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CORRELATION ANALYSIS OF LPR-5, SOST AND MHR WITH POOR PROGNOSIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS COMPLICATED WITH OSTEOPOROSIS

ANALIZA KORELACIJE LPR-5, SOST I MHR SA LOŠOM PROGNOZOM KOD PACIJENATA SA DIJABETESOM TIP 2 KOMPLIKOVANIM OSTEOPOROZOM

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Summary

Background: To evaluate the predictive value of the monocyte/high-density lipoprotein cholesterol ratio (MHR), low-density lipoprotein-associated protein (LRP)-5 and sclerostin protein (SOST) for fractures in patients with osteoporosis due to type 2 diabetes.
Methods: For the osteoporosis group, 218 individuals who received a diagnosis of type 2 diabetes at this facility between January 2023 and December 2024 were selected. Moreover, 90 patients with normal bone mass and 130 patients with decreased bone mass due to type 2 diabetes who were diagnosed at this centre during the same time period were selected as the normal bone mass and reduced bone mass groups, respectively. Changes in MHR, LPR-5, and SOST in each group, and their relationships with fracture severity, were observed. Binary logistic regression was used to analyse the risk factors for fractures in patients with osteoporosis. Receiver operating characteristic (ROC) curves were used to assess the prediction effectiveness of the MHR, LPR-5, and SOST for fractures in individuals with type 2 diabetes-related osteoporosis.
Results: In the osteoporosis group, the MHR and LPR-5 were substantially higher ($P<0.05$) than those in the osteopenia group, and in the osteopenia group, they were significantly higher than those in the normal bone mass group. The MHR and LPR-5 in the fracture group were significantly greater ($P<0.05$) than in the non-fracture group, and they also increased dramatically as the fracture's severity rose

Kratak sadržaj

Uvod: Cilj je bio da se procene prediktivne prediktivne vrednosti odnosa monocita i holesterola visoke gustine (MHR), proteina povezanog sa lipoproteinom niske gustine (LRP-5) i sklerostina (SOST) za frakture kod pacijenata sa osteoporozom usled dijabetesa tipa 2.
Metode: U grupu sa osteoporozom uključeno je 218 osoba kojima je dijabetes tipa 2 dijagnostikovan u ovoj ustanovi između januara 2023. i decembra 2024. Takođe je odabrano 90 pacijenata sa normalnom koštanom masom i 130 pacijenata sa smanjenom koštanom masom usled dijabetesa tipa 2, dijagnostifikovanih u istom periodu, koji su činili grupe normalne i smanjene koštane mase. Posmatrane su promene MHR, LPR-5 i SOST u svakoj grupi i njihova povezanost sa težinom frakture. Za analizu faktora rizika za frakture kod pacijenata sa osteoporozom korišćena je binarna logistička regresija. Za procenu prediktivne efikasnosti MHR, LPR-5 i SOST za frakture kod osoba sa osteoporozom povezanim sa dijabetesom tipa 2 korišćene su ROC krive.
Rezultati: U grupi sa osteoporozom, vrednosti MHR i LPR-5 bile su značajno više ($P<0,05$) nego u grupi sa osteopenijom, a u grupi sa osteopenijom značajno više nego u grupi normalne koštane mase. Vrednosti MHR i LPR-5 u grupi sa frakturama bile su značajno više ($P<0,05$) nego u grupi bez fraktura, a takođe su se značajno povećavale sa porastom težine frakture ($P<0,05$). U poređenju sa grupama osteopenije i normalne koštane mase, nivo

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(P<0.05). Compared to the groups with osteopenia and normal bone mass, the osteoporosis group's serum SOST level was considerably lower (P<0.05), and that in the osteopenia group was significantly lower than that in the normal bone mass group (P<0.05). The serum SOST level in the fracture group was considerably lower than that in the non-fracture group (P<0.05). Multivariate analysis revealed that BMI, FBG, the MHR, the LPR-5, and SOST were independent risk factors for fractures in patients with type 2 diabetes (P<0.05). The MHR, LPR-5, and SOST were significantly more predictive of fractures in patients with osteoporosis and type 2 diabetes than were BMI and FBG (P<0.01). The combined detection of the MHR, LPR-5 and SOST had a sensitivity of 87.5% and a specificity of 83.6% for diagnosing fractures in patients with osteoporosis and type 2 diabetes. While there was no statistically significant difference in the AUC of the individual detections of each index (P>0.05), the area under the curve (AUC) was 0.909, which was significantly greater than the AUC of the individual detections of MHR (Z=3.182, P<0.01), LPR-5 (Z=3.154, P<0.01), and SOST (Z=3.684, P<0.01).

Conclusions: The MHR, LPR-5, and SOST are independent determinants of fractures and contribute to the onset and progression of osteoporosis in people with type 2 diabetes. The combined detection of the above three indicators has high predictive value for fractures in patients with osteoporosis and type 2 diabetes.

Keywords: type 2 diabetes, osteoporosis, fracture, blood lipids, sclerostin

SOST u serumu u grupi sa osteoporozom bio je značajno niži (P<0,05), a u grupi osteopenije značajno niži nego u grupi normalne koštane mase (P<0,05). Nivo SOST u serumu u grupi sa frakturama bio je znatno niži nego u grupi bez fraktura (P<0,05). Multivarijantna analiza pokazala je da su BMI, FBG, MHR, LPR-5 i SOST nezavisni faktori rizika za frakture kod pacijenata sa dijabetesom tipa 2 (P<0,05). MHR, LPR-5 i SOST imali su značajno veću prediktivnu vrednost za frakture kod pacijenata sa osteoporozom i dijabetesom tipa 2 nego BMI i FBG (P<0,01). Kombinovana detekcija MHR, LPR-5 i SOST imala je senzitivnost od 87,5% i specifičnost od 83,6% za dijagnostikovanje fraktura kod pacijenata sa osteoporozom i dijabetesom tipa 2. Iako nije bilo statistički značajne razlike u AUC pojedinačnih parametara (P>0,05), kombinovana površina ispod krive (AUC) iznosila je 0,909, što je bilo značajno više nego AUC pojedinačnih vrednosti MHR (Z=3,182, P<0,01), LPR-5 (Z=3,154, P<0,01) i SOST (Z=3,684, P<0,01).

Zaključak: MHR, LPR-5 i SOST su nezavisni pokazatelji rizika za frakture i doprinose nastanku i progresiji osteoporoze kod osoba sa dijabetesom tipa 2. Kombinovana detekcija ova tri parametra ima visoku prediktivnu vrednost za frakture kod pacijenata sa osteoporozom i dijabetesom tipa 2.

Ključne reči: dijabetes tip 2, osteoporoza, fraktura, krvni lipidi, sklerostin

Introduction

One prevalent chronic metabolic condition whose incidence rate rises yearly is type 2 diabetes (1). This disease is related to factors such as abnormal glucose metabolism, the environment, genetics, and age to some extent. A long-term state of high sugar can cause various complications in the body, the most common of which is osteoporosis, with an incidence rate as high as 60%. Osteoporosis can easily lead to fractures and even disability (2). Therefore, screening for fracture risk factors in patients with type 2 diabetes, especially those with osteoporosis, is of great clinical importance for the early prevention of fractures (3–5). Chronic inflammation and lipid metabolism disorders are involved in the pathophysiological process of osteoporosis in type 2 diabetes. Sclerostin (SOST) is an essential inhibitory factor that regulates glucose metabolism and bone metabolism. It can regulate bone density in patients by binding to the low-density lipoprotein receptor-related protein 5 (LRP5) and inhibiting the Wnt pathway (6). Additionally, in patients with type 2 diabetes, the monocyte/high-density lipoprotein cholesterol ratio (MHR) has some clinical utility in predicting osteoporosis (7).

Both type 2 diabetes mellitus (T2DM) and osteoporosis (OP) are chronic conditions with high prevalence rates around the globe (8). Patients who have both conditions together are far more likely to suffer fractures, particularly at unusual sites (9). Interestingly, individuals with type 2 diabetes mellitus (T2DM) frequently display distinct anomalies in bone metabolism, even though the bone mineral density (BMD) measurement may not be low or even normal, their risk of fracture significantly increases (10–12). This phenomenon is known as the »bone mineral density paradox«, suggesting that traditional BMD-based fracture risk assessment models have obvious limitations in such patients. Thus, there is a pressing need to investigate new biomarkers that more accurately and precisely reflect deterioration in bone integrity and fracture risk in individuals with osteoporosis (DOP) associated with type 2 diabetes (13). The regulation of bone metabolism and its association with metabolic diseases (such as T2DM) have received extensive attention (14). These indicators are believed to reveal the pathological mechanism of DOP and to predict its fracture risk from multiple perspectives, including bone formation inhibition, Wnt signalling pathway disorders, chronic low-grade inflammation, and lipid metabolism imbalance (15).

This study aims to explore the predictive value of serum LRP-5, SOST and MHR levels for fractures in patients with T2DM complicated with osteoporosis, with the expectation of compensating for the deficiencies of existing assessment tools, providing a new theoretical basis and potential predictive tools for the early identification of high-risk patients, optimising intervention strategies and reducing fracture incidence, and having important clinical translational significance.

Materials and Methods

General information

The osteoporosis group consisted of 218 patients, 94 men and 134 women, aged 60 to 80, with an average age of 68.81±4.84 years and an average duration of diabetes of 13.62±5.28 years, who were diagnosed with osteoporosis due to type 2 diabetes at our hospital between January 2023 and December 2024. The average body mass index (BMI) was 22.88±3.47 kg/m^2, and the average fasting blood glucose (FBG) was 8.06±1.40 mmol/L. Based on fracture status, patients were divided into two groups: 121 in the non-fracture group and 96 in the fracture group.

According to fracture severity, the Genant semi-quantitative method was used to classify patients into Grade I (22 cases) and Grade II (44 cases). The degree of vertebral compression >40% was Grade III, the degree of vertebral compression 25–40% was Grade II, and the degree of vertebral compression <25% was Grade I.

For the bone mass reduction group, 130 patients with type 2 diabetes and reduced bone mass at our centre during the same time period were selected. The group consisted of 58 men and 72 women aged 60–77, with an average age of 68.02±4.72 years and an average duration of diabetes of 13.03±5.48 years. The average BMI was 22.05±2.86 kg/m^2, and the average FBG was 8.14±1.10 mmol/L. Another 45 patients diagnosed with type 2 diabetes and normal bone mass at our centre during the same period were selected as the normal bone mass group. The average BMI was 22.40±2.83 kg/m^2, and the average FBG was 8.20±0.98 mmol/L. The general data, including age, sex, disease duration, BMI, and FBG level, did not differ significantly across the three research groups (P>0.05).

This study has obtained medical research ethics approval [No. HKYS-2025-A0237].

Inclusion and exclusion criteria

Inclusion criteria: (1) A T value of ≥-1 was regarded as normal bone mass, while a T value larger than -2.5 to less than -1 denotes decreasing bone mass. When the T value is -2.5, osteoporosis is present. (2) Age 60 to 80 years old; (3) Meet the diagnostic criteria for type 2 diabetes; (4) Complete clinical data.

Exclusion criteria: (1) Those with bone metabolic diseases caused by other reasons; (2) Bone metabolic diseases caused by drugs, such as those who have been treated with hormones for a long time; (3) Those who have been bedridden for a long time and are malnourished; (4) Those with malignant tumours; (5) Those suffering from chronic infectious diseases and immune diseases; (6) People with mental disorders and intellectual disabilities.

Detection methods

Blood samples from 5 mL of fasting elbow vein blood were collected and placed in anticoagulant tubes once all participants had been enrolled. The samples were centrifuged for 10 minutes at 3,000 rpm, and the supernatant was stored at -80 °C for later use. The levels of serum LPR-5 and SOST were determined using the enzyme-linked immunosorbent assay. The reagent kits were purchased from Shanghai Lianmai Bioengineering Co., Ltd. Routine blood parameters were determined via a blood cell analyser. Triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), FBG, total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) were measured using an automatic biochemical analyser. An automated glycated haemoglobin (HbA1c) analyser was used to measure glycated haemoglobin.

Observation indicators

The changes in the MHR, LPR-5, and SOST scores in each group were compared. The determinants of fractures in patients with osteoporosis brought on by type 2 diabetes were examined using univariate and multivariate analysis. Analysis was conducted to assess how well the MHR, LPR-5, and SOST predicted fractures in patients with osteoporosis due to type 2 diabetes, and how these values related to fracture severity.

Laboratory testing reagents and equipment

The main serological indicators in this study include lipoprotein receptor-associated protein 5 (LRP5), osteoprotegerin (SOST), and the monocyte/high-density lipoprotein cholesterol ratio (MHR). After all blood samples were collected, they were left to stand at room temperature for 30 minutes to coagulate, and then centrifuged at 3000 rpm for 15 minutes to separate the serum. The portioned serum samples should be stored in an ultra-low-temperature freezer at -80°C for testing, avoiding repeated freezing and thawing (the maximum number of freeze-thaw cycles should not exceed 2). The specific detection methods and the reagents and equipment used are as follows:

(1) Detection of lipoprotein receptor-associated protein 5 (LPR-5)

Human Lipoprotein Receptor-Associated Protein 5 (LRP5) ELISA Kit, Yunkelong Company, Katie, Texas, USA, catalogue number: CEA143Hu.

(2) Detection of sclerostin (SOST)

Human Sclerostin (SOST) ELISA Kit, R&D Systems, Minneapolis, Minnesota, USA, catalogue number: DSTN01.

(3) High-density lipoprotein cholesterol (HDL-C) detection

HDL-C Gen. 3 Direct Assay Kit, Roche Diagnostics (Basel, Switzerland), catalogue number: 07528504190.

(4) Monocyte Count

A Complete Blood Count (CBC) was performed using an automated blood cell analyser to obtain the differential count of white blood cells, including the absolute count of monocytes: Sysmex XN series fully automatic blood analyser, SYSmex Corporation, Kobe, Japan, Model: XN-9000.

(5) Equipment

Microplate reader: Multiskan SkyHigh microplate Spectrophotometer, Thermo Fisher Scientific (USA), model/item number: Multiskan SkyHigh. Wellwash Versa Microplate washer, Thermo Fisher Scientific (USA), model/item number: Wellwash Versa. Eppendorf Centrifuge 5810R benchtop high-speed refrigerated centrifuge, Eppendorf, Germany, Model: 5810R.

Statistical processing methods

To analyse the data, SPSS 20.0 statistical software was utilised. The symbol $\bar{x}\pm s$ represents measurement data that follows a normal distribution. When comparing two groups, a t-test was used; for comparisons among multiple groups, analysis of variance was used. Count data were expressed as counts or percentages, and the χ^2 test was used for comparisons between groups. Binary logistic regression was used to analyse the influencing factors of fractures in patients with osteoporosis. The predictive efficacy of the MHR, LPR-5 and SOST for fractures in patients with osteoporosis was analysed via receiver operating characteristic (ROC) curves.

Results

Comparison of the MHR, LPR-5 score and SOST score across the groups

In comparison to the groups with osteopenia and normal bone mass, the osteoporosis group's MHR and LPR-5 were considerably higher ($P<0.05$), and those in the osteopenia group were significantly greater than those in the normal bone mass group ($P<0.05$). Compared to the groups with osteopenia

Table I Comparison of MHR, LPR-5, and SOST levels among groups.

Group	n	MHR	LPR-5 (pg/mL)	SOST (pg/mL)
Osteoporosis group	218	0.34±0.08	13.60±3.40	478.43±48.22
Bone loss group	130	0.27±0.06	9.94±2.40	669.34±52.30
Normal bone mass group	90	0.19±0.04	6.57±1.27	778.08±72.29
t		83.035	108.424	551.146
P		<0.001	<0.001	<0.001

Table II Single-factor analysis of fracture in type 2 diabetes patients with osteoporosis.

Group	n	Age (years)	Systolic blood pressure (mmol/L)		Diastolic pressure (mmol/L)	BMI (kg/m^2)	FBG (mmol/L)	HbA1c (%)
Fracture group	96	61.38±5.31	132.48±6.28		73.72±5.27	22.82±3.22	8.43±1.57	8.11±0.97
Non-fracture group	121	60.73±5.28	131.72±7.31		72.16±5.17	24.29±3.13	7.77±1.19	7.61±1.00
t		0.637	0.573		1.551	2.398	2.511	2.605
p		0.526	0.568		0.124	0.018	0.014	0.01
Group	n	LDL-C (mmol/L)	HDL-C (mmol/L)	TC (mmol/L)	TG (mmol/L)	MHR	LPR-5 (pg/mL)	SOST (pg/mL)
Fracture group	96	3.21±0.72	1.15±0.35	5.01±1.02	2.09±0.72	0.38±0.07	15.31±2.92	454.23±36.62
Non-fracture group	121	3.18±0.53	1.16±0.32	4.96±0.97	1.78±0.87	0.31±0.06	12.25±3.14	497.74±47.93
t		0.251	0.156	0.261	2.053	5.903	5.216	5.173
p		0.803	0.877	0.795	0.043	<0.001	<0.001	<0.001

Table III Multifactor analysis of fracture in type 2 diabetes patients with osteoporosis.

Indicator	β	SE	Wald χ^2	P	OR	95%CI
BMI	-0.235	0.109	4.663	0.031	0.791	0.639~0.979
FBG	0.552	0.248	4.935	0.026	1.736	1.067~2.825
HbA1c	0.306	0.322	0.904	0.342	1.358	0.723~2.551
TG	0.690	0.395	3.049	0.081	1.994	0.919~4.328
MHR	22.283	6.903	10.421	0.001	4.76×10^{9}	$6.34\times104\sim3.58\times10^{15}$
LPR-5	0.408	0.115	12.577	<0.001	1.504	1.200~1.884
SOST	-0.029	0.009	10.194	0.001	0.971	0.954~0.989

Table IV Predictive efficacy of MHR, LPR-5 and SOST levels on fracture in type 2 diabetes patients with osteoporosis.

Indicator	Truncation value	Sensitivity (%)	Specificity (%)	AUC	95%CI
BMI	24.33 kg/m^2	75.0	60.7	0.647	0.549~0.736
FBG	8.54 mmol/L	58.3	75.4	0.641	0.544~0.731
MHR	0.35	64.6	80.3	0.793	0.705~0.865
LPR-5	12.85 pg/mL	83.3	63.9	0.761	0.670~0.837
SOST	482.14 pg/mL	79.2	60.7	0.760	0.669~0.837
MHR+LPR-5+SOST	–	87.5	83.6	0.909	0.839~0.956

and normal bone mass, the osteoporosis group's serum SOST level was considerably lower (P<0.05), and it was substantially smaller in the group with osteopenia than in the group with normal bone mass (P<0.05) (*Table I*).

Univariate analysis of fractures in patients with osteoporosis and type 2 diabetes

While the BMI and SOST in the fracture group were considerably lower than those in the non-fracture group (P<0.05), the levels of FBG, HbA1c, TG, MHR, and LPR-5 were significantly higher in the fracture group than in the non-fracture group (P<0.05). There were no statistically significant differences (P>0.05) between the fracture group and the non-fracture group in terms of age, systolic and diastolic blood pressure, LDL-C, HDL-C, and TC values (*Table II*).

Multivariate analysis of fractures in patients with osteoporosis and type 2 diabetes

Multivariate analysis of the indicators with statistically significant differences in the univariate analysis (BMI, FBG, HbA1c, TG, MHR, LPR-5 and SOST) revealed that BMI, FBG, MHR, LPR-5 and SOST were independent influencing factors for fractures in patients with type 2 diabetes (P<0.05) (*Table III*).

Predictive efficacy of the MHR, LPR-5 and SOST for fractures in patients with osteoporosis due to type 2 diabetes

The predictive efficacy of the MHR, LPR-5 and SOST for fractures in patients with osteoporosis due to type 2 diabetes was superior to that of BMI and FBG (P<0.01). The equation Y=19.5×MHR+0.37×LPR-5-0.03×XS was derived after a binary logistic regression analysis to determine whether fractures occurred in individuals with osteoporosis caused by type 2 diabetes. The combination detection of OST+0.34 has 87.5% sensitivity and 83.6% specificity. Significantly higher than the AUC of individual detections of MHR (Z=3.182, P<0.01) and LPR-5 (Z=3.154, P<0.01), the area under the curve (AUC) was 0.909, and SOST (Z=3.684, P<0.01). However, the AUC of each index's individual detections did not differ statistically significantly (P>0.05) (*Table IV*).

Relationships between MHR, LPR-5 and SOST levels and the severity of fractures in patients with osteoporosis due to type 2 diabetes

Patients with type 2 diabetes, osteoporosis, and Grade III fractures had considerably higher MHR and LPR-5 values than those with Grade II and Grade I fractures (P<0.05), while Grade II fractures were significantly higher than Grade I fractures (P<0.05). The serum SOST level of patients with Grade III frac-

Table V Relationship between MHR, LPR-5 and SOST levels and fracture severity in type 2 diabetes patients with osteoporosis.

Item	n	MHR	LPR-5 (pg/mL)	SOST (pg/mL)
Level I	22	0.30±0.02	11.46±1.52	503.91±16.29
Level II	44	0.37±0.02	15.00±1.06	456.84±15.81
Grade III	30	0.47±0.06	18.59±1.41	413.98±15.81
t		67.855	99.056	101.797
P		<0.001	<0.001	<0.001

tures, type 2 diabetes and osteoporosis was significantly lower than that of Grade II patients (P<0.05), and that of Grade II patients was significantly lower than that of Grade I patients (P<0.05) (*Table V*).

Discussion

Patients with type 2 diabetes, owing to long-term poor blood sugar control, suffer from relatively poor or absolute insufficient insulin secretion, which leads to disorders in the metabolism of the three major nutrients (16–18). Moreover, they have calcium and phosphorus metabolism disorders, resulting in destruction of the bone structure, increased bone fragility, and a significant reduction in bone strength, with a significantly increased risk of fractures (19). Type 2 diabetes and osteoporosis are mutually causal. Clinically, it is necessary to actively control blood sugar levels and prevent the occurrence of diabetic complications. Fractures in patients with osteoporosis are extremely harmful, causing families or society to invest large amounts of human, material and financial resources, resulting in a heavy burden on society and families (20). Early identification and screening of high-risk groups for osteoporosis in individuals with type 2 diabetes, along with further intervention measures for these high-risk groups, can reduce the occurrence of osteoporosis and fracture complications (21). This study conducted a univariate analysis on whether fractures occurred in osteoporosis patients with type 2 diabetes and revealed that the levels of FBG, HbA1c, TG, MHR and LPR-5 in the fracture group were significantly greater than those in the non-fracture group, whereas the BMI and SOST were significantly lower than those in the non-fracture group. Further multivariate analysis revealed that patients with type 2 diabetes had fractures that were independently influenced by BMI, FBG, MHR, LPR-5, and SOST. MHR, LPR-5, and SOST significantly exceeded BMI and FBG in predicting fractures in patients with osteoporosis who also had type 2 diabetes (22).

Patients with type 2 diabetes who had osteoporosis had a considerably higher MHR than those with osteopenia or normal bone mass (P<0.05), and those with fractures had a significantly higher MHR than those without fractures (P<0.05) (23). These findings indicate that the MHR is closely related to osteoporosis and fractures in type 2 diabetes patients and increases with increasing fracture grade. The MHR is suggested as a diagnostic indicator for assessing fracture severity in patients with osteoporosis due to type 2 diabetes (24). The MHR is an indicator of inflammation and oxidative stress. There have also been certain studies on osteoporosis caused by type 2 diabetes. On the one hand, chemokines secreted by monocytes cause a large aggregation of inflammatory cells in the local area and simultaneously induce positive telomerase to stimulate monocytes to produce osteoclasts, which further promote bone resorption and lead to the occurrence of osteoporosis (25-28). The sensitivity for predicting fractures in patients with osteoporosis due to type 2 diabetes was 64.6%, the specificity was 80.3%, and the AUC was 0.793, indicating high predictive efficacy.

The serum LPR-5 level in type 2 diabetes patients in the osteoporosis group was significantly higher than in those in the osteopenia group. The normal bone mass group (P<0.05), and the LPR-5 level rose with increasing fracture grade and was substantially higher in the fracture group than in the non-fracture group (P<0.05) (29). Patients with type 2 diabetes who had osteoporosis had a substantially lower serum SOST level than those who had osteopenia or normal bone mass (30). The fracture group's serum SOST level was substantially lower than the non-fracture group's, and it dropped as the severity of the fracture increased. LPR-5 is a transmembrane receptor protein and an auxiliary receptor of the Wnt ligand. It is widely distributed throughout the body's organs and tissues (31). An increase in its expression promotes insulin production and positively affects the insulin signalling pathway, thereby helping osteoblasts encourage bone formation (32). SOST is an important regulator of glucose and bone metabolism. It prevents the Wnt signalling pathway from being activated, thereby inhibiting bone formation, by binding to the shared receptor LPR-5 (33). When the serum LPR-5 is 12.85 pg/mL, the sensitivity for predicting fractures in patients with osteoporosis due to type 2 diabetes is 83.3%, the specificity is 63.9%, and the AUC is 0.761. Moreover, this study revealed that when the serum SOST concentration is 482.14

pg/mL, the sensitivity for predicting fractures in patients with diabetic osteoporosis is 79.2%, the specificity is 60.7%, and the AUC is 0.760.

The combined detection of MHR, LPR-5, and SOST has greater diagnostic efficacy for predicting fractures in patients with type 2 diabetes and osteoporosis (34). Its sensitivity is 87.5%, its specificity is 83.6%, and its AUC is 0.909, which is significantly greater than that of individual detection of each index. This indicates that there are intrinsic connections among the three indicators and that they exhibit some complementarity. The MHR is an indicator of inflammation and lipid oxidative stress, whereas LPR-5 and SOST mainly reflect indicators of the Wnt signalling pathway regulating fracture metabolism (35). When these indicators are abnormal, how to intervene to prevent fractures remains to be further experimentally confirmed.

Conclusion

The MHR, LPR-5, and SOST are independent determinants of fractures and contribute to the onset and progression of osteoporosis in patients with type 2 diabetes. When the MHR, LPR-5, and SOST are identified simultaneously, patients with osteoporosis and type 2 diabetes have a good predictive value for fractures.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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