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Original Article

Gender-effect on the contractile properties of skeletal muscle in streptozotocin-induced diabetic rats

A. Virgen-Ortiz[1], A. Apolinar-Iribe[2], J. Muñiz[3]

[1]Centro Universitario de Investigaciones Biomédicas, Universidad de Colima, C.P. 28045, Colima, Colima, México; [2]Departamento de Física, Universidad de Sonora, Unidad Centro. A.P. 1621. C.P. 83000, Hermosillo, Sonora, México; [3]Instituto Estatal de Cancerología, Secretaria de Salud de Colima, C.P.28010, Colima, Colima, México

Abstract

In the present study, we studied the effect of streptozotocin-induced Type 1 diabetes on contractile properties of soleus muscle in female and young male rats. We hypothesized that the gender affects the contractile function in diabetic rats. Thirty-two Sprague-Dawley rats, male and female, three months old were divided into four groups: Female Non-Diabetic (FND), Female Diabetic (FD), Male Non-Diabetic (MND) and Male Diabetic (MD). Diabetes was induced by a single dose of 60 mg/kg body weight of streptozotocin in citrate buffer pH 4.5 by intraperitoneal route. At 4 weeks after of the dose animals were considered to be diabetic if they had glucose levels ≥20 mmol/L. Soleus muscle mass and twitch force were higher in MND than in FND; in male rats, the diabetes decreased the muscle mass in 34% and the twitch force decayed in 33%; while in diabetic females the muscle mass and twitch force decayed 15% and 10% respectively. Our results showed that the diabetes has gender-dependent effects on the muscle mass and maximal contractile force.

Keywords: Diabetes, Skeletal Muscle, Soleus, Sex-Difference

Introduction

Diabetes mellitus (DM) is a metabolic disorder that continues growing to be a major worldwide epidemic. The prevalence of diabetes is rapidly increasing from 171 million in 2000 to an estimated 366 million in 2030[1]. There are two main types of diabetes: Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) and the prevalence of diabetes has been reported higher in men than women[1]. However, the beta cell failure/death is the cause of development of T1DM[2] and T2DM[3]. Diabetes is characterized by clinical symptoms that include a deficit in the capacity for muscle force development, lower muscle mass, and reduced physical capacity, manifested as fatigue and therefore reduced quality of life. In T1DM, this alteration progressively reduces the physical performance of the patient in daily activities[4-7]. A loss of physical activity in diabetic patients often leads to increased morbidity and mortality, as well as cardiovascular and respiratory diseases[8]. The muscle is the most important regulator of insulin-dependent circulating glucose and an impaired hormonal signaling has a deleterious effect on glucose uptake[9,10]. Investigations on patients and animals with T1DM and T2DM models designed for studying the effect of diabetes on skeletal muscle showed that the muscle mitochondrial ATP production rate and expression of oxidative phosphorylation genes are decreased[11], there is a reduction in the production of force and loss of muscle mass[6,12-14]. Moreover, proteomic profile alterations induced by diabetes have been reported in different studies, increasing the expression of stress response proteins[15], altered expression in the glycolytic enzymes[16], abnormal phosphorylation of ATP synthase[17], increase of glycolytic/fast-twitch muscle fiber and glycolytic enzymes[18], and cytoskeleton defects in the sarcolemmal dystrophin-dystroglycan complex[19].

Although the streptozotocin (STZ)-induced T1DM effects on the muscle have been investigated, there is a lack of knowledge on the effects of gender or the diabetes-induced changes in the skeletal muscle in young patients. Recently, the National Institutes of Health (NIH) of the U.S. has suggested consider the sex as a biological variable in preclinical research[20,21].

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Corresponding author: A. Apolinar-Iribe
E-mail: apolinar@ciencias.uson.mx

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Table 1. Soleus muscle mass and contractile properties.

	Female		Male	
	FND (n = 8)	FD (n = 8)	MND (n = 8)	MD (n = 8)
Soleus muscle mass (g)	0.14 ± 0.01	0.12 ± 0.01	0.24 ± 0.02†	0.16 ± 0.01††
Twitch				
Peak Force (N)	0.55 ± 0.06	0.50 ± 0.04	0.83 ± 0.12†	0.56 ± 0.02††
Muscle quality (kN/kg)	3.72 ± 0.20	3.58 ± 0.25	3.59 ± 0.29	3.56 ± 0.10
Tetanus*				
Maximal Force (N)	1.29 ± 0.08	0.99 ± 0.10††	2.64 ± 0.11†	1.33 ± 0.14††
Muscle quality (kN/kg)	8.97 ± 0.40	6.97 ± 1.00††	11.28 ± 0.99†	8.02 ± 0.70††

*All data correspond to mean ± SD. † p<0.05, non-diabetic female vs non-diabetic male. †† p<0.05, non-diabetic vs diabetic. *At 50 Hz of stimulation, kN = 1 x 103Newton.*

Previous studies show that for a better diabetes care and management is very important improve the knowing their physiopathology specifically gender-based differences, these would help a increasing in the quality of life of the diabetic patients[22,23]. In a clinical study with diabetic elderly patients, the muscle strength was lower in diabetic than nondiabetic men, however there were not differences found in woman; meanwhile, the muscle quality was significantly lower in men and women with diabetes than those without diabetes[14,24]. In STZ-induced experimental diabetes in rats, a study did not find differences in the contractile properties when female and male were compared, however this study lack a comparative analysis between diabetic rats versus healthy rats[25], this comparison is essential to evaluate the diabetes-induced effects in the skeletal muscle functional activity. In the present study, we performed a comparative analysis between females and males on the effect of the experimental diabetes in the mass and contractile properties of soleus muscle from young rats. Our results showed that the diabetes has effects gender-dependent on the mass muscle and maximal contractile force.

Materials and methods

Treatment and care of animals

Animal care and experimental procedures were approved by the Ethics Committee of Colima University, using guidelines based on the Guide for the Care and Use of Laboratory Animals (US Department of Health, NIH). Thirty-two Sprague-Dawley rats, male and female, three months old were divided into four groups: Female Non-Diabetic (FND; body weight= 265±9 g; blood glucose level= 4.94±0.22 mmol/L; n=8), Female Diabetic (FD; body weight= 220±7 g; blood glucose level= 27.69±0.85 mmol/L; n=8), Male Non-Diabetic (MND; body weight= 275±10 g; blood glucose level= 4.95±0.25 mmol/L; n=8) and Male Diabetic (MD; body weight= 207±8 g; blood glucose level= 28.39±0.94 mmol/L; n=8). The diabetes was induced by a single dose of 60 mg/kg body weight of STZ in citrate buffer pH 4.5 by intraperitoneal route[26]. The animals in non-diabetic group received an equivalent volume of the vehicle. At 4 weeks after the STZ injection, the animals (female and male) were considered to be diabetic if they had glucose levels ≥20 mmol/L[27]. Blood glucose was determined by the glucose oxidase technique in blood samples collected from the tail veins. All rats were provided with water and food (rodent laboratory chow, Purina; Composition: 23.9% Protein, 5% Fat, 5.1% Fiber, 7% Minerals), *ad libitum* and were maintained on individual acrylic cages (using a natural bedding, HER-BIO Purina) on a 12:12-h light-dark cycle with an average daily temperature of 24±1°C and average humidity of 60-70%.

Surgery and experimental conditions

Four weeks after the diabetes induction, all rats were subjected to surgical intervention to evaluate contractile activity of the soleus muscle. Rats were anaesthetized with a intraperitoneal injection of sodium pentobarbital (50 mg/kg). The right soleus muscle was dissected free from the adjacent tissues, leaving the bone insertion and blood supply intact. The sciatic nerve was cut as far away as possible from its entry into the muscle. During surgery, saline solution (125 mM NaCl; 5.4 mM KCl; 1.05 mM MgCl2; 1.8 mM CaCl2; and 11 mM glucose, pH=7.4) was applied to protect the tissues. A transverse hole was made in the femur using a micro-drill (F.S.T.18000 - 17; Fine Science Tools, Foster City, CA, USA), and the distal tendon of soleus muscle was tied to a hook then each rat was transferred to a mechanical recording system consisting of a plate mounted on an inclined base that allowed the muscle to be placed perpendicularly to a load transducer (FT10; Grass Co., Quincy, MA, USA). The plate had two posts to hold the steel rod passing through the hole in the femur. The transducer was mounted on an actuator driven by a computer-controlled stepper-motor and wired to an A/D converter to allow display and storage of the force responses. The tendon hook was attached to the transducer. The sciatic nerve was placed on stimulating electrodes wired to a stimulator (S88; Grass Co.). During the experiment, the rat body temperature

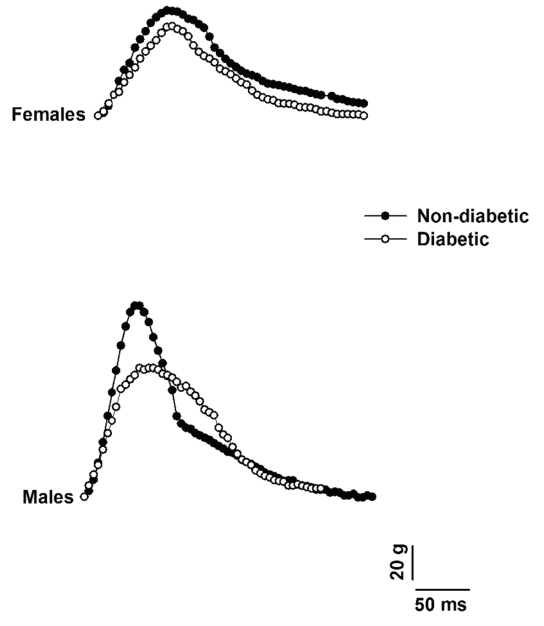

Figure 1. Representative twitches records of soleus muscle in diabetic and non-diabetic rats.

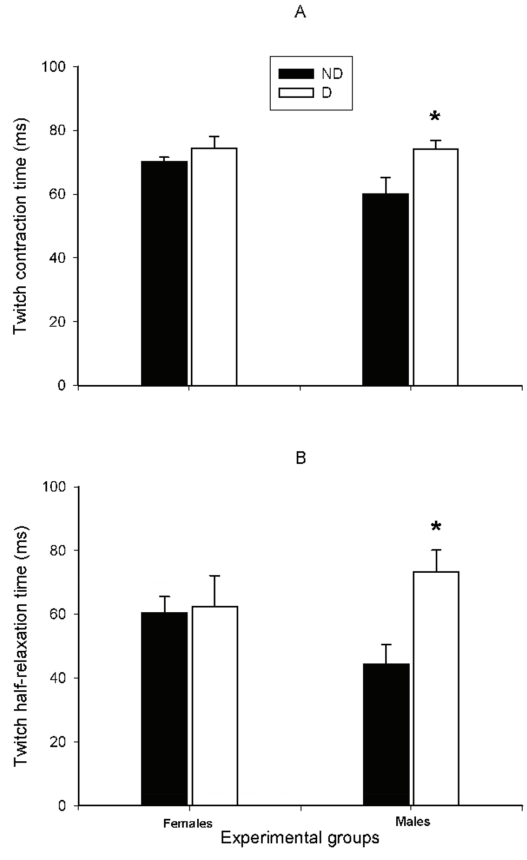

Figure 2. Contraction (A) and half-relaxation times (B) in single twitch from soleus muscle. ND, represent to non diabetic rats; D, represent to diabetic rats. Data correspond to means ± standard error, n=8 by group, * p<0.05.

was maintained at 37°C. The environmental temperature was 24°C. At the end of the experiments, the soleus muscle were excised from the animals and weighed on an analytical balance (Sartorius, Edgewood, NY, USA).

Mechanical properties measurement

At several muscle lengths, single isometric twitches were elicited by supramaximal stimuli (3 volts applied) to the sciatic nerve until reached the maximal force; this length was defied as the optimal length (Lo). At Lo of soleus muscle, single twitches and tetani were recorded (5-100 Hz) elicited by motor nerve stimulation. The muscle was rested for 100 s between each record. Finally, the animals were euthanized by anesthetic overdose (150 mg/kg, intraperitoneally).

Mechanical analysis

The obtained tensions were expressed as force (N). The contractile function of skeletal muscle is dependent on the quantity of muscle mass and due a difference in skeletal muscle mass between healthy and diabetic rats, then for the comparison between groups was used the concept of skeletal muscle quality, defined as the maximal contractile force to muscle mass ratio[14] (in our case soleus muscle mass) and expressed in kN/kg.

Statistical analysis

Comparative analysis between pairs was performed using a Student test with a 95% significance level. The different tensions of frequency were compared with an analysis of variance of one factor and a post hoc Tukey's test. All differences were considered statistically significant with a p≤0.05. Statistical analysis was conducted with software Minitab Release version 12.

Results

The body weight loss after four weeks of the diabetes induction was higher in MD than FD group (MD, 29±5 g; FD, 10±4 g); in contrast in the same time period, the healthy rats gained body weight (MND= 24±3 g; FND= 6±2 g). These results showed that in healthy and diabetic rats body weight variation is gender-dependent. Soleus muscle mass and twitch force were higher in MND than FND (p<0.05, data showed in Table 1). The diabetes significantly decreased 34% the muscle mass and 33% the twitch force in the male rats, while in diabetic females decayed 15% and 10% the muscle mass and the twitch force respectively (Table 1). When the twitch force was normalized to muscle mass, (skeletal muscle quality), there were not differences

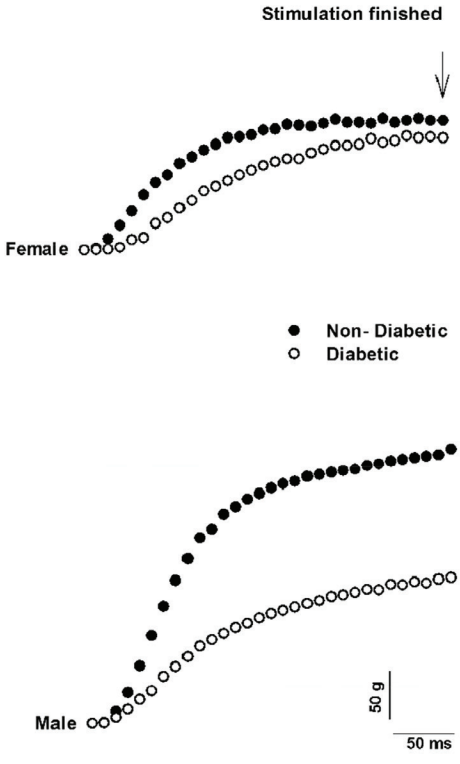

Figure 3. Representative force records elicited with repetitive stimulation (50 Hz) in soleus muscle of diabetic and non-diabetic rats.

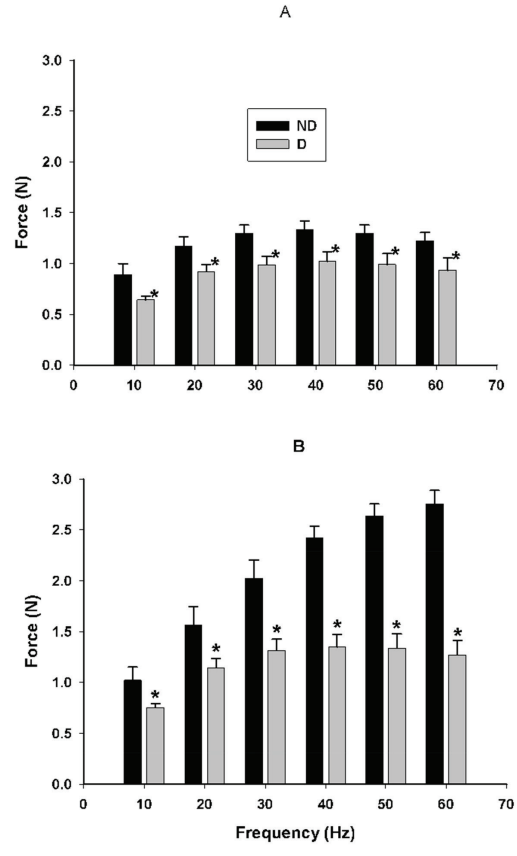

Figure 4. Maximal tetanic force developed for the soleus muscle in female (A) and male rats (B). ND, represent to non diabetic rats; D, represent to diabetic rats. Data correspond to means ± standard error, n=8 by group, *p<0.05.

between females and males in the studied groups. In addition, we studied the relaxation and contraction times of the soleus muscle and as shown in the Figure 1 and Figure 2, the diabetes did not affect the twitch contraction and the half-relaxation times in the females; however, in males, diabetes increased significantly the twitch contraction and the half-relaxation times ($p<0.05$). In relation to the maximal tetanic force developed for the soleus muscle at different stimulation frequencies (Figure 3), the males significantly developed more tetanic force than the females ($p<0.05$, Figure 4) and diabetes reduced force development in both, females and males. However, the effect of diabetes on the tetanic force development is higher in males than in females. The skeletal muscle quality was less in the diabetic rats (Figure 5), and the diabetes effect was significantly greater in males compared with the females ($p<0.05$).

Discussion

We studied the effect of the experimental diabetes in the mass and contractile properties of soleus muscle of young rats from the point of view of sex-based difference. In the literature there few studies carried out to understand differences of gender in the deterioration of skeletal muscle in STZ-induced diabetes. A study in diabetic persons with physical activity showed that there are not differences gender-based on strength and contractile properties[28], and T2DM older adults showed a significantly decrease in the absolute muscle strength in men but not in the woman. Moreover, the muscle quality was significantly lower in both, women and men with diabetes than without diabetes[14]. The experimental diabetes in young rats showed that absolute twitch force decayed significantly in male, however, in female it not changed significantly. Also, we demonstrated that absolute tetanic force and muscle quality decayed significantly in diabetic females and males, but the males are more susceptible to diabetes-induced effect on the muscle than females. Although mechanisms underlying to gender differences in muscle performance during diabetes are still poorly understand, peripheral fatigue can play a key role, recent study showed that diabetic male have higher peripheral fatigue than female[29].

In the diabetic males, the relaxation-half and contraction times of soleus muscle increased respect to non-diabetic males, those is consistent with others studies[30,31]. On the

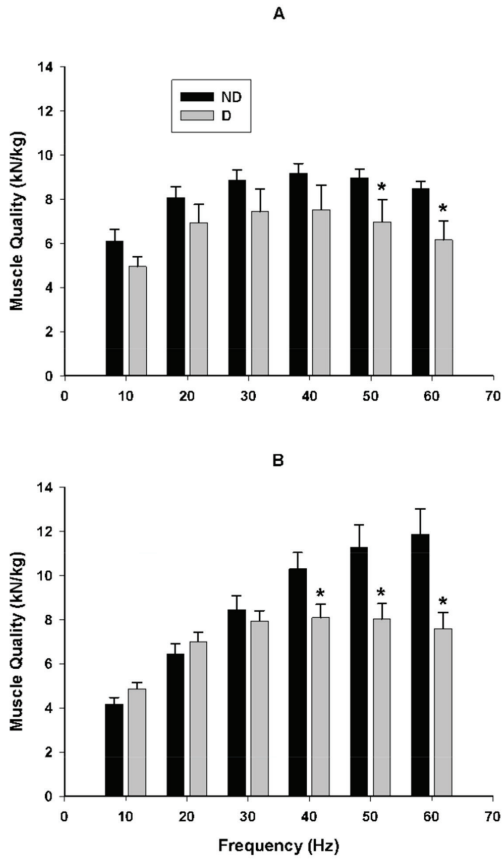

Figure 5. Soleus muscle quality in female (A) and male rats (B) to different frequency. ND, represent to non diabetic rats; D, represent to diabetic rats. Data correspond to means ± standard error, n=8 by group, *p<0.05.

other hand, the relaxation-half and contraction times in the soleus muscle were not altered significantly for diabetes in the females. Although our results were found in the slow soleus muscle, which is mostly the oxidative in rodents and humans, similar results were found in a study using the fast glycolytic extensor digitorum longus muscle (non-oxidative) of non-diabetic and diabetic female rats[32]. The changes showed in the contraction time in diabetic males, that could have been caused by the increased sensitivity to Ca2+ of the contractile properties of skeletal muscles[33] and a Ca2+ diminished release induced by an increase in the calsequestrin expression[34,35], the main calcium binding protein of the sarcoplasmic reticulum, while the augmented in the relaxation-half time could be caused by impaired Ca2+ uptake by sarcoplasmic reticulum[36]. Ca2+ATPasa activity and Ca2+ uptake in skeletal muscle are gender-affected in diabetes[37], this deregulation can explain relaxation and contraction times differences in the current study.

In diabetic males, the increased in the relaxation-half and contraction times, as well as the reduction in the production of soleus muscle force, also may be related to an increase in the proportion of slow oxidative fibers at the expense of fast oxidative glycolytic fibers38. In the cardiac muscle, the contractility is sex-dependent and is related to different protein levels and/or Ca2+-handling functioning systems[38], however, in skeletal muscle are required further investigations. Although the studies reported in literature are limited, there are evidence than female skeletal muscle has less fast fibers amount in comparison to male[39,40]; this difference could result benefic for female in conditions as the diabetes, it supporting that diabetes do not have significant effects on the relaxing and contraction times in soleus muscle.

The muscle mass and the contractile properties of the soleus muscle in male and diabetic female could be explained by the reduction in the testosterone levels in male rats with STZ-induced diabetes[41]. Studies suggest that the gender effect and estrogen on skeletal muscle depends of the type of muscle. Recently, it was shown that in soleus muscle (slow muscle) of pregnant rats (high estrogen levels) increase the fatigue resistance with regard to non-pregnant rat[42]; while estrogen and gender did not affected the fatigue resistance in EDL muscle (fast muscle)[43]. Therefore, our results in the soleus muscle could be explained by the estrogen ability to reduce oxidative stress and promote the formation of cross-bridges[7], but is necessary more studies.

Metabolic differences between male and female muscles may contribute to observed differences in the strength development during this study. A recent study reported a decrease in the alpha-enolase expression pattern in skeletal muscle of diabetic male rats and an increase in female rats, as is known this enzyme plays an important role in the glycolytic metabolism to produce energy (ATP), essential for muscle contraction[41]. Furthermore, it is known that in the diabetes the soleus muscle (mainly composed of slow fibers) accumulates twice of the intramyocellular lipids in comparison with the tibialis muscle (fast fibers)[44]. This suggests that lipids could be used by diabetic skeletal muscle as an alternative source of energy and could be another possible explanation for our results. From the above, during the diabetes the slow muscle would have a bigger availability of lipid reserves to produce ATP. Also, studies performed in rats have shown that lipid oxidation is higher in female skeletal muscles than in male muscles, which may explain why diabetic skeletal muscle has greater functional performance in females than in males[45,46].

Another factor that should be considered is oxidative stress due to a previous study it has been associated with inactivation of the calcium channel voltage-dependent and Ca2+ ATPase[47], as well as a decrease in the generation of force[48]. Previous reports in skeletal muscle show that oxidative stress is higher in male than female[49,50], this suggest that oxidative status differences gender-based would be crucial to the decline in the functional activity of the skeletal muscle in chronic diseases as the diabetes. However, more research is necessary to evaluate the effect of gender on oxidative stress in skeletal muscle generated during diabetes.

Skeletal muscle is fundamental to regulate insulin-dependent blood glucose level. Previous studies have reported that the insulin level is greater in male than in

healthy female rats[51], and moreover, females have a better adaptive response in skeletal muscle to a drastic change of insulin by GLUT-4 regulating expression[52], some studies have reported that GLUT4 expression is higher in female than male[53,54]. However, this sex-based mechanism has not been fully established in diabetes.

In conclusion, our study shows experimental evidence about the differential gender effects on the contractile mechanical properties of the soleus muscle of young diabetic rat. Therefore, this study on gender-based is relevant in improving the understanding about the functional alterations presented in the diabetic patients and, therefore, in future occasions they can receive more appropriate medical care and have a better quality of life.

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes. Diabetes Care 2004;27:1047-53.
2. Tish R, McDevitt H. Insulin-dependent diabetes mellitus. Cell 1996;85:291-97.
3. Johnson JD, Alejandro EU. Control of pancreatic beta-cell fate by insulin signaling. Cell Cycle 2008;7:1343-47.
4. Andersen H, Gjerstad MD, Jakobsen J. Atrophy of foot muscles: a measure of diabetic neuropathy. Diabetes Care 2004;27:2382-85.
5. Andersen H, Poulsen PL, Mogensen CE, Jakobsen J. Isokinetic muscle strength in long-term IDDM patients in relation to diabetic complications. Diabetes 1996; 45:440-45.
6. Andersen H, Schmitz O, Nielsen S. Decreased isometric muscle strength after acute hyperglycaemia in type 1 diabetic patients. Diabet Med 2005;22:1401-07.
7. Krause MP, Riddell MC, Hawke TJ. Effects of type 1 diabetes mellitus on skeletal muscle: clinical observations and physiological mechanisms. Pediatr Diabetes 2011;12:345-64.
8. Güller I, Russell AP. MicroRNAs in skeletal muscle: their role and regulationin development, disease and function. J Physiol 2010;588:4075-87.
9. Ohlendieck K. Pathobiochemical changes in diabetic skeletal muscle as revealed by mass-spectrometry-based proteomics. J Nutr Metab 2012;2012:1-16.
10. Wasserman DH. Four grams of glucose. Am J Physiol Endocrinol Metab 2009;296:E11-21.
11. Karakelides H, Asmann YW, Bigelow ML, Short KR, Dhatariya K, Coenen-Schimke J, Kahl J, Mukhopadhyay D, Nair KS. Effect of insulin deprivation on muscle mitochondrial ATP production and gene transcript levels in type 1 diabetic subjects. Diabetes 2007;56:2683-89.
12. Fortes MAS, Pinheiro CHJ, Guimaraes-Ferreira L, Vitzel KF,Vasconcelos DAA, Curi R. Overload-induced skeletal muscle hypertrophyis not impaired in STZ-diabetic rats. Physiol Rep 2015;3:e12457
13. Zhang Z, Li KW, Zhang W, Ma L, Chen Z. Muscular fatigue and maximum endurance time assessment for male and female industrial workers. Int J Ind Ergon 2014; 44(2):292-7
14. Park SW, Goodpaster BH, Strotmeyer ES, Rekeneire N, Harris TB, Schwartz AV, Tylavsky FA, Newmann AB. Decreased muscle strength and quality in older adults with type 2 diabetes: the health, aging, and body composition study. Diabetes 2006;55:1813-18.
15. Stentz FB, Kitabchi AE. Transcriptome and proteome expressions involved in insulin resistance in muscle and activated T-lymphocytes of patients with type 2 diabetes. Genomics Proteomics Bioinformatics 2007;5:216-35.
16. Iori E, Millioni R, Puricelli L, Arrigoni G, Lenzini L, Trovisan R, James P, Rossi GP, Pinna LA, Tessari P. Glycolytic enzyme expression and pyruvate kinase activity in cultured fibroblasts from type 1 diabetic patients with and without nephropathy. Biochim Biophys Acta 2008;1782:627-33.
17. Højlund K, Yi Z, Lefort N, Langlais P, Bowen B, Levin K, Beck-Nielsen H, Mandarino LJ. Human ATP synthase beta is phosphorylated at multiple sites and shows abnormal phosphorylation at specific sites in insulin-resistant muscle. Diabetologia 2010;53:541-51.
18. Fritzsche K, Bluher M, Schering S, Bochwalow IB, Kern M, Linke A, Oberbach A, Adams V, Punk K. Metabolic profile and nitric oxide synthase expression of skeletal muscle fibers are altered in patient with type 1 diabetes. Exp Clin Endocrinol Diab 2008;116:606-13.
19. Mulvey C, Mullen E, Ohlendieck K. The pathobiochemical role of the dystrophin-dystroglycan complex and the Ca2+-handling apparatus in diabetes-related muscle weakness. Mol Med Report 2008;1:297-06.
20. National Institutes of Health. Consideration of sex as a biological variable in NIH-funded research. National Institutes of Health; 2015.
21. Miller LR, Marks C, Becker JB, Hurn PD, Chen WJ, Woodruff T, McCarthy MM, Sohrabji F, Schiebinger L, Wetherington CL, Makris S, Arnold AP, Einstein G, Miller VM, Sandberg K, Maier S, Cornelison TL, Clayton JA. Considering sex as a biological variable in preclinical research. FASEB Journal 2017;31:29-34.
22. Lundsgaard AM, Kiens B. Gender differences in skeletal muscle substrate metabolism - molecular mechanisms and insulin sensitivity. Front Endocrinol 2014;5:1-15.
23. Siddiqui MA, Khan MF, Carline TE. Gender differences in living with diabetes mellitus. Mater Sociomed 2013; 25:140-2.
24. Volpato S, Bianchi L, Lauretani F, Lauretani F, Bandinelli S, Guralnik JM, Zuliani G, Ferrucci L. Role of Muscle Mass and Muscle Quality in the Association Between Diabetes and Gait Speed. Diabetes Care 2012;35:1672-79.
25. Imam KA, Sarwa M, Wali U, Siddique L, Perveen S. Gender and contractile functions of slow and fast skeletal muscles in streptozotocin induced diabetic sprague dawley Rats. Rom J Diabetes Nutr Metab Dis 2012;19:417-24.
26. Gajdosík A, Gajdosíková A, Stefek M, Navarová J, Hozová R. Streptozotocin-induced experimental diabetes in male wistar rats. Gen Physiol Biophys 1999;8:54-62.
27. Cheng JT, Huang CC, Liu IM, Thing-Fong T, Chih JC. Novel mechanism for plasma glucose-lowering action of metformin in streptozotocin-induced diabetic rats.

Diabetes 2006;55:819-25.
28. Singh-Peters LA, Jones GR, Kenno KA, Jacobi JM. Strength and contractile properties are similar between persons with type 2 diabetes and age, weight, gender and physical activity matched controls. Can J Diabetes 2007;31:357-64.
29. Solianik R, Kreivėnaitė L, Streckis V, Mickevičienė D, Skurvydas A. Effects of age and sex on fatigability and recovery from a sustained maximal isometric voluntary contraction. J Electromyogr Kinesiol 2017;32:61-9.
30. Cotter M, Cameron NE, Lean DR, Roberson S. Effects of long-term streptozotocin diabetes on the contractile and histochemical properties of rat muscles. Q J Exp Physiol 1989;74:65-74.
31. Mcguire M, Macdermott M. The influence of streptozotocin diabetes and metformin on erythrocyte volume and on the membrane potential and the contractile characteristics of the extensor digitorum longus and soleus muscles in rats. Exp Physiol 1999;84:1051-58.
32. Asghar K, Majeed F, Arshad S. Skeletal muscle contractile functions in streptozotocin induced type 1 diabetes mellitus. Pak J Physiol 2012;8:27-31.
33. Stephenson GM, O'Callaghan A, Stephenson DG. Single-fiber study of contractile and biochemical properties of skeletal muscles in streptozotocin-induced diabetic rats. Diabetes 1994;43:622-28.
34. Howarth FC, Glover L, Culligan K, Qureshi MA, Ohlendieck K. Calsequestrin expression and calcium binding is increased in streptozotocin-induced diabetic rat skeletal muscle though not in cardiac muscle. Pflugers Arch-Eur J Physiol 2002;444:52-58.
35. Novák P, Soukup T. Calsequestrin distribution, structure and function, its role in normal and pathological situations and the effect of thyroid hormones. Physiol Res 2011;60: 439-52.
36. Yaras N, Tuncay E, Purali N, Sahinoglu B, Vassort G, Turan B. Sex-related effects on diabetes-induced alterations in calcium release in the rat heart. Am J Physiol Heart Circ 2007; 293:H3584-92.
37. Harmer AR, Ruell PA, Hunter SK, McKenna MJ, Thom JM, Chisholm DJ, Flack JR. Effects of type 1 diabetes, sprint training and sex on skeletal muscle sarcoplasmicreticulum Ca2+ uptake and Ca2+-ATPase activity. J Physiol 2014;592:523-35.
38. Cotter M, Cameron NE, Robertson S, Ewing I. Polyol pathway-related skeletal muscle contractile and morphological abnormalities in diabetic rats. Exp Physiol 1993;78:139-55.
39. Drzymała-Celichowska H, Krutki P. Slow motor units in female rat soleus are slower and weaker than their male counterparts. J Muscle Res Cell Motil 2015;36:287-95.
40. Haizlip KM, Harrison BC, Leinwand LA. SexBased Differences in Skeletal Muscle Kinetics and FiberType Composition. Physiology (Bethesda) 2015;30:30-39.
41. Choi M, Choi JW, Chaudhari HN, Aseer RK, Mukherjee R, Yun JW. Gender-dimorphic regulation of skeletal muscle proteins in streptozotocin-induced diabetic rats. Cell Physiol Biochem 2013;31:408-20.
42. Virgen-Ortiz A, Apolinar-Iribe A, Muñiz J. Differential effects of pregnancy on contractile behavior of rat fast and slow skeletal muscles. Bratisl lek listy 2014;115: 389-94.
43. Tiidus PM, Bestic NM, Tupling R. Estrogen and gender do not affect fatigue resistance of extensor digitorum longus muscle in rats. Physiol Res 1999;48:209-13.
44. Perseghin G, Lattuada G, Danna M. Insulin resistance, intramyocellular lipid content, and plasma adiponectin in patients with type 1 diabetes. Am J Physiol Endocrinol Metab 2003;285:1174-81.
45. Ellis GS, Lanza-Jacoby S, Gow A, Kendrick ZV. Effects of estradiol on lipoprotein lipase activity and lipid availability in exercised male rats. J Appl Physiol 1994;77:209-15.
46. Kendrick ZV, Ellis GS. Effect of estradiol on tissue glycogen metabolism and lipid availability in exercised male rats. J Appl Physiol 1991;71:1694-99.
47. De Angelis KLD, Cestari IA, Barp J, Fernandes TG, Homen de Bittencourt PI, Belló-Klein A, Belló AA, Llesuy S, Irigoyen MC. Oxidative stress in the latissimus dorsi muscle of diabetic rats. Braz J Med Biol Res 2000;33:1363-68.
48. D'Avila KP, Cestari IA, Bittencourt PIH, Leirner AA, Irigoyen MC. Changes in latissimus dorsi isometric contractile properties in streptozotocin-induced diabetic rats. Artificial Organs 1997;2:485.
49. Barreiro EI, Coronell C, Laviña B, Ramírez-Sarmiento A, Orozco-Levi M, Gea J, and behalf of the PENAM project. Aging, sex differences, and oxidative stress in human respiratory and limb muscles. Free Radic Biol Med 2006;41:797-09.
50. Pansarasa OI, Castagna L, Colombi B, Vecchiet J, Felzani G, Marzatico F. Age and sex differences in human skeletal muscle: role of reactive oxygen species. Free Radic Res 2000;33:287-93.
51. Thomas-Moya E, Gianotti M, Proenza AM, Llado I. Paraoxonase 1 response to a high-fat diet: gender differences in the factors involved. Mol Med 2007;13:203-09.
52. Gómez-Pérez Y, Amengual-Cladera E, Català-Niell A, Amengual-Cladera E, Català-Niell A, Thomàs-Moyà E, Gianotti M, Proenza AM, Lladò I. Gender dimorphism in high-fat-diet-induced insulin resistance in skeletal muscle of aged rats. Cell Physiol Biochem 2008; 22:539-48.
53. Rune A, Salehzadeh F, Szekeres F, Kuhn I, Osler ME, Al-KhaliliL. Evidence against asexual dimorphism in glucose and fatty acid metabolism in skeletal muscle cultures fromage-matched men and post-menopausal women. Acta Physiol (Oxf) 2009;197:207-15.
54. Tarnopolsky MA. Sex differences in exercise metabolism and the role of 17- beta estradiol. Med Sci Sports Exerc 2008;40:648-54.