Desmin expression in human cardiomyocytes and selected clinical and echocardiographic parameters in patients with chronic heart failure

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Abstract

Background: Desmin, one of the basic muscular-specific structural proteins, is believed to play an important role in the progression of heart failure (HF). The function of desmin in cardiomyocytes is still unclear. Mechanical, structural and regulatory functions are postulated. Regulatory function of desmin seems the most interesting. Desmin might be involved in the regulation of gene expression, myofibrillogenesis and intercellular signalling, and be responsible for shape and tension of the cell membrane and other organelles. Abnormal accumulation of desmin may disturb the function of myofibrils, lead to unusual tension of sarcolemma and atypical distribution of organelles (nucleus), and impair intra- and intercellular communication.

Aim: Evaluation of desmin expression in specimens derived from right ventricular myocardium during endomyocardial biopsy (EMB).

Methods: The study population consisted of 135 patients (86.7% males, mean age 49.4 ± 14.1 years) presenting with clinical symptoms of HF and LVEF < 45%. During EMB 3-4 samples were taken from the right ventricular myocardium. The immunohistochemical studies of the endomyocardial specimens included immunostaining with desmin-specific antibodies. The study population was divided into three groups: I – 48 patients with normal expression of desmin, II – 54 patients with increased expression and accumulation of desmin and III – 33 patients with low expression of desmin in cardiomyocytes.

Results: The LVEF was significantly higher in group I than in groups II and III. The LV diameter was significantly lower in group I than in groups II and III. Functional status according to NYHA class was the worst in group I compared to group II and III. These differences were statistically significant.

Conclusion: Evaluation of desmin distribution in specimens derived from the right ventricular myocardium may be useful as an objective tool in the assessment of left ventricle status.

Key words: heart failure, desmin, endomyocardial biopsy

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Introduction

Desmin, along with tubulin and actin, belongs to the basic cytoskeletal proteins and is the major muscle-specific, type III intermediate filament (IF) protein.

The function of desmin in cardiomyocytes is still unclear. Mechanical, structural and regulatory functions are postulated. Regulatory function of desmin seems the most interesting. Desmin might be involved in the regulation of gene expression, myofibrillogenesis and intercellular signalling [1-6], and be responsible for shape and tension of the cell membrane and other organelles [7, 8].

Desmin plays an essential role in maintaining muscle cytoarchitecture by forming a scaffold around the myofibrillar Z-disc and by connecting the sarcomeric contractile apparatus to the subsarcolemmal cytoskeleton, the nuclei and mitochondrium [9, 10]. It is particularly abundant in the intercalated disc, the attachment between cardiomyocytes in cardiac muscle. Desmin due to its localisation and interconnections may be considered a protein responsible for integrating contractile function of myofilaments [11].

Abnormal accumulation of desmin may disturb the function of myofibrils, lead to unusual tension of sarcolemma and atypical distribution of organelles

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(nucleus), and impair intra-and intercellular communication. It leads to the development of desmin related myopathy or cardiomyopathy (DRM). Characteristic features of DRM include the presence of intracellular desmin aggregates, frequently involving other proteins [12, 13]. Such aggregation may be a result of mutation in the desmin gene or alterations of other proteins' function.

Currently high and low expression of desmin in the cardiomyocytes are distinguished and according to published data the high expression form is more frequently found [14].

The main aim of this study was to assess the concentration of desmin in cardiomyocytes of patients with chronic heart failure (CHF). Additionally, the relationship between desmin distribution in cardiomyocytes and left ventricular (LV) size and ejection fraction (EF), as the most important parameters of cardiac function, was evaluated.

Methods

Patient characteristics

The study population consisted of 135 patients (mean age 49.4 ± 14.1 years; 86.7% males) presenting with CHF of unknown origin. To include a patient, a clinical diagnosis of CHF with LVEF below 45%, assessed by echocardiography (Sonos 75V), was required.

Following enrollment, endomyocardial biopsy (EMB) was performed using the femoral approach. In each patient 3-4 tissue samples from the free right ventricular (RV) wall, apical and interventricular septum of the RV were collected using a Cordis bioptome (7 F), under continuous ECG monitoring.

All patients underwent coronary angiography to exclude significant coronary artery disease (defined as lumen reduction exceeding 50%) and two-dimensional echocardiography, including measurements of LV end-diastolic diameter (LVEDD) and LVEF using the Simpson equation (from apical four and two chamber view). Echocardiography was performed before a patient's inclusion in the study. Mean LVEF was 31.4 ± 11.2% and LVEDD – 65.1 ± 10.8 mm.

Table I. Clinical characteristics of the whole cohort of patients

Clinical symptoms and concomitant diseases	Study population (n = 135)
Shortness of breath, n (%)	101 (74.8)
Ankle oedema, n (%)	73 (54.1)
Rales, n (%)	25 (18.5)
Chest pain, n (%)	43 (31.9)
Hypertension, n (%)	60 (44.4)
Hypercholesterolaemia, n (%)	40 (29.6)
Renal failure, n (%)	16 (11.9)
Diabetes mellitus, n (%)	21 (15.6)
Gastritis, n (%)	12 (8.9)
Anaemia (Hb < 12 mg/dl), n (%)	12 (8.9)

All patients were assigned to the New York Heart Association (NYHA) classes: I (42 patients; 31%), II (49; 36%), III (36; 27%), and IV (8; 6%). On admission, CHF signs and symptoms were also recorded, including the presence of rales on chest auscultation, ankle oedema, shortness of breath and chest pain. Additionally, concomitant diseases were evaluated (Table I).

Histological and immunohistological evaluation of specimens

The myocardial tissue samples were immediately fixed in 4% formaldehyde, buffered by PBS and embedded in paraffin. Serial sections (4-µm thick) were mounted on poly-L-lysine coated slides. Non-consecutive sections were stained with haematoxylin-eosin [15], Azan (azocarmine G) [16], Mason's method [17] and Mallory's method [18]. Mastocyte content of the tissue was identified with anti-human tryptase mouse monoclonal antibody (DAKO inc. M-7052).

Myocarditis was diagnosed based on morphological assessment of specimens according to Dallas criteria [19] and using immunohistochemical methods for identification of inflammatory cells – T lymphocytes, granulocytes, vascular endothelium and MHC II antigens [20]. Antibodies against CD3 (UCHL-1) (Rabbit antibody anti-human T cell CD3, DAKO, catalogue number A-0452; dilution 1 : 10) and CD45RO (Mouse monoclonal antibody anti-human T cell-Clone OPD4, DAKO, catalogue number M-0834; dilution 1 : 10) were applied to detect T lymphocytes. Antibodies against antigen DPQR (Mouse monoclonal antibody anti-human HLA – DQ, DP, DR Antigen, DAKO, catalogue number M-0775; dilution 1 : 25) identified expression of MHC class II antigens. Antibodies against CD15 (Mouse monoclonal antibody anti-human granulocyte-associated antigen CD15, DAKO, catalogue number M-0733; dilution 1 : 10) identified granulocytes. Inflammatory process on endothelium was identified with antibodies against CD34 (Mouse monoclonal antibody anti-human endothelium CD34, Novocastra, catalogue number NCL-END; dilution 1 : 25).

Dilated cardiomyopathy (DCM) was diagnosed when histological examination revealed the presence of myocytes of abnormal morphology or signs of increased local hypertrophy, local degenerative changes (mainly myocytolysis), abnormal myocyte distribution, including myocyte branching and stroma fibrosis or the presence of lymphocyte infiltration as well as endocardial fibrosis [21].

Vascular myocardial injury was diagnosed when there were thrombi in the coronary arteries, fibrosis of the interstitium, presence of numerous mastocytes (cells promoting fibrosis) or thickening or lumen closure of small vessels. The clinical profile of these patients did not reveal coronary artery disease as a cause of heart failure.

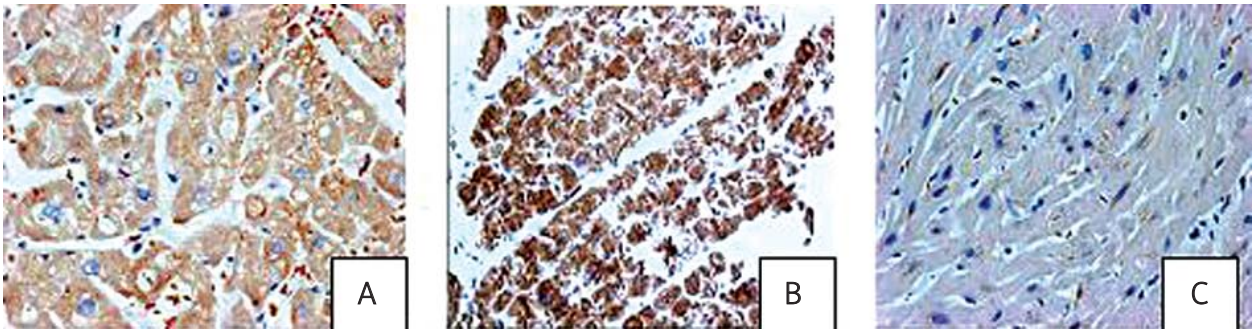

Figure 1. Immunohistochemistry desmin staining. Myocardial sample derived from a patient with heart failure. **A** – normal expression of desmin cardiomyocytes. **B** – accumulation of desmin in a cardiomyocyte firming aggregates. **C** – low expression of desmin in the cardiomyocytes. Magnification 200 ×

Identification and evaluation of desmin

The expression of desmin in myocardial biopsy samples was determined by immunohistochemical assay. This method was previously described elsewhere [22].

The antigen distribution and the immunostaining intensity of a minimum of three stained sections for each case were observed in light microscope (semi-quantitative method). Brown positive pellets were seen in cardiomyocytes of DCM. Desmin positive cell counts and presence of aggregates differed in samples derived from patients with DCM. Analysis of stained slides revealed a difference in the amount of desmin in cardiomyocytes. Three types of desmin presentation were distinguished: normal, high and low. Normal expression of desmin was defined as an even distribution of desmin on slides (not an intensive reaction) – Figure 1 A. High expression of desmin – irregular, more intensive accumulation of desmin on stained slides with formation of aggregates – Figure 1 B. Low expression of desmin was assigned when desmin was barely visible or invisible in cells – Figure 1 C. All samples were evaluated by two independent histopathologists.

Statistical analysis

The values are presented as mean ± standard deviation or numbers and percentages. Parametric data were compared using Student's t-test. Non-parametric data were compared using the χ^2 test (with Yates' correction when needed) or exact Fisher's test.

Multivariable Cox proportional hazards analysis was used to adjust for baseline differences between groups.

Values of $p < 0.05$ were considered significant. The STATISTICA 7.0 package was used.

Results

HE staining

HE stained myocardial tissues obtained from the DCM patients showed typical pathological changes for myocarditis (27% of all study population), vascular disease (35%) and idiopathic DCM (37%).

Immunohistochemical detection of desmin

Desmin expression in the whole cohort

Immunohistochemical staining of desmin revealed three forms of desmin expression in cardiomyocytes. Normal expression of desmin was observed in 36% of the whole study group, high expression in 40%, and low expression in 24%.

Expression of desmin in patients with myocarditis, vascular disease and idiopathic dilated cardiomyopathy

All three forms of intramyocyte desmin expression were found in myocarditis, vascular disease and idiopathic DCM groups. There was no significant difference in the frequency of any desmin expression form in

Table II. Various forms of intramyocyte desmin expression in specific diseases

	Expression of desmin in cardiomyocytes		
	normal (n = 48), n (%)	high (n = 54), n (%)	low (n = 33), n (%)
Idiopathic dilated cardiomyopathy (n = 52)	20 (38.5)*	21 (40.4)	11 (21.2)**
Myocarditis (n = 36)	9 (25.0)	19 (52.8)#	8 (22.2)##
Vascular disease (n = 47)	19 (40.4)	14 (29.8)	14 (29.8)

** p = 0.02 normal vs. low; ** p = 0.01 low vs. high; # p = 0.007 normal vs. high; ## p = 0.003 low vs. high*

the vascular disease group. In the idiopathic DCM group, the number of patients with low expression of desmin was significantly lower. Increased accumulation of desmin was most frequently observed in patients with myocarditis. (Table II). There were no significant differences in LVEF and LVEDD values in patients with myocarditis, vascular disease and idiopathic DCM.

Expression of desmin and NYHA class

Evaluation of severity of heart failure according to the NYHA classification revealed that in the group with normal expression of desmin NYHA class was lower (NYHA 1.58 ± 0.7) compared to the groups with high (NYHA 2.11 ± 0.81) and low expression of desmin, where the NYHA class was highest (NYHA 2.72 ± 0.83). Differences between all three groups were statistically significant (normal vs. high, p = 0.001, high vs. low, p = 0.009, normal vs. low, p = 0.001) (Figure 2).

The majority of patients in NYHA class I and II belonged to the group with normal expression of desmin while the lowest number of such patients was found in the group with low expression of desmin (Figure 3).

Echo examination and desmin distribution

Echocardiographic examination demonstrated that higher values of LVEF and lower values of LVEDD were observed in the group with normal expression of desmin (LVEF 34.1 ± 10.8%; LVEDD 61.4 ± 9.7 mm) than in the groups with high (LVEF 29.0 ± 8.9%; LVEDD 65.9 ± 10.1 mm) and low expression of desmin (LVEF 26.9 ± 7.2%; LVEDD 69.1 ± 12.0 mm). Differences in these echocardio-graphic parameters between normal and abnormal expression of desmin groups were significant (LVEF: normal vs. high p = 0.01, normal vs. low p = 0.001; LVEDD: normal vs. high p = 0.027, normal vs. low p = 0.004) (Table III).

No significant differences were observed between high and low expression of desmin groups (Figures 4 and 5).

Discussion

The analysis of cardiomyocyte desmin expression (normal, high, low) in our patients with heart failure showed significant differences.

For the first time a report documenting a decrease in the amount of desmin in human cardiomyocytes and its focal deficits was published in the year 2004 [23]. It was found in patients with post-infarction CHF in NYHA class IV [23].

Some data suggest that cardiac dysfunction is likely caused by low intracellular expression of desmin [14]. Current data on desmin cardiomyocyte distribution in patients with CHF are based on experimental studies on transgenic animals with desmin gene knockout. We chose immunocytochemistry staining of intracellular myocardial desmin based on the results of an earlier study comparing such a method with immunofluorescence staining [22, 23]. Both methods were used in an Italian study to identify desmin in cardiomyocytes [24].

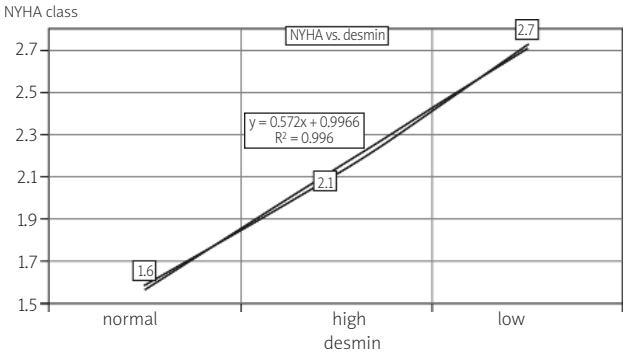

Figure 2. Correlation between desmin expression and NYHA class in all group of desmin expression

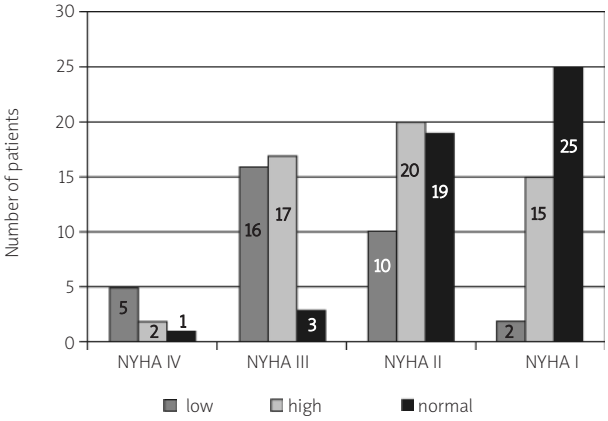

Figure 3. Number of patients vs. NYHA class and expression of desmin

Table III. LVEF and LVEDD in normal, high and low expression of desmin in cardiomyocytes

	LVEF [%]			LVEDD [mm]		
Desmin expression	value	SD	p	value	SD	p
Normal (n = 48)	34.1	10.8	0.01*	61.4	9.7	0.027#
High (n = 54)	29.0	8.9	0.4#	65.9	10.1	0.23^
Low (n = 33)	26.9	7.2	0.001^	69.1	12.0	0.004*

** p normal vs. high expression, # p high vs. low, ^ p normal vs. low*

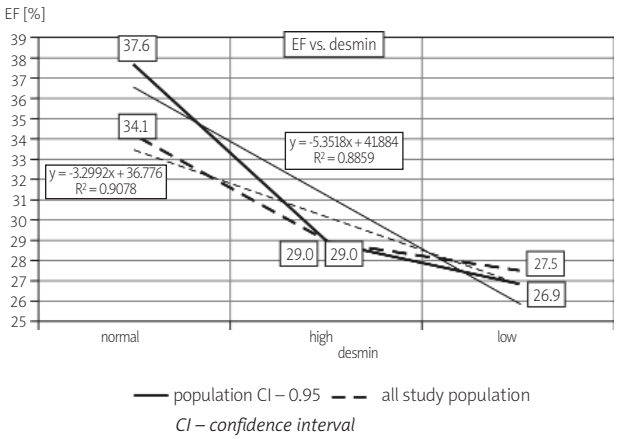

Figure 4. Correlation between desmin expression and LVEF

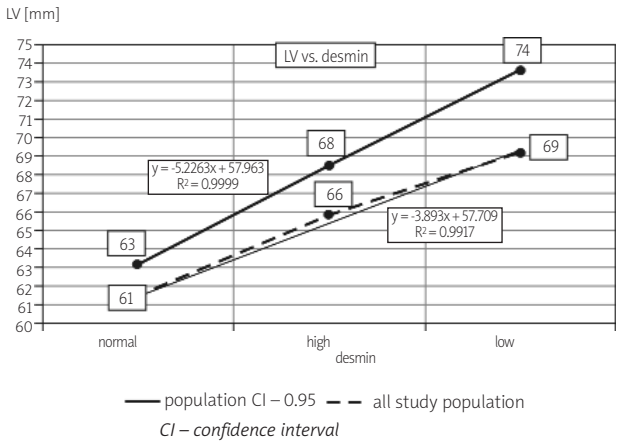

Figure 5. Correlation between desmin expression and LVEDD

The most favourable values of LV diameter and LVEF were observed in the group with normal expression of desmin. High expression of desmin in cardiomyocytes was associated with significantly more abnormal values of these echocardiographic parameters, and the highest values of LV diameter and the lowest of LVEF were found in the group of patients with low expression of desmin. Functional status assessment based on NYHA class demonstrated a similar trend. The average value of NYHA class was the highest in the group with low expression of desmin, lower in the group with high expression, and the lowest in the group with normal accumulation of desmin. Differences between all groups were significant.

Our study showed that increased accumulation of desmin in cardiomyocytes was associated with more abnormal clinical parameters as compared with a group of patients with normal expression of this protein. This may be a result of damage of the desmin network in cardiomyocytes, likely caused by accumulation of cytoskeleton proteins.

In the initial stages of CHF development accumulation of desmin seems to be a result of a compensatory increase of myocardial tension. However, the least favourable values of clinical parameters were discovered in the group with low expression of desmin in cardiomyocytes, which is consistent with published data.

Gradual increase of the size of cardiomyocytes and loss of proper function of contractility fibres is a well known scenario in the development of CHF [25]. Accumulating intermediate filaments disrupt the desmin network and consequently impair its function aimed primarily at protecting structural and functional integrity of myofibrils and being responsible for cell cohesion (e.g. sites of cellular nucleus) [26]. Such changes can affect the LV diameter and LVEF. It seems possible that it leads to loss of ability of the cell to provide an adequate increase of desmin in the end-stage CHF.

As a result, in the setting of CHF less or no desmin can be found in cardiomyocytes compared to normal subjects. Additionally, this effect is intensified by increased size of cardiomyocytes. Thus, patients with low expression of desmin show the most extensive pathology within their cells.

It seems that the suggested classification of desmin distribution into normal, high and low properly reflects the severity of CHF. We believe that this statement is justified based on the values of LV diameter, LVEF and NYHA found in our study. Reduced LVEF is one of the basic parameters of CHF and it directly illustrates abnormal systolic function of the LV. According to some investigators, initial impairment of systolic function results from desmin abnormalities. It leads to abnormal arrangement of sarcomeres and impaired cellular transmission rather than destruction of protein function of the contractile apparatus [27]. Protein content of the contractile apparatus remains intact and so does its response to calcium ions [27]. Increasing LV diameter correlated with deteriorating parameters of desmin in cardiomyocytes in our study population.

The relationship between LVEF, LV diameter and desmin expression suggests that the presence of desmin in cardiomyocytes is important in terms of CHF development. Decreasing LVEF and dilating LV indicate a special role of intermediate filaments and desmin in the pathophysiology of CHF.

Our observations are consistent with those of Italian authors [24], who reported that patients with low expression of desmin in cardiomyocytes had more altered echocardiographic parameters and higher NYHA class. In our population, patients with low expression of desmin demonstrated lower NYHA class (2.61 ± 0.83) as compared with patients from Di Somma's study (NYHA class IV) [24]. This may have resulted from different inclusion criteria. In our study, we included patients with LVEF < 45% (mean value of EF in group with low expression of desmin – 26.9 ± 7.2%), regardless of the NYHA class. In the Italian study, patients with LVEF below 40% (average value 26.3 ± 11.4%) were included, but only if they presented symptoms of NYHA class IV.

The analysis of various forms of intramyocyte desmin accumulation resulted in several findings. In the coronary artery disease group no significant differences in the frequency

of presence of any desmin form were noticed. There were significantly fewer patients with low expression of desmin in the DCM group. Increased accumulation of desmin was most frequently observed in patients with myocarditis.

The aetiology of CHF may be related to the desmin distribution. Desmin abnormalities are most frequently detected in the group with myocarditis, which suggests that inflammatory factors can specifically damage the structure and function of cardiomyocytes.

To our knowledge, there are no other reports investigating the intensity of CHF in patients with normal desmin content. Our study, which included an analysis of NYHA class with respect to the desmin content, is the first report on this topic we are aware of.

Analysis of the discussed parameters (LV diameter, LVEF and NYHA class) did not show any significant statistical difference between patients with different aetiology of CHF in our population. Thus, we can hypothesise that protein abnormalities in cardiomyocytes impact LV diameter and its systolic function, regardless of aetiology of heart failure.

Study limitations

A limitation of our study is desmin assessment only in immunohistochemical assay. We know that in the group of patients with high expression of desmin, aggregates can consist of proteins other than desmin (selenoprotein or mothylin). However, we chose this method for desmin evaluation because we were looking for a simple, easy to perform and relatively cost-effective parameter for establishing the long-term prognosis. In addition, the immunohistochemical assay was confirmed by immunofluorescence assay in our previous paper [22].

Conclusions

Immunohistochemical staining of desmin revealed three forms of desmin expression in cardiomyocytes – normal, high and low. Abnormal expression of desmin in cardiomyocytes is associated with significant enlargement of LV diameter and lower LVEF as well as higher NYHA class.

References

1. Li Z, Mericskay M, Agbulut O, et al. Desmin is essential for the tensile strength and integrity of myofibrils but not for myogenic commitment, differentation, and fusion of sceletal muscle. *J Cell Biol* 1997; 139: 1-16.
2. Milner DJ, Waltzer G, Tran D, et al. Disruption of muscle architectureand myocardial degeneration in mice lacking desmin. *J Cell Biol* 1996; 134: 1255-70.
3. Schultheiss T, Lin ZX, Ishikawa H, et al. Desmin/vimentin intermediate filaments are dispensable for many aspects of myogenesis. *J Cell Biol* 1991; 114: 953-66.
4. Cartaud A, Jaśmin BJ, Changeux JP, et al. Direct involvement of a lamin-B-related (54 kDa) protein in the association of intermediate filaments with the postsynaptic membrane of the Torpedo Marmorata electrocyte. *J Cell Science* 1995; 108: 153-60.
5. Tolstonog GV, Sabasch M, Traub P. Cytoplasmic intermediate filaments are stably associated with nuclear marices and potentially modulate their DNA-binding function. *DNA and Cell Biol* 2002; 21: 213-39.
6. Hutchison CJ. Lamins: building blocks or regulator soft gene expression? *Nat Rev Mol Cell Biol* 2002; 3: 848-58.
7. Milner DJ, Mavroidis M, Weisleder N, et al. Desmin cytosceleton linked to muscle mitochondrial distribution and respiratory function. *J Cell Biol* 2000; 150: 1283-98.
8. Thornell L, Carlsson L, Li Z, et al. Null mutation in the desmin gene gives rise to cardiomyopathy. *J Mol Cell Cardiol* 1997; 29: 2107-24.
9. Thornell LE, Ericson A, Johansson B, et al. Intermediate filament and associated proteins in heart Purkinje fibers: a memebrane-myofibril anchored cytosceletal system. *Ann NY Acad Sci* 1985; 455: 213-40.
10. Fuchs E, Weber K. Intermediate filaments: structure, dynamics, function and disease. *Annu Rev Biochem* 1994; 63: 345-82.
11. Granger BL, Lazarides E. Synemin: a new high molecular weight protein associated with desmin and vimentin filaments in muscle. *Cell* 1980; 22: 727-38.
12. Goldfarb LG, Vicart P, Geoble HH, et al. Desmin myopathy. *Brain* 2004; 127: 723-34.
13. Goebel HH. Congenital myopathies at their molecular dawning. *Muscle Nerve* 2003; 27: 527-48.
14. Asangri R, Kumarapeli K, Wang X. Genetic modyfication of the heart: chaperones and the cytosceleton. *J Mol Cell Card* 2004; 37: 1097-109.
15. Zawistowski S. Technika histologiczna, histologia oraz podstawy histopatologii. *PZWL* 1975; 132-3.
16. Zawistowski S. Technika histologiczna, histologia oraz podstawy histopatologii. *PZWL* 1975; 136-7.
17. Carleton HM. Histological technique for normal and pathological tissues and the identification of parasites. *Oxford University Press,* London – New York – Toronto, 1957; 106.
18. Zawistowski S. Technika histologiczna, histologia oraz podstawy histopatologii. *PZWL* 1975; 133-4.
19. Aretz TH. Myocarditis. The Dallas criteria. *Hum Pathol* 1987; 18: 619-24.
20. Noutsiasis M, Pauschinger M, Schulthesis HP, et al. Advances in the immunohistochemical diagnosis of inflammatory cardiomyopathy. *Eur Heart J* 2002; 4: 154-62.
21. Nożyński J, Konecka-Mrówka D, Zembala-Nożyńska E, et al. Biopsja mięśnia sercowego w kardiologii i kardiochirurgii. *Kardiochir Torakochir Pol* 2004; 1: 110-7.
22. Pawlak A, Gil RJ, Walczak E, et al. Evaluation of desmin activity using immunohistochemical and immumofluorescent staining of myocardial biopsies in patients with chronic heart failure. Comparison of the two methods. *Kardiol Pol* 2007, 65: 229-35.
23. Pawlak A, Gil RJ, Walczak E, et al. Relationship between desmin presence in cardiomyocytes and left ventricle function in patients with chronic heart failure. *Eur J Heart Fail Suppl* 2006; 5:186.
24. Di Somma S, Di Benedetto MP, Salvatore G, et al. Desmin-free cardiomyocytes and myocardial dysfunction in end stage heart failure. *Eur J Heart Fail* 2004; 6: 389-98.
25. Hein S, Kostin S, Heling A, et al. The role of the cytosceleton in heart failure. *Cardiovasc Res* 2000; 45: 273-8.
26. Dalakas MC, Oark KY, Semino-Mora C, et al. Desmin mypathy, a sceletal myopathy with cardiomyopathy coused by mutation in the desmin gene. *N Engl J Med* 2000; 342: 770-80.
27. Paulin D, Li Z. Desmin: a major intermediate filament protein essential for the structural integrity and function of muscle. *Exp Cell Res* 2004; 301: 1-7.

Ekspresja desminy w kardiomiocytach a wybrane parametry kliniczne i echokardiograficzne u chorych z niewydolnością serca

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Streszczenie

Wstęp: Desmina jest jednym z podstawowych białek strukturalnych kardiomiocytów, które może odgrywać ważną rolę w ocenie progresji niewydolności serca. Białku temu przypisuje się pełnienie wielu funkcji w kardiomiocycie, takich jak funkcja mechaniczna, strukturalna i regulatorowa. Desmina poprzez swoją lokalizację w kardiomiocycie może wpływać na regulację ekspresji genów, miofibrylogenezę, sygnalizację międzykomórkową, jak również może być odpowiedzialna za kształt i napięcie błony komórkowej oraz położenie i funkcję innych elementów komórki, w tym np. mitochondriów. Nieprawidłowe rozłożenie desminy w komórce może upośledzać funkcję miofibryli, przyczyniać się do nieprawidłowego rozlokowania organelli (jądra komórkowego) i uszkadzać komunikację wewnątrz- i międzykomórkową.

Cel: Ocena ekspresji desminy w bioptatach pochodzących z prawej komory serca chorych z niewydolnością serca.

Metody: Badaną populację stanowiło 135 chorych (86,7% mężczyzn, średni wiek 49,4 ± 14,1 roku) z klinicznymi cechami niewydolności serca i frakcją wyrzutową lewej komory (LVEF) poniżej 45%. W czasie biopsji endomiokardialnej (EMB) pobierano trzy lub cztery wycinki z prawej komory serca. W pobranych wycinkach dokonywano immunohistochemicznej oceny ekspresji desminy. Badana populacja została podzielona na trzy grupy: I grupę stanowiło 48 chorych z prawidłową ekspresją desminy, II grupę – 54 chorych ze zwiększoną ekspresją desminy, III grupę – 33 chorych ze zmniejszoną ekspresją desminy w kardiomiocytach.

Wyniki: W analizowanej populacji w grupie I wykazano znamiennie wyższą LVEF, istotnie mniejszy wymiar lewej komory i niższą klasę wg NYHA (wykładnik stanu klinicznego) niż w grupach II i III. Obserwowane różnice między poszczególnymi grupami były znamienne statystycznie.

Wnioski: Ocena ekspresji desminy w wycinkach pochodzących z prawej komory serca chorych z niewydolnością serca może być użytecznym narzędziem oceny funkcji lewej komory oraz zmian zachodzących na poziomie komórkowym.

Słowa kluczowe: niewydolność serca, desmina, biopsja mięśnia serca

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