Informativeness of structural and biochemical changes in the muscle tissue of myocardium in the early postmortem period

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A – research concept and design, B – data collection, C – data analysis and interpretation, D – article writing, E – critical review of the article, F – final approval of the article

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Postmortem structural and biochemical changes in the muscle tissue (MT) of myocardium from the positions of forensic examinations (FE) of the prescription of death coming (PDC) were not studied systematically, this fact determining the purpose of the present research.
The aim *of the research consisted in study of structural and biochemical changes in the tissue of myocardium during the early postmortem period (PMP).*
Material and methods. *The muscle tissue of myocardium within the early PMP (3-13 hours) after the coming of death was studied on 30 human corpses. Six BCM in myocardium muscle homogenates (MMH) were determined: BCM_1 – the content of glycogen, BCM_2 – the content of acid phosphatase, BCM_3 – the content of lactate, BCM_4 – the content of lactate dehydrogenase (LDH), BCM_5 – the content of lipofuscin, BCM_6 – the content of cholinesterase. MT was taken with use of special instruments, MT homogenates were prepared following the standard technique. Cytological studies of MT preparations of myocardium as well as their photographic recording were made on an Axiostar microscope (Zeiss, FRG). The optic density (OD) of nuclei and cytoplasm of cardiomyocytes (CMC) in conventional units of OD was measured using VideoTest program (Russia).*
Results. *It was found out that changes in MT of myocardium during the early PMP were characterized by the morphological, biochemical and biophysical regularities that we revealed; their most demonstrative features were as follows: – a gradual and constant reduction of the relative OD of CMC nuclei (Y_{M-7}) and cytoplasm (Y_{M-8}) during 3-13 hours from the moment of death, the rate and stage of these dynamics depending nonlinearly upon PDC; we substantiated and received quantitative regularities (polynomials) for the above biophysical indicators.*
Conclusions. *A comparative morphological study of the ultrastructure of CMC at the early PMP depending upon PDC was performed; - the early PMP is characterized by proper biochemical changes in MT, the most demonstrative of them are as follows: a reduction in the content of glycogen (Y_{M-1})and a dynamic increase in the content of lipofuscin(Y_{M-5}).For all six BCM, representative absolute and relative values of their content in MMH depending upon PDC were obtained; - paired correlative values between biochemical and biophysical markers of the state of MT of myocardium were examined in their systemic relationships and proper SCC were determined by six time intervals of the early PMP, thereby making it possible to substantiate those of them that were criterially significant for increasing the accuracy of diagnosis of PDC.*

Key words: *myocardium, muscle tissue, biochemical changes, early postmortem period*

Informatywność zmian strukturalnych i biochemicznych w tkance mięśniowej mięśnia sercowego we wczesnym okresie pośmiertnym

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Pośmiertne zmiany strukturalne i biochemiczne w tkance mięśniowej (MT) mięśnia sercowego w zakresie badań kryminalistycznych (FE) we wczesnym okresie pośmiertnym (PDC) nie były systematycznie badane, co spowodowało zasadnośc dla podjęcia badań.
Celem *badań było zbadanie zmian strukturalnych i biochemicznych w tkance mięśnia sercowego we wczesnym okresie pośmiertnym (PMP).*
Materiał i metody*. Tkankę mięśniową mięśnia sercowego we wczesnym okresie PMP (3-13 godzin) po nadejściu śmierci badano na 30 zwłokach ludzkich. W homogenatach mięśnia sercowego (MMH) oznaczono sześć BCM: BCM1 – zawartość glikogenu, BCM2 – zawartość kwaśnej fosfatazy, BCM3 – zawartość mleczanu, BCM4 – zawartość dehydrogenazy mleczanowej (LDH), BCM5 – zawartość lipofuscyna, BCM6 – zawartość cholinesterazy. MT pobrano za pomocą specjalnych narzędzi, a homogenaty MT przygotowano standardową techniką. Badania cytologiczne preparatów MT mięśnia sercowego oraz ich fotograficzną rejestrację wykonano na mikroskopie Axiostar (Zeiss, RFN). Gęstość optyczną (OD) jąder i cytoplazmy kardiomiocytów (CMC) w konwencjonalnych jednostkach OD mierzono za pomocą programu VideoTest (Rosja).*
Wyniki. *Stwierdzono, że zmiany w MT mięśnia sercowego we wczesnym okresie PMP charakteryzowały się ujawnionymi przez nas prawidłowościami morfologicznymi, biochemicznymi i biofizycznymi; ich najbardziej charakterystycznymi cechami były: – stopniowe i stałe zmniejszanie względnej OD jąder CMC (Y_{M-7}) i cytoplazmy (Y_{M-8}) w ciągu 3-13 godzin od momentu śmierci, częstość i stopień zaawansowania tych dynamika zależna nieliniowo od PDC; uzasadniliśmy i otrzymaliśmy prawidłowości ilościowe (wielomiany) dla powyższych wskaźników biofizycznych.*
Wnioski. *Przeprowadzone porównawcze badanie morfologiczne ultrastruktury CMC we wczesnym PMP w zależności od PDC wykazało, że; - wczesne PMP charakteryzuje się prawidłowymi zmianami biochemicznymi w MT, najbardziej typowymi są: zmniejszenie zawartości glikogenu (Y_{M-1}) oraz dynamiczne zwiększenie zawartości lipofuscyny (Y_{M-5}); uzyskano wszystkie sześć BCM, reprezentatywne bezwzględne i względne wartości ich zawartości w MMH w zależności od PDC; - zbadano sparowane wartości korelacyjne między markerami biochemicznymi i biofizycznymi stanu MT mięśnia sercowego w ich zależnościach ogólnoustrojowych, a prawidłowy SCC wyznaczono przez sześć przedziałów czasowych wczesnego PMP, co pozwoliło uzasadnić te z nich, które były istotnym kryterium dla zwiększenia dokładności rozpoznania PDC.*

Słowa kluczowe*: mięsień sercowy, tkanka mięśniowa, zmiany biochemiczne, wczesny okres pośmiertny*

At the present stage in the development of forensic medicine scientists have suggested different differential-diagnostic criteria for determining the prescription of death coming (PDC), which give positive results and help in coping with a number of problems that have not been solved yet. But the overwhelming majority of the suggested modern methods of investigation cause difficulties in their introduction into everyday practice, most frequently due to problems with material and technical support for forensic examinations (FE) [1,8].The modern practice and tactics of forensic diagnosis require scientific substantiation of informative diagnostic criteria for assessing PDC, first of all within the early postmortem period (PMP). The above substantiationis caused by a need for an increased accuracy and can be realized by means of objectification of structural and biochemical changes in different organs and tissues of the human organism [7,9,12,14,18,21,24,25]. In particular, the interest of scientists and practitioners in FE is attracted by structural and biochemical changes in the muscle tissue (MT) of different morphological types [3-6,8,15,16,23]. The known methods for diagnosing PDC are based on registration of the existing postmortem rigidity of the body, appearance of cadaveric lividity and some other diagnostic signs [10,11,13]. Nevertheless the use of the above criteria for diagnosing PDC in the majority of cases is not able to form forensic conclusions about PDC with a high reliability and accuracy. At the same time, time-dependent regularities in changes of biochemical (BCM) and biophysical markers (BPM) of the state of MT within the first hours after the coming of death remain insufficiently studied [19].

Postmortem structural and biochemical changes in MT of myocardium from the positions of FE of PDC were not studied systematically, this fact determining the purpose of the present research.

The purpose of the research consisted in study of structural and biochemical changes in the tissue of myocardium during the early PMP.

MATERIALS AND METHODS

The muscle tissue (MT) of myocardium within the early PMP (3-13 hours) after the coming of death was studied on 30 human corpses. Six BCM in myocardium muscle homogenates (MMH) were determined: BCM_1 – the content of glycogen, BCM_2 – the content of acid phosphatase, BCM_3 – the content of lactate, BCM_4 – the content of lactate dehydrogenase (LDH), BCM_5 – the content of lipofuscin, BCM_6 – the content of cholinesterase. MT was taken with use of special instruments, MT homogenates were prepared following the standard technique [8] with subsequent determination of BCM content in MT homogenates by the kinetic method using for this purpose such test systems as SpineLab (Ukraine), DAC-SpeńtroMed and VitalDevelopment (Russia) on a biochemical analyzer Labline-80 (Austria); the content of lipofuscin was determined according to I.A. Volchegorsky's procedure.

Cytological studies of MT preparations of myocardium as well as their photographic recording were made on an Axiostar microscope (Zeiss, FRG). The optic density (OD) of nuclei and cytoplasm of cardiomyocytes (CMC) in conventional units of OD was measured using VideoTest program (Russia). Results of the research were statistically analyzed with help of variation statistics and assessment of normality of distribution and reliability of findings [2,17,20].

The studies were conducted following the basic regulations of *Ethical Principles for Medical Research Involving Human Subjects* approved by the Declaration of Helsinki(1964-2013), ICH GCP (1996), EEU Directive No. 609 (dated November 24, 1986), Orders of the Ministry of Health of Ukraine No. 690 (dated September 23, 2009), No. 944 (dated December 14, 2009) and No. 616 (dated August 03, 2012).

RESULTS AND DISCUSSION

The level of glycogen content in MMH during the analyzed time intervals significantly ranged: from (2.192±0.019) mg/g in 3 hours after death coning to (0.759±0.010) mg/g in 13 hours after the coming of death, reliably ($p<0.001$) differing in different time intervals of the early PMP. It should be noted that the variation coefficient of the absolute content of glycogen during the early PMP in all time intervals ranged within 4.7÷8.4%, this fact being characterized as a low level of variation of a sign (below 10%). For example (tab. 1), as early as in 5 hours after death coming there was a reliable ($p<0.01$) decrease of glycogen content in MMH down to (1.861±0.017) mg/g, in 7 hours it decreased reliably ($p<0.01$) again down to (1.498±0.023) mg/g. During subsequent time intervals a further reduction of the absolute content of glycogen in MMH was registered too: in 9 hours down to (1.413±0.020) mg/g, in 11 hours down to (1.136±0.017) mg/g, and in 13 hours down to (0,759±0,010) mg/g.

The level of content of acid phosphatase in MMH during the analyzed time intervals ranged significantly: from (3.134±0.046) U/g in 3 hours after the coming of death to (2.757±0.025) U/g in 13 hours after death coming, reliably ($p<0.001$) differing during different time intervals of the early PMP. It should be noted that the variation of the absolute value in the content of acid phosphatase was characterized by its increase in time intervals of 5-9 hours. For example (tab. 1), as early as in 5 hours after death coming there was a reliable ($p<0.01$) increase of its content up to (3.475±0.057) U/g, in 7 hours it rose reliably ($p<0.01$) again up to (3.758±0.041) U/g and after that decreased down to (3.616±0.037) U/g.

A similar regularity characterized changes of the absolute content of lactate in MMH: fluctuations from (6.343±0.050) mmol/g in 3 hours after the coming of death to (4.850±0.054) mmol/g in 13 hours after death coming, reliably ($p<0.001$) differing during different time intervals of the early PMP.

The content of LDH in MMH during the analyzed time intervals significantly ranged from (434.8±4.2) U/g in 3 hours after death coming to (254.8±4.2) U/g in 13 hours after the coming of death,

Table 1. Levels in the content of biochemical markers of the state of the muscle tissue in myocardium during the early postmortem period depending upon the prescription of death coming
Tabela 1. Poziomy zawartości markerów biochemicznych stanu tkanki mięśniowej mięśnia sercowego we wczesnym okresie pośmiertnym w zależności od chwili zgonu

Content of biochemical indicators	Postmortem time intervals (hours)					
	3	5	7	9	11	13
BCM_1 – glycogen, mg/g	2.192±0.019	1.861±0.017[a]	1.498±0.023[a,b]	1.413±0.020[a,b]	1.136±0.017[a,b]	0.759±0.010[a,b]
BCM_2 – acidphosphatase, U/g	3.134±0.046	3.475±0.057[a]	3.758±0.041[a,b]	3.616±0.037[a,b]	2.865±0.024[a,b]	2.757±0.025[a,b]
BCM_3 – lactate, mmol/g	6.343±0.050	7.161±0.044[a]	7.865±0.043[a,b]	7.217±0.039[a,b]	5.653±0.043[a,b]	4.850±0.054[a,b]
BCM_4 – lactate dehydrogenase, U/g	434.8±4.2	357.9±3.6[a]	341.3±3.1[a,b]	293.0±2.2[a,b]	276.9±2.0[a,b]	254.7±1.8[a,b]
BCM_5 – lipofuscin, U/g	2.564±0.042	3.423±0.022[a]	3.707±0.027[a,b]	4.147±0.036[a,b]	4.401±0.038[a,b]	5.026±0.038[a,b]
BCM_6 – cholinesterase, U/g	1213.8±8.8	766.3±79.8[a]	947.2±7.0[a,b]	862.0±5.8[a,b]	848.5±5.7[a,b]	834.4±5.4[b]

Note: [a] – reliable differences from the previous interval at the level of $p<0.05$; [b] – reliable differences from the first time interval at the level of $p<0.01$

reliably (p<0.001) differing in different time intervals of the early PMP. It should be noted that the fluctuation of the absolute value in the content of LDH by time intervals was characterized by its continuous decrease (tab. 1): as early as in 5 hours after death coming down to (357.9±3.6) U/g, in 7 hours it reliably (p<0.01) decreased again down to (341.3±3.1) U/g and sharply decreased down to (276.9±2.0) U/g in 11 hours after the coming of death.

The level of lipofuscin content in MMH during the analyzed time intervals changed significantly too: from (2.564±0.042) U/g

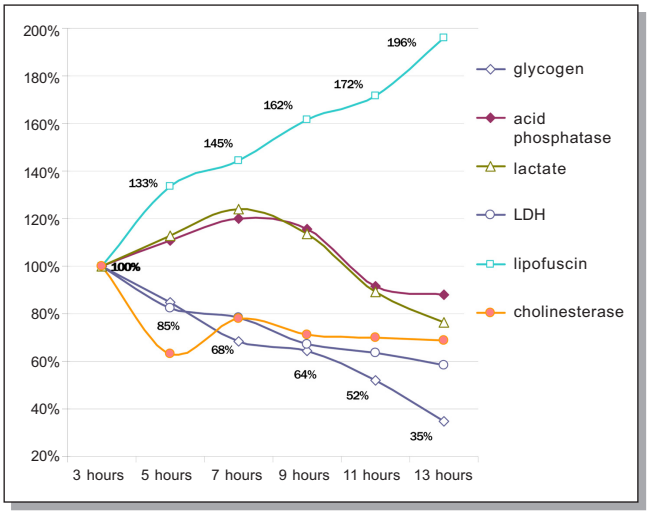

Figure 1. Dynamics in the content of biochemical markers of the state of the muscle tissue in myocardium during the early postmortem period depending upon the prescription of death coming (standardized values)
Rycina 1. Dynamika zawartości markerów biochemicznych stanu tkanki mięśniowej mięśnia sercowego we wczesnym okresie pośmiertnym w zależności od wskazania daty zgonu (wartości standaryzowane)

regularities of biochemical changes in MMH during the early PMP depending upon PDC.

Cytological studies made it possible to reveal qualitative regularities, namely the well preserved transverse and longitudinal streakiness of CMC in 3 hours after the coming of death, an increase in heterochromacity of CMC nuclei within the time intervals of 3-7-9 hours after death coming with manifestations of nuclear chromatolysis at later terms as well as profound lytic processes in the cytoplasm with CMC fragmentation, appearance of granules and "empty" areas. But the above regularities are rather subjective, this fact necessitating biophysical quantitative assessment of the nuclei and cytoplasm. Our cytophotometric study made it possible to objectify changes in CMC (tab. 2) by measuring their OD, determining quantitative regularities (fig. 2) as well as the diagnostic informative value (I, bit) of these indices depending upon PDC.

As it can be concluded from our findings, a change (p<0.01) in OD of CMC nuclei was registered after the 7th hour from the moment of death coming, when it decreased more than by 10% versus the 5th hour from the moment of death, that is from(108.0±1.3) Uto (99.3±0.6) U.A similar regularity characterized changes (p<0.01) in OD of CMC cytoplasm: its change was registered only slightly earlier, by the 5th hour after the coming of death, from (129.7±2.2) Uto (134.9±1.5) U.

Taking into consideration the revealed changes of OD in CMC nuclei and cytoplasm that were nonlinear in time, we found out statistical regularities of these processes, which are presented in the form of polynomials (fig. 2). Indeed, pursuing the aim of substantiation of the criterial significance for certain morphological, biochemical and biophysical markers of changes in MT of myocardium during the early PMP and taking into consideration the consistency of postmortem myocardial changes, we studied correlative relationships between diagnostic signs (markers of changes) and determined the most diagnostically valuable of them (tab. 3). For example, the most significant indices for diagnosis of PDC during the early PMP by the

Table 2. Biophysical markers and quantitative-analytical regularities in changes of optic density of nuclei and cytoplasm of cardiomyocytes during the early postmortem period depending upon the prescription of death coming
Tabela 2. Markery biofizyczne i prawidłowości ilościowo-analityczne w zmianach gęstości optycznej jąder i cytoplazmy kardiomiocytów we wczesnym okresie pośmiertnym w zależności od daty zgonu

Morphological indicators		Postmortem time intervals (hours)					
		3	5	7	9	11	13
Optic density of nuclei (BPM_7)	OD, U	107.1±1.7	108.0±1.3	99.3±0.6 ^{f}	99.3±1.5	93.4±0.8	93.8±0.9
	I, bits	0.360	0.381	0.413	0.361	0.454	0.417
Optic density of cytoplasm (BPM_8)	OD, U	129.7±2.2	134.9±1.5 ^{a}	125.3±1.4 ^{a}	121.4±3.0	126.8±1.0	125.3±0.9
	I, bits	0.207	0.208	0.256	0.202	0.276	0.200

Note: ^{a} – reliable differences from the previous interval at the level of p<0.05

in 3 hours after death coming to (5.026±0.038) U/g in 13 hours after the coming of death, reliably (p<0.001) differing in different time intervals of the early PMP. It should be noted that the variation coefficient of lipofuscin content in MMH by all time intervals was within 10.0%, it characterizing a low level of variation of a sign.

The level of cholinesterase content in MMH ranged from (1213.8±8.8) U/g in 3 hours after death coming to (834.4±5.4) U/g in 13 hours after the coming of death, reliably (p<0.001) differing in different time intervals of the early PMP, and was characterized by a low variation level.

Our analysis of standardized values of BCM (fig. 1) revealed that the dynamics of changes in the content of glycogen and lipofuscin in MMH were the most significant. For example, dynamic changes in the level of these BCM were registered during all time intervals: in 5 hours by 48.0% (an increase in the level of lipofuscin by 33.0% with a simultaneous decrease in the level of glycogen by 15.0%), in 7 hours by 77.0%, in 9 hours by 98.0%, in 11 hours by 120.0%, and in 13 hours by 161.0%. It is these two BCM that most manifestly demonstrate

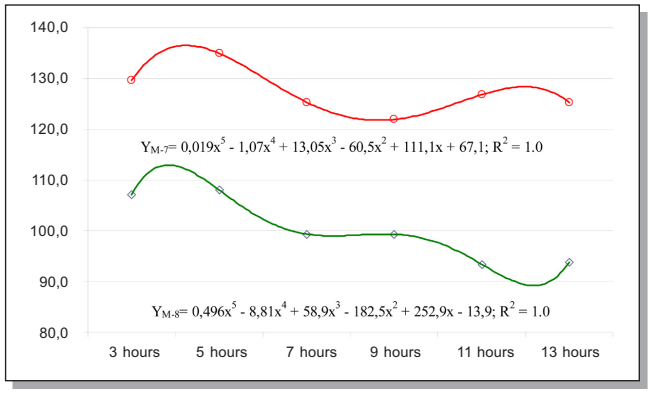

Figure 2. The dynamics of changes in the optic density of nuclei (Y_{M-7}) and cytoplasm (Y_{M-8}) of cardiomyocytes during the early postmortem period depending upon the prescription of death coming
Rycina 2. Dynamika zmian gęstości optycznej jąder (Y_{M-7}) i cytoplazmy (Y_{M-8}) kardiomiocytów we wczesnym okresie pośmiertnym w zależności od daty zgonu

Table 3. Correlative relationships between biochemical and biophysical markers of the state of the muscle tissue of myocardium during the early postmortem period
Tabela 3. Zaleznosci korelacyjne miedzy biochemicznymi i biofizycznymi markerami stanu tkanki miesniowej miesnia sercowego we wczesnym okresie posmiertnym

Markers	BCM_1	BCM_2	BCM_3	BCM_4	BCM_5	BCM_6	BPM_7	BPM_8
BCM_1		0.454	0.561	0.958	-0.986	0.596	0.931	0.570
BCM_2	0.454		0.981	0.326	-0.402	-0.017	0.460	-0.041
BCM_3	0.561	0.981		0.435	-0.518	0.057	0.526	0.071
BCM_4	0.958	0.326	0.435		-0.986	0.747	0.874	0.550
BCM_5	-0.986	-0.402	-0.518	-0.986		-0.698	-0.883	0.534
BCM_6	0.596	-0.017	0.057	0.747	-0.698		0.380	-0.004
BPM_7	0.931	0.460	0.526	0.874	-0.883	0.380		0.698
BPM_8	0.570	-0.041	0.071	0.550	-0.534	-0.004	0.698	
SCC	0.722±0.076	0.371±0.092	0.431±0.093	0.653±0.082	0.670±0.070	0.317±0.110	0.637±0.069	0.138±0.122
p	1.5	5.5	5.5	1.5	1.5	5.5	1.5	8

Notes: BCM_1 – the content of glycogen, BCM_2 – the content of acid phosphatase, BCM_3 – the content of lactate, BCM_4 – the content of lactate dehydrogenase, BCM_5 – the content of lipofuscin, BCM_6 – the content of cholinesterase, BPM_7 – relative optic density of cardiomyocyte nuclei, BPM_8– relative back ground optic density of cardiomyocyte cytoplasm, SCC – system-creating coefficient; p –rank of a diagnostic sign

system-creating coefficient (SCC) were as follows: BCM_1 – the content of glycogen, BCM_4 – the content of LDH, BCM_5 – the content of lipofuscin and BPM_7– relative back ground OD of CMC nuclei.

It should be noted that these four markers of the process of postmortem changes in the myocardium (three characterize biochemical changes, and one is for biophysical changes in CMC nuclei) are actually equally able to be criteria for assessing PDC.

CONCLUSIONS

It was found out that changes in MT of myocardium during the early PMP were characterized by the morphological, biochemical and biophysical regularities that we revealed; their most demonstrative features were as follows:

– a gradual and constant reduction of the relative OD of CMC nuclei (Y_{M-7}) and cytoplasm (Y_{M-8}) during 3-13 hours from the moment of death, the rate and stage of these dynamics depending nonlinearly upon PDC; we substantiated and received quantitative regularities (polynomials) for the above biophysical indicators. A comparative morphological study of the ultrastructure of CMC at the early PMP depending upon PDC was performed;
– the early PMP is characterized by proper biochemical changes in MT, the most demonstrative of them are as follows: a reduction in the content of glycogen (Y_{M-1})and a dynamic increase in the content of lipofuscin(Y_{M-5}).For all six BCM, representative absolute and relative values of their content in MMH depending upon PDC were obtained;
– paired correlative values between biochemical and biophysical markers of the state of MT of myocardium were examined in their systemic relationships and proper SCC were determined by six time intervals of the early PMP, thereby making it possible to substantiate those of them that were criterially significant for increasing the accuracy of diagnosis of PDC.

Prospects of further researches should be aimed to study the postmortem dynamics of BCMfor the structural and biochemical state of MT of other morphofunctional types (of the oesophagus, diaphragm, intercostal muscles) in order to scientifically provide accuracy in diagnosing terms of PDC in the practice of FE.

REFERENCES

1. Bachinsky VT. Advanced diagnostic capabilities of the previous prescription of death (problems and prospects). Materials of scientific conference “Achievement in the galuse of marine medicine and problem nutrition during medical and medical examinations at the forensic examination and at the forensic examination of corpses”, Lviv, 2016; 302-304.
2. Bashynska I, Kovalova O, Malovichko O. et al. Risk Management of Innovative Socially Significant Projects. Inter J Advan Res Engineer Technol. 2020; 11(4): 294-305.
3. Cherkashyna L, Konoval N, Shklyar A, et al. Study of structural and biochemical changes in the muscular tissue of the oesophagus for solving the problem of diagnosing the prescription of death coming. Pol Merkur Lekarski. 2020; 48 (283): 42-44.
4. Cherkashyna L, Konoval N, Shklyar A, et al. The dynamics of changes in biochemical markers of the state of tissue in intercostal muscles during the early postmortem period. Pol Merkur Lekarski. 2020; 48 (283): 45-48.
5. Cherkashyna L, Reminetskyy B, Miz A, et al. The content of lactate in muscle tissue of different types in the early post-mortal period. Pol Merkur Lekarski. 2021; 49(290): 129-132.
6. Cherkashyna L, Shklyar A, Demikhova N, et al. Lipofuscin content in the muscle tissue during the early postmortem period: improvement of forensic diagnosis of the prescription of death coming. Pol Merkur Lekarski. 2020; 48 (284): 35-39.
7. Demikhov O., Dehtyarova I., Demikhova N. Actual aspects of public health policy formation on the example of Ukraine. Bangladesh Journal of Medical Science. 2020; 19 (3); 358-366. https://doi.org/10.3329/bjms.v19i3.45850
8. Garazdyuk MS, Bachynsky VT, Vanchulyak OY, et al. Determining the prescription of death by two-dimensional mapping of polarization-heterogeneous images of polycrystalline liquor films. Clin Exp Pathol, 2016; 15 (1): 36-42.
9. Gaiseniuk F, Driianskaia V, Drannik G, et al. Proinflammatory cytokines in patients with pyelonephritis Lik Sprava, 2013; 6: 32-37.
10. Gladkikh DB. Forensic diagnostics of the prescription of the onset of death by the supravital reaction of the pupils. Abstract of the PhD dissertation, Kyiv, 2016;19.
11. Gurov OM, Kozachenko IM, Kutsenko SV, et al. Determining the prescription of the onset of death in the early post-mortem period by the supravital reaction of the pupils to the action of pilocarpine. Criminal Foren Med.: An Interagency Scientific and Methodological Collection.2014; 59: 443-451.
12. Krynytska I, Marushchak M. The indices of nitric oxide system in rats with carrageenan-induced enterocolitis combined with diabetes mellitus. Romanian J Diab Nutr Metab Dis. 2018; 25(3): 283-288.
13. Kuzovkov AV, Vavilov AY. Objectification of diagnostic algorithms for establishing the limitation of human death by the dynamics of tympanic temperature. Modern Probl Sci Educat. 2017; 2: 12.
14. Loboda A, Smiyan O, Popov S, et al. Child health care system in Ukraine Turk Pediatri Arsivi. 2020, 55: S98-S104.
15. Marushchak M, Krynytska I, Mikolenko A, et al. Chronic heart failure causes osteopathy or is osteopathy a factor in development of chronic heart failure? Asian J Pharmac Clin Res. 2018; 11(1): 111-115. https://doi.org/10.22159/ajpcr.2018.v11i1.17532
16. Marushchak M, Krynytska I, Milevska L, et al. The changes of activity of effector caspase cascade components in case of alimentary obesity in rats. Bangladesh J Med Sci. 2017; 16 (2): 252-258.
17. Moskalenko VM, Voronenko YV. Social Medicine and Health Organization: textbook, Ternopil, 2002; 50-75.
18. Olkhovsky VO, Golubovich LL. Determining the prescription of an onset of death: a monograph, Kharkiv: Brovin OV, 2017; 168-173.
19. Olkhovsky VO, Golubovich LL, Khizhnyak VV. Determining the duration of the post-mortem period in forensic expert practice: current state and prospects. Exp Clin Med. 2016; 4(73): 154-162.
20. Prokopenko O, Holmberg R, Omelyanenko V. Information and communication technologies support for the participation of universities in innovation networks (comparative study). Innovative Marketing. 2018; 14(3): 17-29.

21. Shkatula YV, Badion YA, Kasian SN, et al. Predictive capabilities of using the shock index and its modifications for assessing hemodynamic disorders in victims with traumatic injuries. Azerbaijan Med J. 2021; 1: 117-122.
22. Shkatula YV, Badion YO, Novikov MV. Efficiency of different methods of temporary external hemostasis at the pre-hospital stage of emergency medical care. Novosti Khirurgii. 2021; 28(6): 688-693. doi: 10.18484/2305-0047.2020.6.688
23. Sopel O, Krynytska I, Marushchak M, et al. Differential diagnosis of hepatopulmonary syndrome (HPS): Portopulmonary hypertension (PPH) and hereditary hemorrhagic telangiectasia (HHT). Bosnian J Basic Med Sci. 2017; 17(4): 276-285.
24. Teslyk T, Yarmolenko O, Bumeister V, et al. The remodeling of lungs under the influence of alloxan-induced hyperglycemia. Romanian J Diab Nutr Metab Dis. 2020; 27(1): 45-49. https://doi.org/10.46389/rjd-2020-1008
25. Yarmolenko O., Bumeister V, Demikhova N, et al. The effect of alloxan-induced hyperglicemia on myocardium of experimental animals. Romanian J Diab Nutr Metab Dis. 2020; 27(2): 80-84. https://doi.org/10.46389/rjd-2020-1014

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