differences adjusted by age, menopausal time, and intensity of menopausal symptoms (KBMI).

increased vagal regulation, or by a better interaction between sympathetic and parasympathetic components.

In this context, literature[16-18] shows that protocols evaluating HRV after moderate and intense physical activity can provide HRV recovery in postmenopausal women, reestablishing the parasympathetic predominance, especially in women with longer menopausal time. Those authors[16-18] also suggest that lifestyle is an essential component to improve HRV parameters. This fact may be a convenient general recommendation to be given by clinician following up menopausal and DES women.

It is worth mentioning that HRV can also be influenced by other associated factors, such as comorbidities and lifestyle habits[4,5,7,12]. As already mentioned, overweight and other lifestyle habits were not related to the absence or presence of DES in HRV indices analysis. Additionally, considering the volunteers' age and physiological aging could also influence the ANS due to the loss of the system's complexity[13]. However, the presence of temporary or permanent physiological disorders such as menopause in varied stages did not influence the findings[17,18].

This study has some limitations. The first would be related to the fact that cardiovascular risk was not analyzed. Although increased BMI is a risk predictor for mortality from cardiovascular disease in postmenopausal women, this study showed no differences related to this variable in HRV. The second would be that hypoestrogenism causes a progressive and permanent decrease in serum estrogen levels. However, these postmenopausal clinical aspects were not associated with HRV results with and without DES[17,18]. Finally, it has some limitations related to study design and nonprobabilistic sample. Subsequent studies on DES treatment interventions are necessary to evaluate its impact on the ANS.

CONCLUSIONS

Analysis of cardiac autonomic modulation in postmenopausal women is similar in the presence or absence of DES. Clinical factors, time of menopause, and intensity of symptoms were not associated with HRV indices.

AUTHORS' CONTRIBUTIONS

ADAJ: Data curation, Supervision, Writing – original draft. **TDC:** Supervision, Writing – original draft. **ARN:** Data curation. **FWSF:** Formal analysis. **PMM:** Data curation. **LCA:** Conceptualization. **ECB:** Supervision. **JMSJ:** Conceptualization. **ICES:** Conceptualization, Supervision, Writing – original draft.

REFERENCES

1. Schaumberg DA, Buring JE, Sullivan DA, Dana MR. Hormone replacement therapy and dry eye syndrome. JAMA. 2001;286(17):2114-9. https://doi.org/10.1001/jama.286.17.2114
2. Foulks GN. A new appreciation for dry eye disease. Can J Ophthalmol. 2009;44(4):370-2. https://doi.org/10.3129/i09-148
3. Fonseca EC, Arruda GV, Rocha EM. Dry eye: etiopathogenesis and treatment. Arq Bras Oftalmol. 2010;73(2):197-203. https://doi.org/10.1590/s0004-27492010000200021
4. Vanderlei LCM, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Noções básicas de variabilidade da frequência cardíaca e sua aplicabilidade clínica. Rev Bras Cir Cardiovasc. 2009;24(2):205-17. https://doi.org/10.1590/S0102-76382009000200018
5. Sorpreso ICE, Soares Júnior JM, Fonseca AM, Baracat EC. Female aging. Rev Assoc Med Bras (1992). 2016;61(6):553-6. https://doi.org/10.1590/1806-9282.61.06.553
6. Bagnoli VR, Fonseca AM, Arie WMY, Neves EM, Azevedo RS, Sorpreso IC, et al. Metabolic disorder and obesity in 5027 Brazilian postmenopausal women. Gynecol Endocrinol. 2014;30(10):717-20. https://doi.org/10.3109/09513590.2014.925869
7. Martinelli PM, Sorpreso ICE, Raimundo RD, Leal Junior OS, Zangirolami-Raimundo J, Lima MVM, et al. Heart rate variability helps to distinguish the intensity of menopausal symptoms: a prospective, observational, and transversal study. PLoS One. 2020;15(1):e0225866. https://doi.org/10.1371/journal.pone.0225866
8. Pereira VX, Carvalho TD, Marinovic Junior MA, Norberto AR, Soares Júnior JM, Valenti VE, et al. Linear and nonlinear heart rate variability analysis in gonadal dysgenesis (swyer syndrome): a case report. Int J Cardiovasc Sci. 2021;34(4):486-9. https://doi.org/10.36660/ijcs.20200002
9. Akiyoshi M, Kato K, Owa Y, Sugiyama M, Miyasaka N, Obayashi S, et al. Relationship between estrogen, vasomotor symptoms, and heart rate variability in climacteric women. J Med Dent Sci. 2011;58(2):49-59. PMID: 23896786
10. Esposito Sorpreso IC, Laprano Vieira LH, Longoni Calió C, Abi Haidar M, Baracat EC, Soares Jr JM. Health education intervention in early and late postmenopausal Brazilian women. Climacteric. 2012;15(6):573-80. https://doi.org/10.3109/13697137.2011.635915
11. Catai AM, Pastre CM, Godoy MF, Silva E, Takahashi ACM, Vanderlei LCM. Heart rate variability: are you using it properly? Standardisation checklist of procedures. Braz J Phys Ther. 2020;24(2):91-102. https://doi.org/10.1016/j.bjpt.2019.02.006
12. Dias De Carvalho T, Pastre CM, Rossi RC, de Abreu LC, Valenti VE. Geometric index of heart rate variability in chronic obstructive pulmonary disease. Rev Port Pneumol. 2011;17(6):260-5. https://doi.org/10.1016/j.rppneu.2011.06.007
13. Carvalho TD, Pastre CM, Godoy MF, Fereira C, Pitta FO, Abreu LC, et al. Fractal correlation property of heart rate variability in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2011;6:23-8. https://doi.org/10.2147/COPD.S15099

14. Jones SMW, Guthrie KA, LaCroix AZ, Sternfeld B, Landis CA, Reed SD, et al. Is heart rate variability associated with frequency and intensity of vasomotor symptoms among healthy perimenopausal and postmenopausal women? Clin Auton Res. 2016;26(1):7-13. https://doi.org/10.1007/s10286-015-0322-x

15. Lai S, Mangiulli M, Perrotta AM, Giraldi GDL, Testorio M, Rosato E, et al. Reduction in heart rate variability in autosomal dominant polycystic kidney disease. Kidney Blood Press Res. 2019;44(5):1142-8. https://doi.org/10.1159/000502419

16. Barbosa MPCR, Vanderlei LCM, Neves LM, Takahashi C, Torquato PRS, Fortaleza ACS, et al. Impact of functional training on geometric indices and fractal correlation property of heart rate variability in postmenopausal women. Ann Noninvasive Electrocardiol. 2018;23(1):e12469. https://doi.org/10.1111/anec.12469

17. Barbosa MPCR, Netto Júnior J, Cassemiro BM, Souza NM, Bernardo AFB, Silva AKF, et al. Impact of functional training on cardiac autonomic modulation, cardiopulmonary parameters and quality of life in healthy women. Clin Physiol Funct Imaging. 2016;36(4):318-25. https://doi.org/10.1111/cpf.12235

18. Rezende Barbosa MP, Vanderlei LC, Neves LM, Takahashi C, Torquato PR, Silva AK, et al. Functional training in postmenopause: cardiac autonomic modulation and cardiorespiratory parameters, a randomized trial. Geriatr Gerontol Int. 2019;19(8):823-8. https://doi.org/10.1111/ggi.13690

19. Calio CL, Sorpreso ICE, Haidar MA, Maciel GAR, Baracat EC, Soares Jr JM. Physiotherapeutic approach in early and late post-menopausal Brazilian women. Gynecol Endocrinol. 2013;29(7):670-3. https://doi.org/10.3109/09513590.2013.788627

20. Orri JC, Hughes EM, Mistry DG, Scala AH. Is vigorous exercise training superior to moderate for CVD risk after menopause? Sports Med Int Open. 2017;6;1(5):E166-E171. https://doi.org/10.1055/s-0043-118094