disease in the Russian Federation 2016-2020. Summary report on the data of the All-Russian Register of renal replacement therapy of the Russian Dialysis Society]. Nefrologiya i dializ [Nephrology and dialysis. 2022; 24(4) (In Russ.).]
2. Dudko M.Yu., O.N. Kotenko O.N., Malkoch A.V. Znachenie skrininga naseleniya v vyyavlenii hronicheskoĭ bolezni pochek [The importance of population screening in the detection of chronic kidney disease]. Lechashchij vrach [Attending physician. 2019; 1: 50-52 (In Russ.).]
3. Essaian A.M., Arutyunov G.P., Melikhov O.G. Rasprostranennost' hronicheskoj bolezni pochek sredi pacientov, obrativshihsya v uchrezhdeniya pervichnoj mediko-sanitarnoj pomoshchi. Rezul'taty prospektivnogo nablyudatel'nogo issledovaniya v 12 regionah Rossii [Prevalence of chronic kidney disease in primary care patients. results of a prospective observational study in 12 regions of Russia]. Klinicheskaya nefrologiya [Clinical nephrology. 2021; 13 (3): 6-16 (In Russ.).]
4. Klinicheskie rekomendacii. Hronicheskaya bolezn' pochek (HBP) [Clinical recommendations. Chronic kidney disease (CKD)]. Nefrologiya [Nephrology. 2021; 25(5): 10-82 (In Russ.).]
5. Sarycheva A.A., Davitashvili S.A. Upravlenie pochechnymi riskami v klinicheskoj praktike. Sovremennye vozmozhnosti nefroprotekcii [Management of renal risks in clinical practice. Modern possibilities of nephroprotection]. Kremlin medicine. Clinical Bulletin [Kremlevskaya medicina. Klinicheskij vestnik. 2022; 4: 53-59 (In Russ.).]
6. Yagudina R.I., Kotenko O.N., Serpik V.G., Abdrashitova G.T. Ekonomicheskoe bremya hronicheskoj bolezni pochek v Rossijskoj Federacii [The economic burden of chronic kidney disease in the Russian Federation]. Farmakoekonomika: teoriya i praktika [Pharmacoeconomics: theory and practice. 2014; 2 (4): 34-39 (In Russ.).]
7. World Health Organization. URL: https://www.who.int/ru/
8. Federal State Statistics Service. URL: https://rosstat.gov.ru
9. Yakutsk Republican Medical Information and Analytical Center. URL: https://yakmed.ru/#/home
10. Bochud M. On the rationale of population screening for chronic kidney disease: a public health perspective. Public Health Reviews. 2015; 36:11
11. Ikechi G., Okpechi [et al.] Early Identification of CKD-A Scoping Review of the Global Populations. Kidney International Reports. 2022; 7: 1341-1353.
12. Boris Bikbov [et al.] Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. Vol. 395 February 29, 2020.
13. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements. 2013. Vol.3.
14. Levey A.S., Grams M.E., Inker L.A. Uses of GFR and albuminuria level in acute and chronic kidney disease. N Engl Med 2022; 386: 2120-2128.
15. Levey A.S., Titan S.M., Powe N.R. Kidney disease, race, and GFR estimation. Clin J Am Soc Nephrol. 2020; 15(8): 1203-1212.
16. Van der Velde M. [et al.] Lower estimate glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. Kidney int. 2011; 12:1341–1352.
17. Xia J. [et al.] Cigarette smoking and chronic kidney disease in the general population: a systemic review and meta-analysis of prospective cohort studies. Nephrol Dial Transplant. 2017; 3: 475-487.

SCIENTIFIC REVIEWS AND LECTURES

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BIOLOGICAL MARKERS IN PREDICTING THE COURSE OF SPINAL MUSCULAR ATROPHY AND THEIR IMPORTANCE IN ORGANIZING MEDICAL CARE

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A correlation between the levels of blood biomarkers and clinical manifestations of SMA in patients of the main regional healthcare institution of the Samara region was carried out.

Differences in creatinine, creatine phosphokinase, and lactate dehydrogenase levels among patient groups and their association with motor impairment did not show statistical significance. Differences in CPK levels between groups may be related to age, weight, gender, and levels of physical activity of patients. The data obtained from the study of the history of repeated hospitalizations do not provide reliable information due to the limited sample and heterogeneity of the data. The results of this work indicate the ineffectiveness of assessing the levels of creatinine, CPK and LDH in order to monitor and predict the course of SMA, as well as the inappropriateness of repeating these laboratory studies in patients with SMA 5q.

Keywords: creatine phosphokinase, creatinine, neurofilament, neuromuscular diseases, nusinersen, hereditary disease, pathogenetic therapy, risdiplam, spinal muscular atrophy.

Introduction. Spinal muscular atrophy (SMA) is a genetically heterogeneous group of CNS disorders characterized clinically by the loss of motor skills, progressive symmetric peripheral paralysis due to degeneration of motor neurons, and resultant atrophy of striated muscles, which leads to difficulty in swallowing, general paralysis, and respiratory failure. SMA predominantly develops in childhood and is a major hereditary cause of infant mortality (Araujo et al. 2009). The worldwide prevalence of SMA is estimated to be 8.5-10.3 per 100,000 newborns, with carrier frequencies ranging from 1 in 35 to 1 in 60 (Kimizu et al. 2021). SMA is most commonly caused by autosomal inheritance mutations, resulting in a roughly equal distribution among both genders, although the gender frequency differs slightly according to SMA type (Verhaart et al. 2017, Gayduk & Vlasov 2019). The most common forms, known as SMA 5q, have no clear association with cognitive

and affective disorders in numerous studies, which have nonetheless highlighted the lack of detailed information about neuropsychiatric status (Mix et al. 2021, Zappa et al. 2021, Rivière et al. 2007, Gayduk et al. 2022).

The genetic nature of SMA 5q variants calls for molecular-genetic research methods as essential tools for confirming the diagnosis. Here, the most relevant method is testing for the copy numbers of *SMN1* and *SMN2* using multiplex ligation-dependent probe amplification (MLPA) (Hong et al. 2020, Mercuri et al. 2018, Feng et al. 2020, Lopez-Lopez et al. 2020). At the time of writing, laboratory diagnostic methods other than MLPA do not accurately determine the presence of the disease or provide predictions regarding its progression and severity. However, some studies suggest that certain nonspecific biomarkers hold promise for monitoring disease progression and assessing treatment effectiveness (Alves et al. 2020, Freigang et al. 2021, Yuan et al. 2017, Kobayashi et al. 2013, Kolb et al. 2016, Gayduk et al. 2022). These biomarkers include plasma levels of creatine phosphokinase (CPK), creatinine, and neurofilaments (NF). For instance, a study involving 238 patients demonstrated an inverse between serum creatinine levels and disease severity in children and adolescents, with correction for age and muscle mass (Alves et al. 2020). Creatinine levels were highest in patients with type III SMA and lowest in patients with type I, but decreasing with age regardless of clinical subtype.

A study population of 22 infants diagnosed with preclinical SMA underwent repeated measurement of plasma creatinine levels and evoked potentials electromyography (EMG) over the course of a year (Alves et al. 2020). Results showed decreasing creatinine levels and evoked potential amplitudes during the first three months, in consideration of earlier findings that decreasing creatinine levels preceded the decline in evoked potential amplitudes in 8 of 12 type III SMA patients. Another study conducted with adult patients demonstrated a correlation between plasma CPK and creatinine levels and disease severity, indicating their potential utility in predicting treatment efficacy (Freigang et al. 2021).

NF are cytoskeletal proteins that provide structural integrity to neurons, particularly in their axons. Elevated levels of NF are present in blood and cerebrospinal fluid during ongoing neurodegenerative processes in several diseases and in traumatic brain injury. In the case of SMA, plasma levels of NF are more indicative for disease prognosis and treatment monitoring in children than in adult patients (Yuan et al. 2017).

Broader research on SMA biomarkers has revealed other analytes that correlate with the degree of motor function impairment; the Biomarkers for SMA (BforSMA) study published in 2013 identified 200 plasma markers correlating with motor and other impairments in infants with SMA up to two years of age (Kobayashi et al. 2013). The authors selected the most significantly correlating plasma metabolites to create the commercially available diagnostic panel known as SMA-MAP. Further studies with the SMA-MAP panel revealed statistically significant deviations in infants with SMA compared to healthy infants up to 6 months of age (Kolb et al. 2016).

Serum lactate dehydrogenase (LDH) is a cytoplasmic enzyme, which serves as a common indicator of tissue damage (Zhang et al. 2012). Despite its broad application at many local healthcare institutions, there is scant evidence for the fitness of LDH as a biomarker for SMA.

As noted above, EMG is among the most effective instrumental diagnostic methods for evaluating neuromuscular function (Querin et al. 2018). Changes in electrophysiological parameters in SMA patients correlate with the number of *SMN2* copies, SMA type, motor function assessment results, and patient age. EMG results also serve for assessing the patient's response to specific therapies (Weng et al. 2021, Kariyawasam et al. 2020). The application of techniques such as EMG with motor unit number index (MUNIX) and motor unit size index (MUSIX) enables the detection of subtle electrophysiological changes, which is valuable for identifying specific patterns for differential diagnosis and therapy monitoring (Querin et al. 2018, Nandedkar et al. 2010). However, at the time of writing, there are no universal and cost-effective diagnostic and prognostic EMG-based tools, which poses a major challenge in providing medical care to SMA patients in Russia and around the world.

Thus, the currently most available and widely used blood biomarkers (serum creatinine, CK, and LDH) have the potential for utilizing as a tool for disease course monitoring. This approach is considerably cheaper than SMA-MAP (USD 500 per test), and calls for lower labor input than tests involving motor unit examinations.

The aim of this study was to investigate differences in an abbreviated panel of blood biomarkers (serum creatinine, CK, and LDH), EMG data, and clinical manifestations (including psychological/psychiatric impairments), among SMA patients at the main regional healthcare institution in the region of Samara, Russia Federation. Our goal was to obtain data that could contribute to the development of a practical and effective method for predicting the course of the disease, with potential application as an endpoint in intervention/treatment studies.

Materials and Methods. In a retrospective study of archived data from the V.D. Seredavin Samara Regional Clinical Hospital (SRCH), we assembled 112 medical records from 58 patients from hospitalizations spanning from January 2008 to February 2022. Patients were divided into groups based on gender, age (children under 18 years and adults), and the ICD-10 diagnostic categories (G12.0, G12.1, G12.8, and G12.9). When available, we included data from subsequent hospitalizations. The analysis included clinical data from general and neurological examinations, laboratory test indicators (LDH, CK, creatinine levels), and instrumental diagnostic methods (EMG). Statistical analysis was performed using MedCalc and IBM SPSS Statistics (Version 27, license from Samara State Medical University, 2022) with descriptive statistics and non-parametric methods due to the small sample size and non-normal distributions of the data. The Kruskal-Wallis test, a non-parametric equivalent of one-way analysis of variance (ANOVA), was used to compare median values between groups, with pairwise comparisons adjusted for multiple comparisons using the Dunn method. The data were described using the median, first and third quartiles, absolute frequencies, and percentages (indicated in parentheses).

Results. From January 2008 to February 2022, 58 SMA patients (38.4 [quartiles 13.7, 55.0] years old) had been registered at SRCH, of whom 32 (55.2%) were female. Among the 58 patients, 21 were children (12.3 [6.6, 13.9] years old), including 14 (24.1%) girls. The diagnosis of "Infantile spinal muscular atrophy, Type I, Werdnig-Hoffmann" (G12.0) was established in 7 patients (12.0%), all of whom were children: 5 (8.6%) girls and 2 (3.4%) boys. The oldest such patient was 14.3 years old, and the youngest was 4.8 years old (median of 7.7 [6.8, 12.7] years). The diagnosis of G12.1, encoding SMA II, III, and IV, was assigned to 43 patients (74.1%) (median age of 37.3 [14.5, 55.6] years), including 14 (24%) children, 9 (15.5%) of whom were girls, and 29 (50.0%) adults, 13 (22.4%) of whom were women. The diagnosis of

G12.8 was assigned to 6 adult patients: 3 (5.2%) women and 3 (5%) men, with mean age 59.3 [37.3, 62.1] years. Two women, aged 40 and 52 years, were diagnosed with G12.9, "Unspecified spinal muscular atrophy."

According to the general and neurological examinations, all patients included in the study were clinically stable, in a satisfactory condition, and not on mechanical ventilation. Data on motor impairments were obtained from the results of neurological examinations recorded in all medical records. Motor impairments ranged from mildly expressed proximal lower paraparesis (n=13, 22.4%) to severely pronounced tetraparesis (n=7, 12.1%) (Table). Assessment of the mental status primarily involved evaluating the level of consciousness and rapport using the clinical-psychopathological method, without the use of neuropsychological tests. All patients were responsive, and could understand and accurately follow instruc-

Socio-demographic, clinical and laboratory characteristics of the study sample of patients with SMA, depending on the nosological category

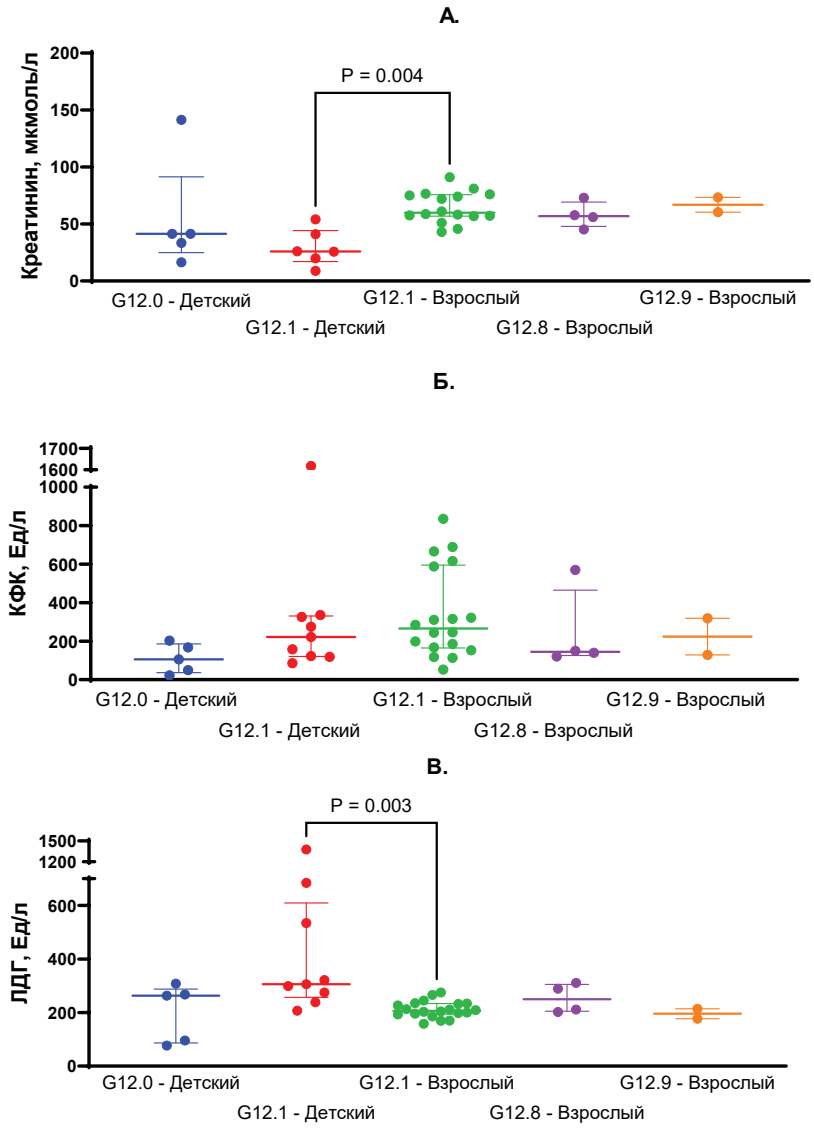
Diagnostic categories according to ICD-10	G12.0	G12.1		G12.8	G12.9	Всего		Статистика
Age Group Gender	Children	Children	Adults	Adults	Adults	Children	Adults	
Socio-demographic indicators of the sample Sample size, n (%)								
W:	5 (8.6%)	9 (15.5%)	13 (22.4%)	3 (5.2%)	2 (3.4%)	14 (24.1%)	18 (31.0%)	χ2=4,163, df=4, p=0.384, for gender distribution between groups
M:	2 (3.4%)	4 (6.9%)	16 (27.6%)	3 (5.2%)	0	6 (10.4%)	19 (32.8%)	
Total:	7 (12.1%)	14 (24.1%)	29 (50.0%)	6 (10.4%)	2 (3.4%)	21 (36.2%)	37 (63.8%)	
Age - Median (Interquartile interval), years								
W:	7.7 (4.2)	13.2 (7.8)	50.8 (19.69)	63.6 (16.3)	45.8 (6.2)	11.8 (7.7)	51.4 (22.9)	KW=40.125, df=4, p<0.001 to compare the age between groups
M:	10.2 (3.7)	12.7 (8.7)	47.1 (30.0)	55.0 (8.9)		12.7 (8.0)	48.6 (28.5)	
Total:	7.7 (5.8)	12.9 (8.3)	49.1 (24.8)	59.3 (15.5)	45.8 (6.2)	12.3 (7.4)	50.8 (24.1)	
Assessment of motor functions during neurological examination, graduation taking into account the sum of the scores of the four limbs								
W:	6.3	14.3	13.4	12	15.3	11.5	13.4	KW=14.196, df=4, p=0.007 to compare the amount of points between groups
M:	2	11.8	13.2	16.7		9	13.7	
Total:	5.1	13.4	13.3	14.3	15.3	10.6	13.6	
Bulbar syndrome								
W:	1 (1.7%)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.7%)	0 (0)	χ2=5,418, df=4, p=0.247 to distribute cases of bulbar syndrome between groups
M:	1 (1.7%)	0 (0)	2 (3.4%)	0 (0)	0 (0)	1 (1.7%)	2 (3.4%)	
Total:	2 (3.4%)	0 (0)	2 (3.4%)	0 (0)	0 (0)	2 (3.4%)	2 (3.4%)	
Laboratory and instrumental indicators								
Creatinine is the Median (Interquartile gap), mmol/l								
W:	41.4 (54.0)	25.9 (5.4)	74.1 (15.1)	65.4 (7.6)	66.9 (6.5)	33.4 (18.6)	73.1 (14.6)	KW= 15.0324, df=4, p=0.005 to compare creatinine between groups
M:	28.9 (12.5)	31.4 (22.6)	57.9 (6.1)	50.6 (5.3)		28.9 (30.0)	57.4 (7.4)	
Total:	41.4 (8.0)	25.9 (15.9)	61 (18.9)	56.9 (8.3)	66.9 (6.5)	33.4 (18.5)	60.4 (17.5)	
KFC - Median (Interquartile interval), Units/l								
W:	168.0 (48.4)	190.0 (129.9)	222.5 (157.7)	345.3 (224.4)	224.05 (94.9)	168.0 (138.7)	222.5 (189.7)	KW=6. 460, df=4, p=0.167 to compare CFCs between groups
M:	36.4 (13.5)	972.0 (3341.5)	303.6 (453.5)	144.4 (5.0)		206.0 (1236.2)	264.6 (390.7)	
Total:	106.1 (118.1)	248.4 (201.7)	265.6 (349.3)	144.4 (119.8)	224.0 (94.9)	168.0 (188.2)	245.0 (236.9)	
LDH is the Median (Interquartile interval), Units/l								
W:	267.5 (22.5)	287.0 (56.2)	211.0 (39.4)	299.7 (10.8)	195.5 (18.5)	275.0 (44.4)	214.0 (70.4)	KW= 14.2622, df=4, p=0.006 to compare LDH between groups
M:	86.2 (9.2)	684.1 (421.0)	204.0 (26.9)	206.7 (4.2)		534.0 (588.7)	204.0 (15.3)	
Total:	263.0 (172.1)	305.7 (259.0)	206.5 (37.7)	250.0 (85.5)	195.5 (18.5)	287 (72.9)	210 (37.4)	

tions, within the constraints of their motor capabilities. Some pediatric patients showed emotional lability (n=6, 10.3%), fatigue (n=10, 17.2%), and tearfulness (n=3, 5.2%).

During their examinations, all patients underwent a biochemical blood analysis to measure creatinine, CK, and LDH levels (Table). Diagnosis confirmation through molecular-genetic testing conducted by the laboratories of the Federal State Budgetary Scientific Institution "Medico-Genetic Scientific Center named after Academician N.P. Bochkov," was performed on 10 children and 2 adult patients at the time of data collection. EMG was performed on all patients with limb muscles using surface or needle electrodes. Specific electromyographic changes characteristic of SMA were detected in all patients, but quantitative descriptions of these changes were often lacking, which hindered establishing correlations between the EMG findings and other clinical results. The research results are presented in Table. There were no statistically significant differences in creatinine and CK medians between the G12.0, G12.1, G12.8, and G12.9 groups, nor were there any significant associations with motor impairments (Figure). However, we did detect subgroup differences in LDH levels between the G12.1 Children and G12.1 Adult subgroups: G12.1 Children VS G12.1 Adult (median [1 and 3 quartiles]): 305.7 [275.0, 534.0] VS 206.5 [195.0, 233.0], mean rank difference = 16.84, Dunn's p=0.003.

Analysis of archival medical records of patients (n=4, 6.9%) with repeated hospitalizations showed highest CK levels (up to 9000 U/L) in patients of the G12.1 group at clinical onset, followed by a decline in subsequent 3-17 months, depending on the records date. Individual data from cases with repeat hospitalizations also indicated increased CK levels in patients of the G12.0 and G12.1 groups upon initiating disease-modifying therapy with nusinersen or risdiplam. Archival data did not reveal significant correlations between CK levels, disease stage, and the age at start of therapy.

Discussion. The total number of patient records is greater than the number of persons due to inclusion of elderly patients with a milder course of the disease, who had been regularly hospitalized for the 14 years of record collection. Statistical analysis of laboratory test results and neurological examination data obtained from 112 archival medical records of 58 SMA patients diagnosed with G12.0, G12.1, G12.8, and G12.9 codes did not show any associations between creatinine and CK levels with diagnostic categories. Numerically higher CK levels in the G12.1, G12.8, and G12.9 groups compared to the G12.0 group were not statistically significant and were more likely related to age, weight, gender, and the level of physical activity of the patients. These factors were also likely to have been associated with the corresponding group differences in LDH levels. Due to limited sample size and heterogeneity of the data, results for patients with repeat hospitalizations did not support strong conclusions about time-dependent individual changes biomarker levels. Similarly, the collected data on the patients' mental status was insufficient to identify group differences or establish associations with biomarker levels; emotional lability, fatigue, and tearfulness are not specific symptoms.



Levels of creatinine (А), CPK (Б) and LDH (В) in patients with diagnoses G12.0, G12.1, G12.8 and G12.9, taking age into account

Conclusions. Routine laboratory diagnostic methods for SMA, particularly the measurement of creatinine and CK levels, did not reveal differences between the ICD subgroups, nor any association with severity of motor impairments. Although serum LDH levels did show significant differences among the groups, these differences were likely related to body weight and age rather than disease progression and motor impairments. Therefore, we cannot draw strong conclusions regarding the effectiveness of assessing creatinine, CK, and LDH levels for evaluating and predicting the course of the disease. As such, we do not recommend these laboratory tests as part of current clinical practice. Further research is needed to identify possible correlations between baseline CK levels and clinical presentation dynamics, and response to

pathogenetic therapies such as nusinersen, onasemnogen abeparvovec, and risdiplam. Results also highlight the need for prospective investigations of the possible relationship between psychiatric impairments or symptoms, motor manifestations of SMA 5q, and the three widely accessible biomarker levels.

Limitations. The study included archival material from the main regional institution, therefore omitting data from SMA patients residing in the greater Samara Oblast who have not undergone diagnosis and treatment at our hospital. Additionally, the advanced age of some patients in the sample raises concerns about the accuracy of their diagnosis; genetic confirmation was only available in 12 subjects. The study is subject to the typical limitations of a retrospective design. The limited amount of data also does not allow for a comprehensive assessment of the dynamic changes in present blood biomarker levels in individual patients.

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Reference

1. Alves C, Zhang R, Johnstone AJ, Garner R, Nwe PH, Siranosian JJ & Swoboda KJ: Serum creatinine is a biomarker of progressive denervation in spinal muscular atrophy. Neurology 2020; 94(9): e921–e931. doi:10.1212/WNL.0000000000008762

2. Araujo AP, Araujo M, Swoboda KJ et al.: Vascular perfusion abnormalities in infants with spinal muscular atrophy. J Pediatr 2009;155(2):292–294. doi:10.1016/j.jpeds.2009.01.071

3. Feng Y, Ge X, Meng L, Scull J, Li J, Tian X et al.: The next generation of population-based spinal muscular atrophy carrier screening: comprehensive pan-ethnic SMN1 copy-number and sequence variant analysis by massively parallel sequencing. Genet Med 2017;19(11):936–944. doi:10.1038/gim.2016.215.

4. Freigang M, Wurster CD, Hagenacker T, Stolte B, Weiler M, Kamm C et al.: RNA Sequencing of patient-specific motor neurons differentiating from induced pluripotent stem cells resolves motor neuron disease-associated pathways. Cell Rep 2020;33(4):108302.

5. Gayduk AJ & Vlasov YaV: Spinal muscular atrophy in the Samara region: epidemiology, classification, prospects for medical care [In Russ.]. Zh Nevrol Psikhiatr Im S S Korsakova 2019;119(12):88-93. doi:10.17116/jnevro201911912188

6. Gayduk AJ, Cumming P, Chernikova VV, Vlasov YaV, Smirnova D: Comprehensive neuropsychiatric and laboratory-instrumental diagnostics for determining therapeutic management tactics in patients with spinal muscular atrophy: regional experience [In Russ.]. Russ Med Bio Bull I.P. Pavlov 2022;30(3):323–334. doi:10.17816/PAVLOVJ100672

7. Gayduk AJ, Vlasov YaV, Smirnova DA: Application of modern technologies in early diagnosis programs for orphan diseases in Russia and abroad [In Russ.]. Zh Nevrol Psikhiatr Im S S Korsakova 2022;122(6):30–39. doi:10.17116/jnevro202212206130

8. Hong JM, Zhao M, He J, Huang XJ, Zhao ZY, Chen WJ et al.: Genetic screening method for analyzing survival motor neuron copy number in spinal muscular atrophy by multiplex ligation-dependent probe amplification and droplet digital polymerase chain reaction. Chin Med J (Engl) 2020;133(20):2510–2511. doi:10.1097/CM9.0000000000001102.

9. Kariyawasam D, D'Silva A, Howells J, Herbert K, Geelan-Small P, Lin CS et al.: Motor unit changes in children with symptomatic spinal muscular atrophy treated with nusinersen. J Neurol Neurosurg Psychiatry 2020;92(1):78–85. Advance online publication.

10. Kimizu T, Ida S, Okamoto K et al.: Spinal Muscular Atrophy: Diagnosis, Incidence, and Newborn Screening in Japan. Int J Neonatal Screen 2021;7(3):45. doi:10.3390/ijns7030045

11. Kobayashi DT, Shi J, Stephen L, Ballard KL, Dewey R, Mapes J et al.: SMA-MAP: a plasma protein panel for spinal muscular atrophy. PloS one 2013; 8(4): e60113.

12. Kolb SJ, Coffey CS, Yankey JW, Krosschell K, Arnold WD, Rutkove SB et al.: Baseline results of the NeuroNEXT spinal muscular atrophy infant biomarker study. Ann Clin Transl Neurol 2016;3(2): 132–145. doi:10.1002/acn3.283

13. Lopez-Lopez D, Loucera C, Carmona R, Aquino V, Salgado J, Pasalodos S et al.: SMN1 copy-number and sequence variant analysis from next-generation sequencing data. Hum Mutat 2020;41(12):2073–2077. doi:10.1002/humu.24120.

14. Mercuri E, Finkel RS, Muntoni F, Wirth B, Montes J, Main M et al.: Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscul Disord 2018;28(2):103–115.

15. Mix L, Schreiber-Katz O, Wurster CD et al.: Executive function is inversely correlated with physical function: the cognitive profile of adult Spinal Muscular Atrophy (SMA). Orphanet J Rare Dis 2021;16(1):10. doi:10.1186/s13023-020-01661-9.

16. Nandedkar SD, Barkhaus PE, Stålberg EV.: Motor unit number index (MUNIX): principle, method, and findings in healthy subjects and in patients with motor neuron disease. Muscle & nerve 2010;42(5):798–807. doi:10.1002/mus.21824.

17. Querin G, Lenglet T, Debs R, Stojkovic T, Behin A, Salachas F et al.: The motor unit number index (MUNIX) profile of patients with adult spinal muscular atrophy. Clin Neurophysiol 2018;129(11), 2333–2340. doi:10.1016/j.clinph.2018.08.025

18. Rivière J.: Locomotion autonome et cognition spatiale: le paradoxe de l'amyotrophie spinale infantile [Self-produced locomotion and spatial cognition: a new light from spinal muscular atrophy]. Arch Pediatr 2007;14(3):279–284. doi:10.1016/j.arcped.2006.10.011.

19. Verhaart I, Robertson A, Wilson IJ et al.: Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy - a literature review. Orphanet J Rare Dis 2017;12(1):124.

20. Weng WC, Hsu YK, Chang FM, Lin CY, Hwu WL, Lee WT, Lee NC et al.: CMAP changes upon symptom onset and during treatment in spinal muscular atrophy patients: lessons learned from newborn screening. Genet Med 2021;23(2):415–420. doi:10.1038/s41436-020-00987-w

21. Yuan A, Rao MV, Veeranna & Nixon RA. Neurofilaments and Neurofilament Proteins in Health and Disease. Cold Spring Harb Perspect Biol 2017;9(4):a018309.

22. Zappa G, LoMauro A, Baranello G, Cavallo E, Corti P, Mastella C, Costantino MA: Intellectual abilities, language comprehension, speech, and motor function in children with spinal muscular atrophy type 1. Neurodev Disord 2021;13(1):9. doi:10.1186/s11689-021-09355-4

23. Zhang Y, Huang JJ, Wang ZQ, Wang N, Wu ZY.: Value of muscle enzyme measurement in evaluating different neuromuscular diseases. Clin Chim Acta 2012;413(3-4):520-4.