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Assessment of myostatin and C-Terminal telopeptide of type I collagen (CTX-1), As a diagnostic medical parameter linked with skeletal muscular tissue condition

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Abstract

Skeletal muscular tissue plays vital functions like locomotion, metabolism, and systemic health, and muscular tissue dysfunction is linked to various pathological circumstances such as Muscular Dystrophy (MD), sarcopenia, and osteoporosis. myostatin (MSTN), a negative regulator of muscular tissue growth, and the C-Terminal Telopeptide of type I collagen (CTX-1), a bone resorption marker, are increasingly studied as potential biomarkers for muscular tissue-bone interactions. This investigation aimed to investigate the medical relevance of MSTN and CTX-1 concentrations in affected individuals with skeletal muscular tissue conditions compared with Healthy Controls (HCs), and to assess their association with demographic, anthropometric, and comorbid circumstances. A case-HCs investigation was conducted from December 2024 to February 2025 at hospitals in Baghdad. Ninety peripheral blood samples were collected, including 50 from affected individuals with muscular tissue illnesses (aged 27–77 years) and 40 from HCs (aged 20–73 years). Anthropometric data (BMI, skeletal muscular tissue bulk) were recorded using the InBody device. ELISA quantified serum MSTN and CTX-1 concentrations. Statistical analyses comprised t-tests, chi-square, and correlation tests (SPSS v26). Affected individuals displayed significantly higher BMI and lower skeletal muscular tissue bulk in comparison with HCs ($p < 0.05$). Woman predominance and smoking prevalence were greater among affected individuals ($p < 0.01$). MSTN concentrations were slightly higher in affected individuals (456.44 ng/ml) than in HCs (443.08 ng/ml), while CTX-1 concentrations were slightly lower (17.69 vs. 19.28 ng/ml), but both variations were insignificant. No significant influence on biomarker concentrations related to sex criteria. The most frequent coexisting illnesses were hypertension and diabetes (21.8%). Circulating MSTN and CTX-1 alone may not serve as reliable biomarkers in cases of sarcopenia.

Keywords: Skeletal muscular tissue, MSTN, CTX, ELISA

Introduction

Skeletal muscular tissue is one of the major and most metabolic active tissues in the body of human, establishing around 50-75% of total stores of proteins and 40% of total weight of bodies. Its major functions comprise motion, preserving balances, forming heats, and metabolising energies. Also, it behaves as a vital facility of protein storages and offers mechanical protections for internal organs [1]. Preserving function of muscular tissues and the skeleton bulk is critical for general health, and consequently, fragility of muscular tissue of skeleton meaningfully participates to illnesses, disability, and declined qualities of lives.

Musculoskeletal conditions incorporate a broad range of circumstances, comprising trauma-induced lesions, inactivity-induced muscular tissue wasting, muscular tissue-degenerative condition, and genetic or non-genetic muscular tissue diseases, all of which damage strength of muscular tissues and pathways of metabolites [2]. MD particularly is marked via a progressive losing of muscular tissue bulks and strengths, frequently accompanied via deterioration of bones, resulting in osteoporosis. This condition significantly raises the predisposition of falls, breaks, and functional declines. Consequently, understanding the biochemical variables that control muscular tissue is crucial for improving active therapeutic and preventive approaches. Among these crucial regulators of stability of muscular tissue, CTX-1 and MSTN have gained raising attention. MSTN is a member of the transforming growth variable-beta (TGF-β) family and works as an effective negative regulator of muscular tissue differentiation and growth. Raised concentrations of MSTN have been linked with atrophy of muscular tissue and degeneration in some circumstances of pathology, while inhibition or deletion of gene of MSTN has been found to result in significant hypertrophy of muscular tissue [3, 4].

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The CTX is a recognized biochemical indicator of resorption of bones, as raised serum concentrations of CTX are linked with enhanced loss and resorption of bones, representing fragility of skeleton [5].

The recent investigation aimed to detect serum concentrations of MSTN and CTX, appraise their combined impact on health of skeletal muscular tissue, and determine their potential usage as dependable biomarkers in the analysis of early sarcopenia.

Materials and methods

Subject

Samples of blood were obtained from affected individuals with muscular tissue illnesses who were visiting Medical City and Al-Wasiti, Saad Al-Watari hospitals in Baghdad, among Dec 2024 and Feb 2025. The protocol of investigation was approved via the Iraqi Ministry of Health. A total of 90 blood samples were collected. 55 samples from affected individuals diagnosed with muscular tissue illness (aged 27-77 years), and 35 samples from healthy individuals (aged 20-73), serving as a HCs group, were comprised in this work. For all participants, body bulk index (BMI) and skeletal muscular tissue bulk (SMM) were measured using an InBody device (InBody Co., Ltd/South Korea), and anthropometric indexes were recorded.

Blood collection and preparation

Three milliliters of peripheral venous blood were drawn from each participant using a sterile disposable syringe. The samples were allowed to clot for 30 minutes at room temperature. Then, they were centrifuged at 3000 rpm for 5 minutes to separate the serum. The obtained serum was transferred into a clean Eppendorf tube and stored at a low temperature in a refrigerator until laboratory analysis.

Immunological investigation: Serum concentrations of MSTN and C-terminal telopeptide of type I collagen (CTX) were measured using enzyme-linked immunosorbent assay (ELISA) based on Biotin double antibody sandwich technology (Shanghai YL Biont, China).

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences program [6]. T-test, LSD (Least Significant Variation), and Duncan's test were used to compare mean values among groups. Chi-Square test was used to compare percentages. The concentrations of statistical significance were defined as follows: $P \leq 0.05$: Significant; $P \leq 0.01$: Highly significant; $P \geq 0.05$ NS: Non-significant.

Results and Discussion

Table 1 represents that the proportion of women in the patient group (48, 87.27%) was significantly higher than in the HCs group (25, 71.43%). Regarding smoking, the patient group comprised 47 smokers, representing the majority (85.45%), in comparison with 8 non-smokers (14.55%). The results indicate that smoking is widespread among the patient group and may be a potential predisposition variable. In comparison with 3 affected individuals in the HCs group, the age group under 50 comprised 7 (12.73%) affected individuals. The age group of 50–60-year comprised 19 affected individuals (34.55%), in comparison with 9 (25.71%) of HCs. The 61–70-year age group comprised 22 affected individuals (40.00%), in comparison with 5 (14.29%) of HCs. This investigation displayed that the majority of MD (MD) affected individuals were woman, which is corresponding to preceding indication that influences of sex both illness phenotypes and onsets. Montañez *et al.* (2017) [7] stated that in tonic-dystrophic MD type 2, women frequently displayed early muscular tissue fragility, while men mostly experienced pain of muscular tissue, representing that these medical indices are sex-dependent. Correspondingly, sex-linked dissimilarities in the advances of congenital MD and responses to therapy have been detected in models of mice [8].

Table 1: Demographic distribution according to sex, smoking status, and age of affected individuals compared with the HCs group

Variable		Affected individuals No. (%)	HCs No. (%)	P-value
Sex	Male	7 (12.73%)	10 (28.57%)	0.0001 **
	Woman	48 (87.27%)	25 (71.43%)	
Smoking	Yes	8 (14.55%)	3 (8.57%)	0.0001 **
	No	47 (85.45%)	32 (91.43%)	
Age groups (year)	<50 yr.	7 (12.73%)	18 (51.43%)	0.0083 **
	50-60 yr.	19 (34.55%)	9 (25.71%)	
	61-70 yr.	22 (40.00%)	5 (14.29%)	
	>70 yr.	7(12.73%)	3 (8.57%)	
Total		55	35	--

** (P≤0.01).

The recent investigation represents that age distribution analysis revealed the highest illness burden among individuals aged 50–70 years, corresponding to previous studies highlighting age as a determining variable in illness onset and severity. It's observed that initial onset of type II myotonic MD forecasts greater involvement of multi-system, in addition to age-related pulmonary weakening linked with Duchenne MD (DMD) [9, 10]. When viewed collectively, these outcomes propose that age significantly impacts illness severity, advance and outcomes.

Independently, smoking damages skeletal muscular tissue via declining synthesis of proteins, raising oxidative stress, and weakening mitochondrial effectiveness. The smoking' extensive prevalence among affected individuals with diabetic neuropathy is a significant modifiable predisposition variable. Collectively, these outcomes propose that smoke may worsen muscular fragility of tissue in diabetic neuropathy affected individuals and highlight the significance of smoke cessation in clinical managements [11, 12].

The recent outcomes are corresponding to continuing research highlighting smoke, sexes, and ages, as significant predisposition variables for MD and its advances. Besides, the predominance of woman, the mid- to late-life burden, and the robust linking with smoke emphasize the interplay among environmental and biological variables in development of illness.

Table 2 represents the illnesses distributions among the group of patients. The most common coexisting illness (21.82%) was co-morbidity with diabetes and hypertension, followed via 20.0% of MD alone, and then hypertension with both MD (16.36%). Other coexisting illnesses comprised 9.09% of MD with hypertension and diabetes, hypothyroidism, problems of kidney, and liver illness (3.64% each), obesity (5.45%), diabetes mellitus and isolated hypertension (each 7.27%), while osteoporosis was the least common (1.82%). These outcomes reveal that the majority of affected individuals suffered from various chronic illnesses, with cardiometabolic circumstances (diabetes and hypertension) and MD being the most predominant and statistically significant (p≤0.01), representing the strong linking of these illnesses with the group of studied cases.

Table 2: Distribution of investigation samples via illness category among the patient group

Illnesses	No	Percentage (%)
Muscular tissue dystrophy	11	20.00
Hypertension	4	7.27
Diabetics	4	7.27
Obesity	3	5.45
Renal issue	2	3.64
Hypothyroid	2	3.64
Liver illness	2	3.64
Osteoporosis	1	1.82
Hypertension and diabetes	12	21.82
Hypertension and muscular tissue dystrophy	9	16.36
Hypertension, diabetes, and muscular tissue dystrophy	5	9.09
Total	55	100%
P-value	--	0.0001 **

** (P≤0.01).

This work detected that the most common coexisting illness was the co-occurrence of diabetes and hypertension with MD, representing a strong link through muscular illnesses and cardiometabolic circumstances. Initial vascular dysfunction was found in more than 50% of children with weakened regulation of pressure of blood, additional strengthening the close linking among diabetes, hypertension, and the problem of neuromuscular illnesses. The noticeable prevalence of MD and its co-occurrence with metabolic circumstances associated to muscular illnesses is a complex and prominent indicator of coexisting illness [13].

The anti-hypertensive agent losartan has been observed to worsen muscular tissue atrophy in cases of limbic dystrophy. On the other hand, deletion of MSTN in obese and diabetic mouses conserves functions of kidney and declines hypertension [14,15], emphasizing the complicated association among cardiac metabolism and muscular tissue integrity. It has been observed that diabetic affected individuals (9.1%) have hypertension, MD, or both, observing the metabolic influence on health of muscular tissues. Diabetic inflammation is linked with muscular tissue atrophy through the activation of NF-κB and STAT3 [16], and multiple endocrine conditions are linked with type 1 tonic muscular tissue atrophy [17], suggesting a shared endocrine-muscular tissue mechanism.

Less common coexisting illnesses, including obesity, kidney illness, hypothyroidism, liver illness, and osteoporosis, suggest systemic involvement. Diabetes, for example, is linked with Becker Muscle Dystrophy (BMD), and accelerated muscular tissue deterioration has also been observed in cystic fibrosis, further signifying that Becker dystrophy affected individuals may be at predisposition of metabolic dysfunction [18,19].

The results presented in Table 3 indicate significant variations among affected individuals and HCs across the studied parameters. The mean BMI was greater in affected individuals (31.72 ± 0.96 kg/m^2) than in HCs (29.02 ± 0.65 kg/m^2), and this raise was significant (t=2.601, p=0.0426). In contrast, skeletal muscular tissue bulk (SMM) was markedly lower in affected individuals (18.74 ± 0.73) in comparison with HCs (27.07 ± 1.31), with a highly significant variation (t=2.763, p=0.0001).

Table 3: Comparison of Body Bulk Index (BMI) and Skeletal Muscular Tissue Bulk Index (SMM) among affected individuals and HCs groups

Group	BMI (kg/m^2)	SMM or SMI (Kg/m^2)
	Means ±SE	
Affected individuals	31.72 ±0.96	18.74 ±0.73
HCs	29.02 ±0.65	27.07 ±1.31
T-test	2.601 *	2.763 **
P-value	0.0426	0.0001

* (P≤0.05), ** (P≤0.01)

These outcomes are corresponding to previous reports linking obesity to neuromuscular conditions. Obesity is a common endocrine complication in the DMD illness, accounting for approximately 50% of 11-year-old DMD affected individuals, and is linked with fractures and sleep apnea, which are often exacerbated via long-term glucocorticoid therapy [20, 21]. Elevated body bulk index (BMI) is a recurring and medically significant feature in all subtypes of DMD. Skeletal muscular tissue bulk (SMM) was significantly declined in affected individuals in comparison with HCs, corresponding to other studies that observed a marked decrease in lean muscular tissue bulk in Facioscapulohumeral Dystrophy (FSHD) despite similar BMIs among the groups of cases and HC. Correspondingly, loss of muscular tissue and progressive gain of fat have been detected in the DMD [22, 23]. These outcomes highpoint the paradox of declined muscular tissue bulk and raised BMI, representing the sequential alterations in composition of body that happen with the illness. The metabolic influences of obesity, hyperinsulinemia and resistance of insulin, in affected individuals with DMD illness and the BMD are well recognized through their influence on distribution of GLUT4 in muscular tissues [24, 25]. The recent outcomes also propose that raised declined muscular tissue bulk and obesity synergistically participate to metabolic dysfunction, including resistances of insulin and systemic inflammations. Generally, these data emphasize that management of weight is an integral portion of therapy of MD, aiming to improve metabolic

difficulties and enhance functional outcomes.

The mean serum MSTN level in the recent investigation, as shown in the figure, was slightly higher in the affected individuals (456.44 ± 44.78 ng/mL) in comparison with the HCs group (443.08 ± 35.07 ng/mL). However, this variation was not statistically significant (t=124.76, p=0.8320). This indicates that despite the numerical variation, MSTN concentrations did not differ significantly among the two groups, suggesting that the presence of illness in the patient group may not have a direct effect on serum MSTN concentrations.

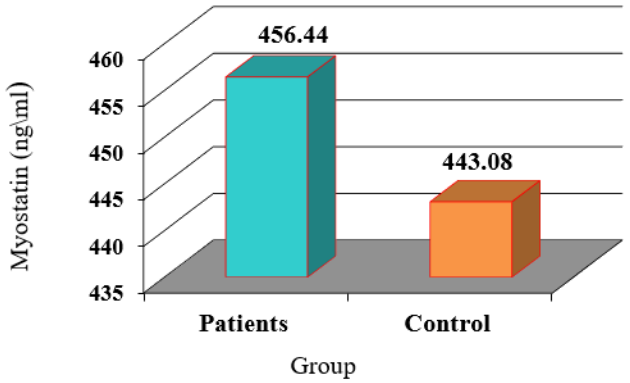

Figure 1: Comparison among affected individuals and HCs in Myostain

The recent MSTN outcomes contradict previous reports showing declined circulating MSTN in neuromuscular conditions. Significantly lower concentrations were found in seven genetic circumstances and correlated with illness severity [26]. Low MSTN concentrations have also been observed in the DMD illness and spinal muscular atrophy (SMA) [27], supporting its potential as a biomarker for these circumstances. Conversely, the recent outcomes are more in line with other studies showing elevated MSTN expression in atrophic muscular tissue [28], representing illness stage or tissue-specific organization. In BMD, MSTN concentrations vary based on the therapy [29]. Consequently, these discrepancies probably form the impacts of illness type and advances, therapies, and methodological variations in detections.

Its circulating concentrations may not consistently reflect illness activity, although MSTN is a known negative regulator of muscular tissue growth [4]. The inconsistent results of inhibition trials of MSTN highpoint the requirement for a more detailed grasp of its biological roles [30]. Generally, the absence of significant variations in serum MSTN concentrations among groups of cases and HC emphasizes the complexity of its regulations. Consequently, future works should classify MSTN via therapy status, severity, and subtype of illness, and participate it with complementary biomarkers to improve diagnostic monitoring and accuracy.

The results in Figure 2 indicate that mean serum CTX concentrations were slightly lower in affected individuals (17.69 ± 0.08 ng/ml) in comparison with the HCs group (19.28 ± 2.10 ng/ml); however, this variation was not statistically significant, as evidenced via the t-test value (6.152) and the p-value of 0.6074, which is well above the significance threshold of 0.01. This suggests that CTX concentrations do not differ statistically significantly among affected individuals and HCs groups, implying that bone resorption activity, as measured via CTX, may not be significantly affected

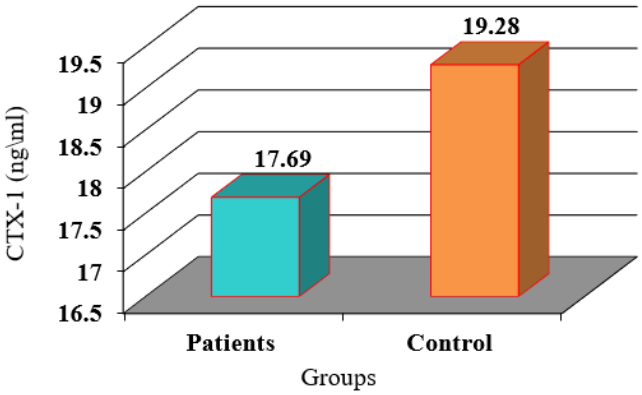

Figure 2: Comparison among affected individuals and HCs in CTX-1

This observation suggests that CTX concentrations may exhibit some variability among patient and HCs groups, but they may not serve as a strong, independent marker in this context. In comparison with preceding research, the recent outcomes are corresponding to certain researches and diverge from others. For instance, a significant positive correlation was observed among glycemic markers, mostly HbA1c, and CTX [31], with individuals

displaying the highest concentrations of CTX. Likewise, a biphasic linking among metabolism of glucose and CTX was emphasized, with moderate concentrations of CTX conferring protective impacts, while raised concentrations improve the dysglycemia predisposition [32]. These outcomes emphasize the probable function of CTX as a metabolic biomarker. On the other hand, the recent investigation did not observe such correlation, perhaps because of variations linked to properties of population, type of illness, size of sample, or therapeutic interventions.
An investigation appraising CTX as a predictor of predisposition of osteonecrosis following aggressive dental procedures in affected individuals taking bisphosphonates observed that the outcomes did not assist CTX as a reliable predictor [33]. Another investigation established that role of CTX encompasses beyond metabolism of bones, as raised concentrations of CTX were negatively linked with measures of physical performance, including mobility and balance, in older adults [34]. Values of reference have been updated through groups of sex and age, with an emphasis on the physiological variability of CTX, predominantly during aging and growth [35].

Table 4: Comparison of MSTN and CTX-1 concentrations among males and women

Parameters	Means ±SE		P-value
	Male	Woman	
MSTN (ng\ml)	428.03 ±109.08	460.58 ±49.15	0.812 NS
CTX-1 (ng\ml)	15.27 ±5.16	18.04 ±2.29	0.360 NS

NS: Non-Significant

The results in Table 4 revealed a low level of both MSTN and CTX-1 in male in comparison with woman in comparison with woman. However, the p-values for both comparisons (0.812 for MSTN and 0.360 for CTX-1) indicate that these variations were not statistically significant, suggesting that gender did not exert a meaningful effect on either parameter in this sample.

These results align with an investigation that revealed insignificant sex-related variation in urinary CTX-II among healthy individuals or osteoarthritis affected individuals, despite slightly higher mean values in women [36].

Conclusions

Musculoskeletal circumstances are linked with alterations in composition of body and serious coexisting illnesses; however, circulating CTX-1 and MSTN alone may not be valid self-determining biomarkers. Their understanding needs incorporation with metabolic, medical and demographic profiles to enhance prognostic and diagnostic accuracy. While concentrations of CTX represent limited variability of sex, MSTN displays slight biological variations. Consequently, although no significant variations of sex were detected in this investigation, preceding evidence proposes that MSTN may apply sex-linked impacts on health of muscular tissues, calling for additional investigation in more and larger diverse cohorts.

Conflict of interest

The authors stated no conflict of interest.

References

1. Iafelice R. Hold on to your muscular tissue, be free of illness: Optimize your muscular tissue bulk to battle aging and illness while promoting total fitness and lasting weight loss. Gatekeeper Press.2023
2. Xia Q, Huang X, Huang J, Zheng Y, March ME, Li J, and Wei Y. The role of autophagy in skeletal muscular tissue illnesses. *Front. physiol*. 2021; 12: 638983.doi:10.3389/fphys.2021.638983.
3. Chen MM., Zhao YP, Zhao Y, Deng SL, and Yu, K. Regulation of MSTN on the growth and development of skeletal muscular tissue. *Front. Cell Dev. Biol*. 2021; *9*: 785712.doi.org/10.3389/fcell.2021.785712.
4. Dewasi G, Nagda P. Bahl G, Jain V. and Gupta, SK. MSTN-driven muscular tissue hypertrophy: A double-edged sword in muscular tissue physiology. *J. of Rare Dis.*2025; 4 (1): 29.:29. doi.org/10.1007/s44162-025-00086-x
5. Meier C, Eastell R, Pierroz DD, Lane NE, Al-Daghri N, Atsushi Suzuki A, Napoli N, Mithal A, Chakhtoura M, and El-Hajj Fuleihan G.

Biochemical Markers of Bone Fragility in Affected individuals with Diabetes. *J. Clin. Endocrinol. Metab*. 2023, 108(10): 923–936.doi: 10.1210/clinem/dgad255.

6. SPSS (2019). Statistical Packages of Social Sciences-SPSS/ IBM Statistics 26 step via step. 16th Edition.
7. Montagnese F, Mondello S, Wenninger S, Kress W, and Schoser B. Assessing the influence of age and gender on the phenotype of myotonic dystrophy type 2. *J. Neurol.* ,2017; *264* (12): 2472-2480. doi: 10. 1007/ s00415-017-8653-2.
8. Chakraborty D, Borthakur S, Sarkar R, and Singh MD. Gender disparities in myotonic dystrophy 1. *Life Sci.,* 2025; 373: 123659.doi: 10.1016/j.lfs.2025.123659.
9. Ivanovic V, Peric S, Pesovic J, Tubic R, Bozovic I, Petrovic Djordjevic, I., Savic-Pavicevic, D, Meola, G. and Rakocevic-Stojanovic, V. Medical score for early diagnosis of myotonic dystrophy type 2. *Neuro. Sci.* 2023; 44(3): 1059-1067.dio: 10.1007/s10072-022-06507-9.
10. Crescimanno G, Greco F, Bertini M, Maltese, G. and Marrone, O. Age-related burden of swallowing in adult affected individuals affected via Duchenne MD. *J. Neuromuscul. Dis*. 2023 10(5): 955-962. doi: 10.3233/JND-230055.
11. Decker ST, Kwon OS, Zhao J, Hoidal JR, Heuckstadt T, Richardson RS, Sanders KA, and Layec G. Skeletal muscular tissue mitochondrial adaptations induced via long-term cigarette smoke exposure. *Am. J. Physiol. Endocrinol. Metab.* 2021. 321(1): 80-89. doi: 10.1152/ajpendo.00544.2020.
12. Nowak A and Pawliczak R. Cigarette smoking and oxidative stress. Alergologia *Polska-Polish Journal of Allergology*, 2022. 9(2): 89-98. doi. org/ 10.5114 /pja. 2022. 116285.
13. Marui FR, Bianco HT, Bombig MTN, Palmeira, NG, Thalenberg JM, Povoa FF, Izar MCDO, Fonseca FAH, Oliveira ASD, and Povoa RM. Behavior of blood pressure variables in children and adolescents with Duchenne MD. *Arq Bras Cardiol.*, 2018; 110(6): 551-557.doi: 10.5935/abc.20180085.
14. White Z, Milad N, Tehrani AY, Chen WWH, Donen G, Sellers SL, and Bernatchez P. Angiotensin II receptor blocker losartan exacerbates muscular tissue damage and exhibits weak blood pressure-lowering activity in a dysferlin-null model of Limb-Girdle MD type 2 B. *PLoS One*; 2019. 14(8): e0220903.doi: 10.1371/ journal. pone.0220903.
15. Butcher JT, Mintz JD, Larion S, Qiu S, Ruan, L, Fulton DJ, and Stepp, DW, raised muscular tissue bulk protects against hypertension and renal injury in obesity. *J Am Heart Assoc,* 7(16): e009358. doi: 10.1161/ JAHA.118.009358.
16. Perry BD, Caldow MK, Brennan-Speranza TC, Sbaraglia M, Jerums G, Garnham A, Wong C, Levinger P, ul Haq MA, Hare DL, and Price SR. Muscular tissue atrophy in affected individuals with Type 2 Diabetes Mellitus: roles of inflammatory pathways, physical activity, and exercise. *Exerc Immunol Rev.* 2016; 22: 94-109.
17. Takeshima K, Ariyasu H, Ishibashi T, Kawai S, Uraki S, Koh J, Ito H, and Akamizu T. Myotonic dystrophy type 1 with diabetes mellitus, mixed hypogonadism, and adrenal insufficiency. *Endocrinol. Diabetes Metab. Case Rep.*2018;18: 17-143. doi: 10.1530/EDM-17-0143.
18. Motohashi K, Murakami T, Otani D, Nakamura T, Kato T, Seguchi O, Ogura M, Yabe D, and Inagaki N. Decreased β-cell function in a case with Becker MD accompanied via post-transplant diabetes. *Endocrinol. Diabetes Metab. Case Rep.* 2025(3): e250038. doi: 10.1530/EDM-25-0038.
19. Berli MC, Azaiez N, Götschi T, Pfirrmann CW, Uçkay I, Sutter R, Waibel FW, and Rosskopf AB. Muscular tissue atrophy in diabetic affected individuals with Charcot foot: a case-HCs investigation. *Skeletal Radiol.* 2023;52(9):1661-1668. doi: 10.1007/s00256-023-04328-1.
20. Weber DR, Hadjiyannakis S, McMillan HJ. Noritz G, and Ward LM. Obesity and endocrine management of the patient with Duchenne MD. *Pediatrics,*2018; 142(Supplement_2): S43-S52.doi: 10.1542/peds.2018-0333F.
21. Billich N, Adams J, Carroll K, Truby H, Evans M, Ryan MM, and Davidson ZE. The relationship

among obesity and medical outcomes in young people with Duchenne MD. *Nutrients.* 2022; 14(16): 3304.doi: 10.3390/nu14163304.

22. Vera K, McConville M, Kyba M, and Keller-Ross M. Sarcopenic obesity in facioscapulohumeral MD. *Front. Physiol.* 2020; 11: 1008. doi: 10.3389/fphys.2020.01008.
23. Billich N, Evans M, Truby H, Ryan MM, and Davidson ZE. The association among dietary variables and body weight and composition in boys with Duchenne MD. *J Hum Nutr Diet.* 2022;35(5):804-815. doi: 10.1111/jhn. 12987. Epub 2022 Feb 1.
24. Cannalire G, Biasucci G, Sambati V, Toschetti T, Bellani M, Shulhai AM, Casadei F, Di Bari ER, Ferraboschi F, Parenti C, and Pera, MC. Beyond Muscular Tissue Fragility: Unraveling Endocrine and Metabolic Dysfunctions in DMD, a Narrative Review. *Biomedicines* 2025; 13(7): 1613. doi.org/10.3390/biomedicines13071613.
25. Thiab S, Azeez JM, Anala A, Nanda M, Khan S, Butler AE, and Nandakumar M. Human-Induced Pluripotent Stem Cells (iPSCs) for Illness Modeling and Insulin Target Cell Regeneration in the Therapy of Insulin Resistance: A Review. *Cells.* 2025 ;14(15):1188. doi: 10.3390/cells14151188.
26. Bello L, Hoffman EP, and Pegoraro E. Is it time for genetic modifiers to predict prognosis in Duchenne MD? *Nat. Rev. Neurol*. 2023;19(7):410-423. doi: 10.1038/s41582-023-00823-0.
27. Piemonte F, Petrillo S, Capasso A, Coratti G, D'Amico A, Catteruccia M, Pera MC, Palermo C, Pane M, Abiusi E, and Cicala G. MSTN Concentrations in SMA Following Illness-Modifying Therapys: A Multi-Center Investigation. *Ann. Clin. Transl. Neurol.* 2025 ;12 (7): 1368-1377. doi: 10.1002/ acn3.70070.
28. Sun Z, Xu D, Zhao L, Li X, Li S, Huang X, Li C, Sun L, Liu B, Jiang Z., and Zhang L. A new therapeutic effect of fenofibrate in Duchenne MD: The promotion of MSTN degradation. Br. J. pharmacol. 2022. 179(6): 1237-1250.doi: 10.1111/ bph.15678. Epub 2021 Dec 23.
29. Marozzo R, Pegoraro V, and Angelini C. MiRNAs, MSTN, and muscular tissue MRI imaging as biomarkers of medical features in Becker MD. *Diagnostics (Basel).* 2020; 10(9), p.713.doi: 10.3390/ diagnostics10090713.
30. Wagner KR. The elusive promise of MSTN inhibition for MD. *Curr Opin Neurol.* 2020; 33(5): 621-628.doi: 10.1097/WCO.0000000000000853.
31. Xuan Y, Sun LH, Liu DM, Zhao L, Tao B, Wang WQ, Zhao HY, Liu JM, and Ning G. Positive association among serum concentrations of bone resorption marker CTX and HbA1c in women with normal glucose tolerance. *J. Clin. Endocrinol. Metab.* 2015 100(1): 274-281. doi: 10.1210/jc.2014-2583.
32. Liu TT, Liu DM, Xuan Y, Zhao L, Sun LH, Zhao DD, Wang XF, He Y, Guo XZ, Du R, and Wang JQ, Liu JM, Zhao HY, and Tao B. The association among the baseline bone resorption marker CTX and incident dysglycemia after 4 years. *Bone Res.* 2017; 4:5:17020. doi: 10.1038/ boneres. 2017.20.
33. Salgueiro M, Stribos M, Zhang LF, Stevens M, Awad ME, and Elsalanty M. Value of pre-operative CTX serum concentrations in the prediction of medication-related osteonecrosis of the jaw (MRONJ): a retrospective medical investigation. *EPMA J.* 2019; *10*(1): 21-29. doi: 10.1007/s13167-019-0160-3.
34. Kirk B, Lieu N, Vogrin S, Sales M, Pasco, JA, and Duque G. Serum concentrations of C-Terminal Telopeptide (CTX) are linked with muscular tissue function in community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2022; 77(10): 2085-2092.doi: 10.1093/gerona/glac008.
35. Chubb SAP, Vasikaran SD, and Gillett MJ. Reference intervals for plasma β-CTX and P1NP in children: a systematic review and pooled estimates. *Clin. Biochem.* 2023.118: 110582. doi: 10.1016/j. clinbiochem. 2023.05.001. Epub 2023 May 13.
36. Arunrukthavon P, Heebthamai D, Benchasiriluck P, Chaluay S, Chotanaphuti T, and Khuangsirikul S. Can urinary CTX-II be a biomarker for knee osteoarthritis? *Arthroplasty*. 2020.2(1): 6. doi: 10. 1186/ s42836-020-0024-2.