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Expression and clinical significance of LncRNA Kcnq1ot1 in type 2 diabetes mellitus patients with osteoarthritis

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Abstract

Objective We aimed to investigate the expression of lncRNA Kcnq1ot1 in T2DM patients with OA, as well as its correlation with serum inflammatory factors and clinical outcomes of the patients.

Methods This prospective observational cohort study included a total of 50 patients with type 2 diabetes mellitus (T2DM), 50 patients with osteoarthritis (OA), and 51 patients with both T2DM and OA between March 2020 and March 2023. The serum TNF-α, interleukin (IL)-6, IL-1β and C-reactive protein (CRP) levels were measured using enzyme-linked immunosorbent assay (ELISA). To determine the expression of LncRNA Kcnq1ot1, RT-qPCR was used. Demographic, clinical statistics, lipid metabolism and nutritional indicators were collected. All data used SPSS 26.0 to statistical analyses.

Results The T2DM + OA group had significantly higher BMI and LDLC levels compared to the T2DM group ($p < 0.05$). The serum levels of LncRNA Kcnq1ot1 were significantly higher in the T2DM + OA group compared to the OA group and T2DM group ($p < 0.05$). Pearson's analysis supported a positive correlation between LncRNA Kcnq1ot1 and IL-6 and IL-1β levels. In addition, LncRNA Kcnq1ot1 could be a potential biomarker for diagnosing the occurrence of T2DM patients with OA. Moreover, LncRNA Kcnq1ot1, BMI, IL-6, Low density lipoprotein cholesterol (LDLC) were the risk factors for T2DM patients with OA.

Conclusion This study showed that the serum LncRNA Kcnq1ot1 levels was remarkably elevated in T2DM patients with OA. This study might provide new targets and a comprehensive approach to treatment in T2DM patients with OA.

Keywords LncRNA Kcnq1ot1, T2DM, OA, Inflammatory factors

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Introduction

The incidence of diabetes mellitus (DM) is increasing worldwide [1, 2]. According to statistics, the global prevalence of DM is projected to reach 7.7% (366 million people) by 2030 and rise to 5.9 billion by 2035 [3]. China has seen a tenfold increase in the prevalence of DM in the past 30 years, making it the country with the largest population of individuals with DM in the world [4, 5]. As the incidence of diabetes continues to rise, the occurrence of related complications also increases [6]. Osteoarthritis (OA) is a common complication in patients with type 2 diabetes mellitus (T2DM) [7]. Evidence suggests that diabetes may be an independent risk factor for OA [8]. Studies have shown that the risk of developing OA in diabetes patients is more than four times higher than in non-diabetic individuals, and the incidence increases with the duration of diabetes, with higher rates in patients with poor long-term glycemic control [9, 10]. Therefore, there is an urgent need to investigate the pathogenesis of DM-associated OA and to prevent diabetic osteoarthritis from the perspective of early risk factors for disease progression.

Long non-coding RNAs (lncRNAs) are a class of non-coding RNAs with a length exceeding 200 nucleotides. They can affect the expression of downstream target mRNAs through various pathways, regulating target proteins, and therefore have important implications in many physiological and pathological processes [11, 12]. The full name of lncRNA Kcnq1ot1 is KCNQ1 overlapping transcript 1, located at the KCNQ1 locus on 11p15.5, and it is involved in the pathophysiology of various diseases [13]. Recent studies have demonstrated that LncRNA Kcnq1ot1 influences cell proliferation, apoptosis, and fibrosis in human renal proximal tubular epithelial cells under hyperglycemic conditions by regulating the miR-18b-5p/SORBS2 axis and the NF-κB pathway [14]. Furthermore, lncRNA Kcnq1ot1 alleviates the functional impairment of osteoarthritic chondrocytes, specifically by enhancing their proliferation, reducing apoptosis, and improving the synthesis of extracellular matrix components through the miR-218-5p/PIK3C2A axis [15]. These suggested that lncRNA Kcnq1ot1 played a certain role in the progression of diabetes and osteoarthritis. However, there is currently no clinical research on the expression and significance of lncRNA Kcnq1ot1 in T2DM patients with OA.

In this prospective observational cohort study, we aimed to investigate the expression of lncRNA Kcnq1ot1 in T2DM patients with OA, as well as its correlation with inflammatory factors and clinical outcomes of the patients. We selected LncRNA Kcnq1ot1 due to its emerging role in the regulation of inflammatory processes and its potential involvement in metabolic disorders, particularly type 2 diabetes mellitus (T2DM). Recent studies have indicated that LncRNA Kcnq1ot1 may play a critical role in modulating inflammatory pathways, which are known to be significantly associated with both T2DM and osteoarthritis (OA). Additionally, we included Body Mass Index (BMI) as it is a well-established indicator of obesity and metabolic health, which are critical factors in the pathogenesis of T2DM. Interleukin-6 (IL-6) was chosen due to its recognized role as a pro-inflammatory cytokine that is often elevated in both T2DM and OA, indicating systemic inflammation. Low-Density Lipoprotein Cholesterol (LDLC) was included because of its association with cardiovascular risks, which are heightened in T2DM patients.

Methods

Subjects

This prospective observational cohort study included a total of 50 patients with T2DM, 50 patients with OA, and 51 patients with both T2DM and OA, treated at our hospital between March 2020 and March 2023. The cohort consisted of 38 males and 63 females, providing a comprehensive view of gender representation in the study population. The diagnosis of T2DM followed the criteria outlined in the Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes (2017 edition) [16], including: (1) typical symptoms of diabetes (polyuria, polydipsia, polyphagia, unexplained weight loss); (2) fasting plasma glucose concentration higher than 7.0 mmol/L, or plasma glucose concentration higher than 11.1 mmol/L, or a 2-hour plasma glucose concentration higher than 11.1 mmol/L during oral glucose tolerance test (OGTT). The diagnosis of OA was based on the criteria outlined in the Chinese Guidelines for the Diagnosis and Treatment of Osteoarthritis (2019 edition) [17], which included clinical symptoms and imaging findings after excluding other types of joint diseases. Specifically: (1) joint pain during activity; (2) morning stiffness, characterized by joint stiffness and tightness lasting 15 to 30 min after waking up; (3) radiographic evidence of asymmetric joint space narrowing, subchondral bone sclerosis and/or cystic changes, and osteophyte formation. The diagnosis of T2DM with OA was made when the criteria for both T2DM and OA were met. All patients included in the study were aged 18 years or older. The exclusion criteria were as follows: (1) patients with gestational diabetes mellitus or type 1 diabetes mellitus; (2) patients who had recently received anti-inflammatory or immunosuppressive therapy; (3) patients with severe infections, severe liver or kidney diseases, malignancies, or cardiovascular dysfunction; (4) patients with acute complications of diabetes or other severe complications; (5) patients with rheumatoid arthritis, gout, ankylosing spondylitis, or other spinal joint diseases. The study was approved by our hospital ethics committee. All subjects agreed to

participate in this study and signed an informed consent form.

Blood sampling measurement

The serum TNF-α, interleukin (IL)-6, IL-1β and C-reactive protein (CRP) levels were measured using enzyme-linked immunosorbent assay (ELISA). Blood samples of fasting cubital venous (5 mL) were collected within 24 h after admission for all cases. Samples were centrifuged at 2000 g for 15 min, following with ELISA tested using commercially available kits (TNF-α MBS824943 MyBioSource, IL-6 MBS175877 MyBioSource, CRP MBS177184 MyBioSource, IL-1β MBS175901 MyBioSource).

Reverse transcription-quantitative polymerase chain reaction (RT-qPCR)

To determine the expression of LncRNA Kcnq1ot1, RT-qPCR was used. To obtain RNA from serum of all patients, we utilized the RNAiso Plus kit (procured from Takara, Japan), and subsequently performed reverse transcription into cDNA using the Prime-ScriptTM one-step qRT-PCR kit (obtained from TAKARA, Dalian, China). For RT-qPCR, we employed the SYBR Premix ExTaq (TaKaRa) and the ABI PRISM7300 Sequence Detection System (from Applied Biosystems). The primer sequences of LncRNA Kcnq1ot1 is: Forward 5'-TTGGTAGGATTT TGTTGAGG-3', Reverse 5'-CAACCTTCCCCTACTAC C-3'. GAPDH served as an internal control. The mRNA expressions were calculated by the $2^{-\Delta\Delta}$Ct method.

Data collection and scale scoring

Demographic and clinical characteristics such as age, BMI, gender, diastolic blood pressure (DBP), systolic blood pressure (SBP), etc., were documented. A routine blood test was conducted using an automated biochemical analyzer (Hitachi 7600, Hitachi Corporation, Japan), and measurements of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting plasma glucose (FPG) were recorded.

Statistical analysis

Normally distributed data are presented as mean ± standard deviation (SD), while non-normally distributed data are presented as median (range). One-way analysis of variance (ANOVA) followed by Tukey's post hoc test was used for comparisons among the three patient groups. Correlation analysis was performed using Pearson's rank correlation and Spearman's rank correlation. Receiver operating characteristic (ROC) curve analysis was used to analyze the role of LncRNA Kcnq1ot1 in diagnosing the occurrence of osteoarthritis in patients with diabetes. Logistic regression analysis was conducted to identify risk factors for the occurrence of osteoarthritis in patients with diabetes. A p-value of < 0.05 was considered statistically significant. All data were analyzed using SPSS 26.0.

Results

Clinical characteristics of all participants

This prospective observational cohort study included 50 T2DM patients (T2DM group, $n = 50$), 50 OA patients (OA group, $n = 50$) and 51 T2DM patients with OA (T2DM + OA group, $n = 51$). When comparing demographic data and clinical data among the three groups, we found that significantly lower FPG and TG levels in the OA group compared to the T2DM + OA group (Table 1, $p < 0.05$). Furthermore, the T2DM + OA group had significantly higher BMI and LDLC levels compared to the T2DM group ($p < 0.05$). There were no significant differences in age, gender, SBP, DBP, TC, and HDLC among the three groups.

Serum levels of LncRNA Kcnq1ot1 and inflammatory factors in all patients

To further investigate the relationship between LncRNA Kcnq1ot1, inflammatory cytokines, and the occurrence of OA in T2DM patients, we measured the levels of serum LncRNA Kcnq1ot1, TNF-α, IL-6, IL-1β, and CRP using PCR and ELISA in all three patient groups. As shown in Fig. 1, the serum levels of LncRNA Kcnq1ot1

Table 1 Demographic and clinical data of all subjects

Variable	T2DM + OA, $n = 51$	T2DM, $n = 50$	OA, $n = 50$	P_1	P_2
Age, y	56 (48–67)	60 (43–71)	58 (48–67)	0.168	0.883
Sex, *n* (%)	29 (56.9)	28 (56.0)	27 (54.0)	0.999	0.776
BMI	25.15 ± 2.07	23.61 ± 2.51	25.41 ± 1.94	0.001	0.822
SBP (mmhg)	134.46 ± 13.54	132.65 ± 14.45	130.79 ± 14.72	0.800	0.400
DBP (mmhg)	87.63 ± 10.80	89.71 ± 9.10	86.30 ± 10.34	0.555	0.783
FPG (mmol/L)	9.15 ± 1.35	8.80 ± 1.52	5.55 ± 0.82	0.349	< 0.001
TC (mmol/L)	3.43 ± 0.65	3.20 ± 0.66	3.29 ± 0.67	0.177	0.538
TG (mmol/L)	1.85 ± 0.35	1.76 ± 0.34	1.48 ± 0.51	0.524	< 0.001
HDLC (mmol/L)	1.20 ± 0.15	1.16 ± 0.15	1.18 ± 0.15	0.427	0.698
LDLC (mmol/L)	2.72 ± 0.55	2.40 ± 0.52	2.72 ± 0.52	0.008	0.999

P_1 comparison between T2DM + OA group and T2DM group. P_2 comparison between T2DM + OA group and OA group

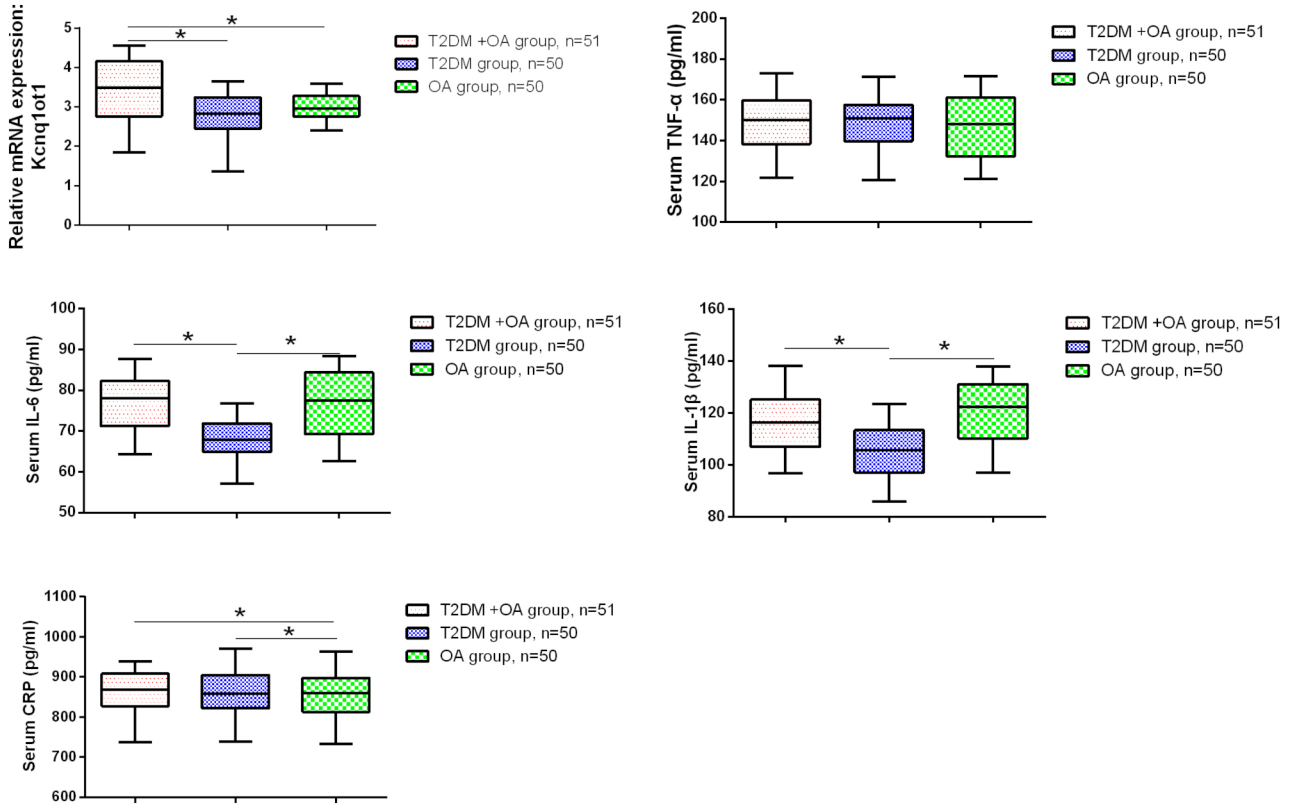

Fig. 1 Comparisons of LncRNA Kcnq1ot1 and other serum biomarkers in all subjects. *$P < 0.05$ vs. corresponding group

Table 2 Correlation analysis among LncRNA Kcnq1ot1, TNF-α, IL-6, IL-1β and CRP

	LncRNA Kcnq1ot1	CRP	IL-6	IL-1β	TNF-α
LncRNA Kcnq1ot1					
Pearson's correlation	1	-0.073	0.196	0.213	0.074
p		0.468	0.049	0.033	0.462
CRP					
Pearson's correlation	-0.073	1	0.022	-0.063	-0.068
p	0.468		0.824	0.535	0.498
IL-6					
Pearson's correlation	0.196	0.022	1	0.383	-0.017
p	0.049	0.824		< 0.001	0.863
IL-1β					
Pearson's correlation	0.213	-0.063		1	-0.089
p	0.033	0.535	0.383		0.375
TNF-α			< 0.001		
Pearson's correlation	0.074	-0.068	-0.017	-0.089	1
p	0.462	0.498	0.863	0.375	

were significantly higher in the T2DM + OA group compared to the OA group ($p < 0.05$). Additionally, the T2DM + OA group had significantly higher levels of LncRNA Kcnq1ot1, IL-6, and IL-1β in serum compared to the T2DM group ($p < 0.05$). Pearson's analysis supported a positive correlation between LncRNA Kcnq1ot1 and IL-6 and IL-1β levels (Table 2).

Correlation between serum LncRNA Kcnq1ot1 levels and patients' clinical outcome

Subsequently, Spearman's rank correlation analysis was performed to examine the relationship between LncRNA Kcnq1ot1 levels and clinical factors in all patients. As shown in Table 3, there was no significant correlation between LncRNA Kcnq1ot1 levels and age, BMI, SBP, DBP, TG, LDLC, and HDLC. However, LncRNA

Table 3 Correlation between serum LncRNA Kcnq1ot1 levels and the clinical data of the patients

Variable	LncRNA Kcnq1ot1	
	Spearman's correlation	*P*
Age	-0.194	0.052
BMI	0.096	0.339
SBP	-0.042	0.674
DBP	0.069	0.490
FPG	0.284	0.004
TC	0.208	0.037
TG	-0.013	0.897
HDLC	0.100	0.322
LDLC	0.084	0.403

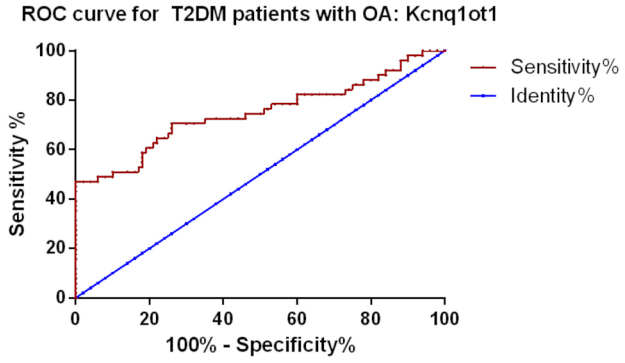

Fig. 2 ROC curves for LncRNA Kcnq1ot1 for the occurrence of osteoarthritis in patients with T2DM

Table 4 Logistic regression for risk factors of T2DM patients with OA

Variables	Odds ratio	95% CI	*P*
Age	1.094	0.957–1.251	0.189
Sex	1.837	0.262–13.408	0.532
BMI	0.550	0.329–0.918	0.022
SBP	0.950	0.884–1.021	0.160
DBP	1.028	0.939–1.125	0.547
FPG	1.029	0.539–1.966	0.931
TC	1.073	0.182–6.336	0.938
TG	1.367	0.064–29.430	0.842
HDLC	0.024	0.001–11.578	0.237
LDLC	0.119	0.019–0.746	0.023
CRP	0.997	0.981–1.014	0.748
IL-6	0.650	0.509–0.831	0.001
IL-1β	0.897	0.084–1.001	0.051
TNF-α	0.999	0.931–1072	0.978
LncRNA Kcnq1ot1	0.115	0.020–0.688	0.016

Kcnq1ot1 levels were positively correlated with serum FPG and TC levels ($p < 0.05$). These results suggested that LncRNA Kcnq1ot1 is associated with clinical outcomes in patients.

Diagnosis value of LncRNA Kcnq1ot1 for the occurrence of osteoarthritis in patients with T2DM

We draw ROC curves to assess the diagnosis value of LncRNA Kcnq1ot1 for the occurrence of osteoarthritis in patients with T2DM (Fig. 2). The results indicated that LncRNA Kcnq1ot1 could be a potential biomarker for diagnosing the occurrence of T2DM patients, the AUC of LncRNA Kcnq1ot1 was 0.748, with a cutoff value of 3.14, sensitivity of 70.6%, and specificity of 76.0%.

Logistic regression for risk factors of T2DM patients with OA

Finally, we used entry method for logistic regression to analyze the risk factors of T2DM patients with OA. For logistic regression, we used the entry method. It was found that LncRNA Kcnq1ot1, BMI, IL-6, LDLC were the risk factors for T2DM patients with OA (Table 4).

Discussion

For patients with T2DM complicated by OA, effective diagnostic methods are lacking in the early stages, often leading to the detection of pathological changes only after structural and functional alterations have occurred, missing the optimal treatment window. Moreover, the altered microenvironment caused by diabetes further increases the difficulty of treatment and affects prognosis [8]. Therefore, we attempted to explore the risk factors for T2DM complicated by OA and identify serum biomarkers indicative of changes. Our findings revealed a significant elevation in serum levels of lncRNA Kcnq1ot1 in patients with T2DM complicated by OA.

More and more studies have focused on changes in serum biomarkers in patients with T2DM complicated by OA. Luo et al. found that the expression levels of matrix metalloproteinases (MMPs) in synovial fluid were significantly higher in patients with DM with OA compared to OA patients and healthy controls [18]. Wang et al.'s meta-analysis indicated an inverse relationship between serum magnesium levels and the prevalence of DM, metabolic syndrome (MetS), and hyperuricemia (HU) in OA patients [19]. Ashoor et al. confirmed that the serum level of Insulin-like growth factor 1 (IGF-1) was significantly decreased in the DM + OA group compared to the DM or OA group alone [20]. Maxime et al. suggested that distinct lipid and protein profiles in articular cartilage between OA patients with and without DM, suggesting differences in several metabolic pathways such as lipid regulation [21]. These findings are consistent with our study results. After measuring the levels of lipid metabolism factors in the three patient groups, we found that the TC level was altered in T2DM patients, and the LDLC level was altered in OA patients compared to T2DM + OA patients. We also found that T2DM + OA patients had higher BMI, which may be associated with

changes in lipid metabolism levels and a higher prevalence of MetS in overweight/obese patients [22].

Activation of the LncRNA Kcnq1ot1 pathway has been found to enhance inflammatory responses in various diseases. In atherosclerosis, Knockdown of Kcnq1ot1 activates the miRNA and tumor necrosis factor-α-induced protein 1 (TNFAIP1) pathway, inhibiting oxidative low-density lipoprotein (ox-LDL)-induced inflammatory response [23]. In transient ischemic attack (TIA), the expression level of LncRNA Kcnq1ot1 is positively correlated with the inflammatory marker high-sensitivity C-reactive protein (hs-CRP) levels, suggesting its involvement in the regulation of TIA-induced inflammation [24]. Moreover, LncRNA Kcnq1ot1 can serve as a molecular sponge for miR-130a-3p, upregulating relevant target proteins and enhancing inflammatory responses, thereby exacerbating hydrogen peroxide (H2O2)-mediated myocardial cell injury [25]. In diabetic nephropathy, Kcnq1ot1 is overexpressed in human glomerular mesangial cells (HGMC) cultured in high glucose (HG), and it mediates proliferation, extracellular matrix (ECM) accumulation, inflammation, and oxidative stress in HG-treated HGMC cells [26]. These research findings suggest a close association between LncRNA Kcnq1ot1 and inflammatory responses. Therefore, in our study, we measured the levels of serum LncRNA Kcnq1ot1 and inflammatory markers in all patients. The results showed a significant elevation of serum LncRNA Kcnq1ot1 levels in T2DM patients with OA, positively correlated with IL-6 and IL-1β. Additionally, we found a positive correlation between serum LncRNA Kcnq1ot1 levels and LDLC levels, indicating a potential association between LncRNA Kcnq1ot1 and lipid metabolism in patients. Similarly, Aili et al. demonstrated that knockdown of Kcnq1ot1 improved cell viability and suppressed inflammatory response, thereby ameliorating OA [27]. Liu et al. also confirmed the critical role of Kcnq1ot1-related signaling pathways in osteoarthritis [28]. Interestingly, Y Liu et al. reported contrary findings, suggesting that overexpression of Kcnq1ot1 reduces chondrocyte dysfunction by targeting miRNA and activating the PI3K-related pathway [15]. These results collectively highlight the important role of LncRNA Kcnq1ot1 in OA. However, no clinical studies have investigated the role of LncRNA Kcnq1ot1 in T2DM patients with OA. We are the first to demonstrate the upregulation of LncRNA Kcnq1ot1 in T2DM patients with OA in a clinical study, and logistic regression analysis showed that LncRNA Kcnq1ot1 is a risk factor for T2DM patients with OA.

There are several limitations to this study. Firstly, it is a single-center study with a relatively small sample size. Secondly, our analysis only assessed the levels of LncRNA in the serum of patients and did not measure the levels of LncRNA in the articular cartilage of patients. Finally, further research is needed to elucidate the molecular mechanisms by which LncRNA Kcnq1ot1 is involved in the development of T2DM patients with OA.

This study has several limitations that should be acknowledged. Firstly, one significant limitation is the lack of detailed analysis regarding gender differences in the expression of biomarkers among the patient cohort. Given that females are more prone to developing osteoarthritis (OA) and that gender may influence the pathophysiology of both type 2 diabetes mellitus (T2DM) and OA, future studies should aim to explore these differences comprehensively. The absence of this analysis in our current study limits the generalizability of our findings and may overlook critical insights into the role of gender in T2DM patients with OA. Additionally, the study's observational design restricts the ability to establish causality between LncRNA Kcnq1ot1 and the clinical outcomes observed. Furthermore, the relatively small sample size may limit the statistical power to detect significant differences in biomarker expression between subgroups. Finally, the study was conducted at a single center, which may affect the external validity of our results.

Conclusion

Serum LncRNA Kcnq1ot1 levels was remarkably elevated in T2DM patients with OA. In addition, serum LncRNA Kcnq1ot1 levels was a risk factor for T2DM patients with OA. This study might provide new targets and a comprehensive approach to treatment in T2DM patients with OA.

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Author contributions

Hai Hu: Conceptualization, Methodology, Resources, Writing - Original Draft, Writing - Review & Editing, Can Zhou: Conceptualization, Methodology, Writing - Review & Editing, Binbin Jiang: Investigation, Supervision, Song Wu: Investigation, Supervision, Ting Cai: Investigation, Supervision, Jie Yu: Investigation, Supervision, Liguo Zhu: Investigation, Supervision, Biao Zhou: Investigation, Supervision,

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest disclosure
The authors declare that they have no conflicts of interest.

Clinical trial number
Not applicable.

Ethics approval
This study was approved by the Ethics Review Committee of The Third Xiangya Hospital, Central South University(K23891). All patients provided written informed consent, and the study was conducted in accordance with the Declaration of Helsinki. All authors confirm that all methods are carried out in accordance with relevant guidelines and regulations.

Patient consent statement
All patients provided written informed consent.

Consent for publication
Not applicable.

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References

1. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the international diabetes federation diabetes atlas. Diabetes Res Clin Pract. 2019;157:107843. https://doi.org/10.1016/j.diabres.2019.107843
2. American Diabetes A. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2021. Diabetes care. 2021;44(Supplement 1):S15-S33. https://doi.org/10.2337/dc21-S002
3. Idf DA. International diabetes federation diabetes atlas. International Diabetes Federation Brussels, Belgium; 2013.
4. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. JAMA. 2013;310(9):948–59. https://doi.org/10.1001/jama.2013.168118
5. Weng J-P, Bi Y. Epidemiological status of chronic diabetic complications in China. Chin Med J (Engl); 2015. pp. 3267–9.
6. Harding JL, Pavkov ME, Magliano DJ, Shaw JE, Gregg EW. Global trends in diabetes complications: a review of current evidence. Diabetologia. 2019;62:3–16.
7. Veronese N, Cooper C, Reginster J-Y, et al. Type 2 diabetes mellitus and osteoarthritis. Elsevier; 2019. pp. 9–19.
8. Eymard F, Parsons C, Edwards MH, et al. Diabetes is a risk factor for knee osteoarthritis progression. Osteoarthr Cartil. 2015;23(6):851–9.
9. Kapur A, Harries AD, Lönnroth K, Wilson P, Sulistyowati LS. Diabetes and tuberculosis co-epidemic: the Bali declaration. Lancet Diabetes Endocrinol. 2016;4(1):8–10.
10. Cannata F, Vadalà G, Ambrosio L, et al. Osteoarthritis and type 2 diabetes: from pathogenetic factors to therapeutic intervention. Diab/Metab Res Rev. 2020;36(3):e3254.
11. Chi Y, Wang D, Wang J, Yu W, Yang J. Long Non-Coding RNA in the pathogenesis of cancers. Cells Sep. 2019;1(9). https://doi.org/10.3390/cells8091015
12. Yang Y, Yujiao W, Fang W, et al. The roles of MiRNA, LncRNA and circrna in the development of osteoporosis. Biol Res Sep. 2020;16(1):40. https://doi.org/10.1186/s40659-020-00309-z
13. Yang F, Qin Y, Wang Y, et al. LncRNA Kcnq1ot1 mediates pyroptosis in diabetic cardiomyopathy. Cell Physiol Biochem. 2018;50(4):1230–44.
14. Jie R, Zhu P, Zhong J, Zhang Y, Wu H. LncRNA Kcnq1ot1 affects cell proliferation, apoptosis and fibrosis through regulating miR-18b-5p/SORBS2 axis and NF-κB pathway in diabetic nephropathy. Diabetol Metab Syndr. 2020;12:1–11.
15. Liu Y, Zhao D, Wang X, Dong Y, Ding F. LncRNA Kcnq1ot1 attenuates Osteoarthritic chondrocyte dysfunction via the miR-218-5p/PIK3C2A axis. Cell Tissue Res. 2021;385:115–26.
16. Diabetes Branch of Chinese Medical A. Guidelines for prevention and treatment of type 2 diabetes in China (2017 edition). Chin J Pract Intern Med. 2018;38:292–344.
17. Zhang Z, Huang C, Jiang Q et al. Guidelines for the diagnosis and treatment of osteoarthritis in China (2019 edition). Annals Translational Med. 2020;8(19).
18. Luo S, Shi Q, Chen J, et al. Expression and significance of MMPs in synovial fluid, serum and PBMC culture supernatant stimulated by LPS in osteoarthritis patients with or without diabetes. Exp Clin Endocrinol Diabetes. 2019;127(04):195–202.
19. Wang Y, Wei J, Zeng C, et al. Association between serum magnesium concentration and metabolic syndrome, diabetes, hypertension and hyperuricaemia in knee osteoarthritis: a cross-sectional study in Hunan Province, China. BMJ Open. 2018;8(9):e019159.
20. Ashoor LS, Ali TM, Hasan H. IGF-1, leptin & AIP in relation to osteoarthritis with and without diabetes mellitus Type2. Ibn AL-Haitham J Pure Appl Sci. 2017;27(3):462–9.
21. Eveque-Mourroux MR, Emans PJ, Boonen A, et al. Heterogeneity of lipid and protein cartilage profiles associated with human osteoarthritis with or without type 2 diabetes mellitus. J Proteome Res. 2021;20(5):2973–82.
22. Berenbaum F. Diabetes-induced osteoarthritis: from a new paradigm to a new phenotype. Postgrad Med J. 2012;88(1038):240–2.
23. Xu C, Chen L, Wang R-J, Meng J. LncRNA Kcnq1ot1 knockdown inhibits ox-LDL-induced inflammatory response and oxidative stress in THP-1 macrophages through the miR-137/TNFAIP1 axis. Cytokine. 2022;155:155912.
24. Yu S, An J, Sun R, Feng J, Yu M. LncRNA Kcnq1ot1 predicts further cerebral events in patients with transient ischemic attack. Front Pharmacol. 2022;13:961190.
25. Xin H, Li C, Cai T, Cao J, Wang M. LncRNA Kcnq1ot1 contributes to hydrogen peroxide-induced apoptosis, inflammation, and oxidative stress of cardiomyocytes via miR-130a-3p/ZNF791 axis. Cell Biol Int. 2022;46(12):2018–27.
26. Xu Y, Zhan X. LncRNA Kcnq1ot1 regulated high glucose-induced proliferation, oxidative stress, extracellular matrix accumulation, and inflammation by miR-147a/SOX6 in diabetic nephropathy (DN). Endocr J. 2022;69(5):511–22.
27. Aili D, Wu T, Gu Y, Chen Z, Wang W. Knockdown of long non–coding RNA Kcnq1ot1 suppresses the progression of osteoarthritis by mediating the miR–211–5p/TCF4 axis in vitro. Experimental Therapeutic Med. 2021;21(5):1–10.
28. Liu C, Gao J, Su G, Xiang Y, Wan L. MicroRNA-1202 plays a vital role in osteoarthritis via Kcnq1ot1 has-miR-1202-ETS1 regulatory pathway. J Orthop Surg Res. 2020;15(1):1–9.

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