The polymorphisms of MIR31HG gene is correlated with alcohol-induced osteonecrosis of the femoral head in Chinese Han male population

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**Background:** Alcoholic osteonecrosis of the femoral head (ONFH) is a multifaceted illness that seriously disturbs the patients’ quality of life. The role of IncRNAs in alcoholic ONFH has attracted widespread attention in recent years. This study mainly explored whether MIR31HG polymorphism affects the risk of ONFH.

**Methods:** There were 733 males (308 alcohol-induced ONFH patients and 425 healthy controls). Seven single nucleotide polymorphisms from MIR31HG were genotyped using the Agena MassARRAY platform. Odds ratio (OR) and 95% confidence intervals (CI) via logistic regression was applied to assess the contribution of MIR31HG variants to alcoholic ONFH susceptibility.

**Results:** We found that rs10965059 was related to a lower risk of alcoholic ONFH in the overall, age, and necrotic sites analysis. Rs10965064 also showed a risk-reducing effect in the occurrence of alcoholic ONFH patients older than 40 years old.

**Conclusions:** We confirmed that MIR31HG variants have a significant correlation with the occurrence of alcoholic ONFH among the Chinese Han male population. Our findings may provide new ideas for understanding the effect of MIR31HG on the prevention and diagnosis of alcoholic ONFH.

**KEYWORDS**
osteonecrosis of the femoral head, MIR31HG, polymorphism, case-control study, gene

**Abbreviations:** ONFH, Osteonecrosis of the femoral head; OR, odds ratio; CI, confidence intervals; MAF, minor allele frequency; HWE, Hardy-Weinberg Equilibrium; CT, computed tomography; MRI, nuclear magnetic resonance imaging; LD, linkage disequilibrium.
Introduction

Osteonecrosis of the femoral head (ONFH) is a common hip illness characterized by impaired microvascular circulation leading to the death of bone cells. It eventually causes structural changes, collapse of the femoral head, and joint dysfunction. It is reported that the age of patients with ONFH is mostly 30–50 years old, and the incidence rate is gradually increasing with the increase of age (1). There are 8.12 million ONFH patients in China, with approximately 150,000 to 200,000 newly diagnosed ONFH patients yearly (2). Some research showed that one of the common causes of ONFH was excessive drinking (3, 4). Besides, Cui et al. reported that alcoholic ONFH accounted for 30.7% of all femoral head necrosis in China (5). Nevertheless, it has been found in clinical practice that only some people who drink excessively suffer from femoral head necrosis, which suggested that genetic susceptibility may contribute to the occurrence of alcoholic ONFH. Meanwhile, a large number of reports confirmed that genetic variants were related to alcoholic ONFH predisposition (6–8).

Long non-coding RNAs (lncRNAs) refers to non-coding RNA with a length of over 200 nucleotides, which can regulate the physiological and pathological activities of organisms by participating in gene transcription and post-transcriptional regulation, epigenetic modification, and translation (9, 10). Recently, lncRNAs have aroused researchers’ concern in bone development, differentiation, and osteonecrosis. For example, Tang et al. found that lncRNA-OG could promote the differentiation of osteoblasts (11). Liu et al. indicated that lncRNA AK077216 facilitated bone resorption and osteoclastogenesis (12). Besides, a study performed by Xiang et al. which reported that lncRNA RP11-154D6 was reduced in ONFH patients and involved in the progression of ONFH (13).

MIR31HG (also named as lncHIFCAR, LOC554202) is described to participate in proliferation, differentiation, invasion of cancer cells (14, 15). In addition, researchers have discovered that MIR31HG silence promoted osteogenic differentiation and relieved the inflammation-induced inhibition of osteogenesis (16). However, the role of MIR31HG in alcoholic ONFH development remains elusive. However, the role of MIR31HG in alcoholic ONFH development remains elusive.

Here, we explored the association of MIR31HG genetic variations with alcoholic ONFH susceptibility among the Chinese Han male population. This will help to provide new understandings for MIR31HG into the pathogenesis of alcoholic ONFH.

Methods

Study subjects

A total of 733 Chinese Han males (308 alcoholic ONFH patients and 425 healthy controls) were enrolled. All patients were randomly selected from Hainan Affiliated Hospital of Hainan Medical University. The patients met the criteria as following: 1) exceeded 400 mL/week (17) alcohol intake for more than 6 months; 2) diagnosed ONFH within one year after drinking alcohol; 3) no rheumatoid arthritis, hyperlipidemia, spinal cord cavitation, decompression sickness, osteoporosis, cardiovascular disease, and virus infection; 4) no history of steroid use; 5) The diagnosis of alcoholic ONFH by X-ray, nuclear magnetic resonance imaging (MRI), and computed tomography (CT). The stage of alcoholic ONFH patients were identified by the Ficat Classification system (18). Healthy people were selected based on 1) drinking habits or greater than 400 mL alcohol intake per week for more than 6 months; 2) no history of the traumatic disease (ONFH, rheumatoid arthritis, hyperlipidemia, spinal cord cavitation, decompression sickness, osteoporosis, cardiovascular disease, etc...), and no steroid use. The study protocol was approved by the Ethics Committee of the Hainan Affiliated Hospital of Hainan Medical University, in compliance with the declaration of Helsinki. And the signature consent of participants was received.

SNP genotyping

Seven SNPs in MIR31HG were chosen with a minor allele frequency (MAF) >5% in 1000 Genomes Chinese Han Beijing population. Total DNA was isolated from peripheral blood cells by GoldMag blood DNA Kit (GoldMag Co. Ltd, Xi’an, China), and the concentration were evaluated via NanoDrop 2000 (Thermo Scientific, USA). SNP genotyping was completed through the Agena MassARRAY platform and the data were analyzed using the Agena Typer 4.0 software.

Data analysis

Student t-test was applied to evaluate age difference between the two groups. Hardy-Weinberg equilibrium (HWE) in controls was calculated using χ² test. The linkage between MIR31HG polymorphisms and alcoholic ONFH susceptibility was examined by odds ratio (OR) and 95% confidence interval (CI) through logistic regression. Linkage disequilibrium (LD) was analyzed by Haplovie software. Multifactor dimensionality reduction (MDR) was conducted to evaluate the SNP-SNP interactions in the risk of ONFH. False positive report probability (FPRP) values and statistical power were calculated (19). P < 0.05 was identified a significant difference.

Results

Participants and selected SNPs in MIR31HG

As listed in Table 1, this study included 308 alcoholic ONFH patients and 425 healthy controls, with an average age of 43.37 ±
The age distribution between the two groups was well-matched ($p=0.478$).

We chose and genotyped seven SNPs (rs1332184, rs72703442, rs2025327, rs55683539, rs2181559, rs10965059, rs10965064) in the intron region of MIR31HG, and all SNPs in line with HWE ($p>0.05$). And we found that rs10965059 could reduce the susceptibility of alcoholic ONFH in the allele model ($p<0.001$, OR = 0.48, 95%CI=0.35-0.66, Table 2).

### Alcoholic ONFH risk assessment

The association of seven SNPs in MIR31HG and alcoholic ONFH risk was evaluated (Table 3). The results revealed that MIR31HG- rs10965059 was related to a lower risk of alcoholic ONFH under codominant ($p<0.001$, OR=0.43, 95%CI=0.30-0.62), dominant ($p<0.001$, OR=0.42, 95%CI=0.30-0.61) and additive models ($p<0.001$, OR=0.45, 95%CI=0.32-0.62).

Age stratification showed that rs10965059 decreased the susceptibility to alcoholic ONFH individuals older than 40 years in the allele ($p<0.001$, OR=0.36), codominant ($p<0.001$, OR=0.45), dominant ($p<0.001$, OR=0.31), and additive models ($p<0.001$, OR=0.33, 9 Table 4). Rs10965064 only reduced the alcoholic ONFH susceptibility under the dominant model ($p=0.049$, OR=0.67).

Besides, the necrotic sites stratification results (Table 5) indicated that rs10965059 played a protective role in alcoholic bilateral ONFH in the allele (OR=0.45, $p<0.001$), codominant (OR=0.40, $p<0.001$), dominant (OR=0.39, $p<0.001$), and recessive model (OR=0.42, $p<0.001$).

### Table 1 Characteristics of ONFH patients and controls in this study.

| Variables       | Cases (n=308)        | Controls (n=425)   | $p$ value |
|-----------------|----------------------|-------------------|-----------|
| Age, years      | 43.37 ± 11.34        | 42.73 ± 12.88     | 0.478     |
| ≤40             | 187 (61%)            | 246 (58%)         |           |
| >40             | 121 (39%)            | 179 (42%)         |           |
| Clinical stages | I-II                 | 218 (71%)         |           |
| III-IV          | 90 (29%)             |                   |           |
| Hip lesions     | Unilateral           | 65 (21%)          |           |
| Bilateral       | 243 (79%)            |                   |           |
| Course, months  | >22                   | 103 (33%)         |           |
| ≤22             | 205 (67%)            |                   |           |

$p$ value was calculated from student’s t test.

### Table 2 Basic information of the selected SNPs in MIR31HG.

| SNP             | Chr : Position | Role | Allele A/B | MAF   | HWE $p$ | OR (95% CI) | $p$   | HaploReg                                      |
|-----------------|----------------|------|------------|-------|---------|-------------|-------|-----------------------------------------------|
| rs1332184       | 9:21504203     | Intron | A/G       | 0.291 | 0.256   | 1.17 (0.93-1.48) | 0.178 | Enhancer histone marks, DNAase                |
| rs72703442      | 9:21515795     | Intron | A/C       | 0.172 | 0.160   | 1.09 (0.82-1.44) | 0.552 | Enhancer histone marks, Motifs changed        |
| rs2025327       | 9:21531629     | Intron | C/T       | 0.141 | 0.114   | 1.00 (0.94-1.74) | 0.122 | Enhancer histone marks, DNAase, Motifs changed, Selected eQTL hits |
| rs55683539      | 9:21542134     | Intron | T/C       | 0.244 | 0.245   | 0.98 (0.78-1.26) | 0.938 | Enhancer histone marks, DNAase, Motifs changed, Proteins bound |
| rs2181559       | 9:21543938     | Intron | A/T       | 0.378 | 0.352   | 1.12 (0.90-1.39) | 0.298 | Enhancer histone marks, DNAase, Motifs changed, Proteins bound, Selected eQTL hits |
| rs10965059      | 9:21544062     | Intron | T/C       | 0.096 | 0.181   | 0.48 (0.35-0.66) | <0.001 | DNAase, Motifs changed, Proteins bound         |
| rs10965064      | 9:21553538     | Intron | G/C       | 0.356 | 0.369   | 0.94 (0.76-1.17) | 0.585 | DNAase, Motifs changed                        |

Human (GRCh38.p13) reference is used for SNP annotation.

SNP, Single nucleotide polymorphism; MAF, Minor allele frequency; HWE, Hardy-Weinberg equilibrium; OR, Odds ratio; 95% CI, 95% confidence interval.

$p$ values were calculated from $\chi^2$ test. Bold values indicate statistical significance.
### TABLE 3  Association of MIR31HG polymorphisms with alcohol-induced ONFH.

| SNP ID   | Model       | Genotype | Case  | Control | Crude analysis | Adjusted analysis |
|----------|-------------|----------|-------|---------|----------------|------------------|
|          |             |          | OR (95% CI) | p | OR (95% CI) | p |
| rs1332184| Codominant  | GG       | 159   | 238     | 1.00           | 1.00             |
|          |             | AA       | 30    | 33      | 1.36 (0.80-2.32) | 0.258          |
|          |             | AG       | 119   | 154     | 1.16 (0.85-1.58) | 0.361          |
|          | Dominant    | GG       | 159   | 238     | 1.00           | 1.00             |
|          |             | AA+AG    | 149   | 187     | 1.19 (0.89-1.60) | 0.241          |
|          |             | AA       | 30    | 33      | 1.28 (0.76-2.15) | 0.347          |
|          | Additive    | ---------| ------|---------| ---------------| ---------------|
|          |             |          | 1.16 (0.93-1.46) | 0.191 | 1.17 (0.93-1.46) | 0.185 |
| rs72703442| Codominant  | CC       | 209   | 298     | 1.00           | 1.00             |
|          |             | AA       | 7     | 10      | 1.00 (0.37-2.67) | 0.997          |
|          |             | AC       | 92    | 116     | 1.13 (0.82-1.57) | 0.460          |
|          | Dominant    | CC       | 209   | 298     | 1.00           | 1.00             |
|          |             | AA+AC    | 99    | 126     | 1.12 (0.82-1.54) | 0.483          |
|          |             | AA       | 7     | 10      | 0.96 (0.36-2.56) | 0.939          |
|          | Additive    | ---------| ------|---------| ---------------| ---------------|
|          |             |          | 1.09 (0.82-1.45) | 0.546 | 1.09 (0.82-1.45) | 0.545 |
| rs2025327| Codominant  | TT       | 231   | 338     | 1.00           | 1.00             |
|          |             | CC       | 10    | 5       | 2.88 (0.97-8.55) | 0.056          |
|          |             | CT       | 67    | 87      | 1.11 (0.77-1.59) | 0.569          |
|          | Dominant    | TT       | 231   | 338     | 1.00           | 1.00             |
|          |             | CC+CT    | 87    | 92      | 1.21 (0.85-1.71) | 0.288          |
|          |             | AA       | 7     | 10      | 0.94 (0.36-2.56) | 0.939          |
|          | Additive    | ---------| ------|---------| ---------------| ---------------|
|          |             |          | 1.26 (0.93-1.71) | 0.131 | 1.27 (0.94-1.73) | 0.121 |
| rs55683539| Codominant  | CC       | 176   | 248     | 1.00           | 1.00             |
|          |             | TT       | 18    | 32      | 0.79 (0.43-1.46) | 0.454          |
|          |             | TC       | 114   | 144     | 1.12 (0.82-1.53) | 0.493          |
|          | Dominant    | CC       | 176   | 248     | 1.00           | 1.00             |
|          |             | TT+TC    | 132   | 176     | 1.06 (0.79-1.42) | 0.715          |
|          |             | TC+CC    | 290   | 392     | 1.00           | 1.00             |
|          |             | TT       | 18    | 32      | 0.76 (0.42-1.38) | 0.369          |
|          | Additive    | ---------| ------|---------| ---------------| ---------------|
|          |             |          | 0.99 (0.78-1.26) | 0.939 | 0.99 (0.78-1.25) | 0.927 |
| rs2181559| Codominant  | TT       | 121   | 183     | 1.00           | 1.00             |
|          |             | AA       | 46    | 57      | 1.22 (0.78-1.92) | 0.387          |
|          |             | AT       | 141   | 185     | 1.15 (0.84-1.58) | 0.380          |
|          | Dominant    | TT       | 121   | 183     | 1.00           | 1.00             |
|          |             | AA+AT    | 187   | 242     | 1.17 (0.87-1.58) | 0.306          |
|          |             | AA       | 46    | 57      | 1.13 (0.75-1.72) | 0.558          |
|          | Additive    | ---------| ------|---------| ---------------| ---------------|
|          |             |          | 1.12 (0.90-1.38) | 0.307 | 1.12 (0.90-1.38) | 0.304 |
| rs10965059| Codominant  | CC       | 249   | 277     | 1.00           | 1.00             |
|          |             | TT       | 2     | 8       | 0.28 (0.06-1.32) | 0.108          |
|          |             | TC       | 55    | 137     | 0.45 (0.31-0.64) | <0.001         |
|          | Dominant    | CC       | 249   | 277     | 1.00           | 1.00             |
|          |             | TT+TC    | 57    | 145     | 0.44 (0.31-0.62) | <0.001         |
|          |             | TC+CC    | 304   | 414     | 1.00           | 1.00             |
|          |             | TT       | 2     | 8       | 0.34 (0.07-1.62) | 0.175          |

(Continued)
### TABLE 3 Continued

| SNP ID | Model     | Genotype | Case  | Control | Crude analysis | Adjusted analysis |
|--------|-----------|----------|-------|---------|----------------|-------------------|
|        |           |          |       |         | OR (95% CI)    | p     | OR (95% CI)    | p     |
|        | Additive  |          |       |         | 0.46 (0.33-0.64) | <0.001 | 0.45 (0.32-0.62) | <0.001 |
| rs10965064 | Codominant | CC      | 128   | 171     | 1.00           |       | 1.00           |       |
|         |           | GG      | 39    | 60      | 0.87 (0.55-1.38) | 0.551 | 0.87 (0.54-1.38) | 0.545 |
|         |           | GC      | 141   | 194     | 0.97 (0.71-1.33) | 0.855 | 0.97 (0.71-1.33) | 0.857 |
|         | Dominant  | CC      | 128   | 171     | 1.00           |       | 1.00           |       |
|         |           | GG+GC   | 180   | 254     | 0.95 (0.70-1.28) | 0.719 | 0.95 (0.70-1.28) | 0.719 |
|         | Recessive | GC+CC   | 269   | 365     | 1.00           |       | 1.00           |       |
|         |           | GG      | 39    | 60      | 0.88 (0.57-1.36) | 0.570 | 0.88 (0.57-1.36) | 0.562 |

SNP, single nucleotide polymorphism; OR, odds ratio; 95% CI, 95% confidence interval.
p values were calculated by logistic regression analysis.
Bold values indicate statistical significance (p < 0.05).

### TABLE 4 Relationships between MIR31HG SNPs and alcohol-induced ONFH susceptibility based on stratification by age.

| SNP    | Model     | Genotype |  > 40 years | ≤ 40 years |
|--------|-----------|----------|-------------|------------|
|        |           |          | Case | Control | OR (95% CI) | p   | Case | Control | OR (95% CI) | p   |
| rs10965059 | Allele    | C        | 340  | 380    | 1.00       |     | 213  | 311    | 1.00       |     |
|         |           | T        | 34   | 106    | 0.36 (0.24-0.54) | <0.001 | 25   | 47     | 0.78 (0.46-1.30) | 0.336 |
|         | Codominant | CC      | 154  | 142    | 1.00       |     | 95   | 135    | 1.00       |     |
|         |           | TT      | 1    | 5      | 0.20 (0.02-1.73) | 0.142 | 1    | 3      | 0.44 (0.04-4.41) | 0.488 |
|         |           | TC      | 32   | 96     | 0.31 (0.20-0.50) | <0.001 | 23   | 41     | 0.80 (0.44-1.42) | 0.440 |
|         | Dominant  | CC      | 154  | 142    | 1.00       |     | 95   | 135    | 1.00       |     |
|         |           | TT+TC   | 33   | 101    | 0.31 (0.20-0.49) | <0.001 | 24   | 44     | 0.77 (0.44-1.36) | 0.369 |
|         | Recessive | TC+CC   | 186  | 238    | 1.00       |     | 118  | 176    | 1.00       |     |
|         |           | TT      | 1    | 5      | 0.28 (0.03-2.40) | 0.243 | 1    | 3      | 0.47 (0.05-4.62) | 0.514 |
|         | Additive  | C       | ---  | ---    | ---        |     | ---  | ---    | 0.33 (0.21-0.51) | <0.001 |
|         |           | T       | ---  | ---    | ---        |     | ---  | ---    | 0.77 (0.45-1.30) | 0.323 |

SNP, single nucleotide polymorphism; OR, odds ratio; 95% CI, 95% confidence interval.
p values were calculated by logistic regression analysis.
Bold values indicate statistical significance (p < 0.05).

### TABLE 5 Association between MIR31HG polymorphisms and ONFH risk stratified by necrotic sites.

| SNP    | Model     | Genotype | OR (95% CI) | p   |
|--------|-----------|----------|-------------|-----|
| rs10965059 | Allele    | C        | 1.00        |     |
|         |           | T        | 0.45 (0.32-0.65) | <0.001 |
|         | Codominant | OC      | 1.00        |     |
|         |           | TT      | 0.34 (0.07-1.60) | 0.171 |
|         |           | TC      | 0.40 (0.27-0.59) | <0.001 |
|         | Dominant  | OC      | 1.00        |     |
|         |           | TT+TC   | 0.39 (0.27-0.58) | <0.001 |
|         | Recessive | TC+CC   | 1.00        |     |
|         |           | TT      | 0.43 (0.09-2.03) | 0.284 |
|         | Additive  | C       | 1.00        |     |
|         |           | T       | 0.42 (0.29-0.61) | <0.001 |

SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval.
p values were calculated from logistic regression.
Bold values indicate statistical significance (p < 0.05).
Haplotype analysis and MDR analysis

We analyzed the haplotype of MIR31HG gene. Table 6 represented that there was no linkage between haplotypes and alcoholic ONFH susceptibility ($p>0.05$). Besides, we found a LD block formed by rs72703442, rs2025327, and rs55683539 (Figure 1).

The Fruchterman-Rheingold of SNP-SNP interaction was presented in Figure 2. The results of Supplemental Table 1

| SNP | Haplotype | Frequency in cases | Frequency in controls | With adjustment | Without adjustment |
|-----|-----------|--------------------|-----------------------|-----------------|--------------------|
|     |           | OR (95% CI)        | p                     | OR (95% CI)     | p                  |
| rs72703442|rs2025327|rs55683539 ATT | 0.171 | 0.157 | 1.11(0.84-1.48) | 0.462 | 1.11(0.84-1.48) | 0.464 |
| rs72703442|rs2025327|rs55683539 CTT | 0.073 | 0.087 | 0.83(0.57-1.21) | 0.330 | 0.83(0.57-1.21) | 0.345 |
| rs72703442|rs2025327|rs55683539 CCC | 0.140 | 0.114 | 1.26(0.93-1.71) | 0.142 | 1.26(0.93-1.71) | 0.153 |
| rs72703442|rs2025327|rs55683539 CTC | 0.384 | 0.362 | 1.10(0.89-1.35) | 0.388 | 1.10(0.89-1.35) | 0.393 |

SNP, Single nucleotide polymorphism; OR, Odd ratios; CI, Confidence interval.

FIGURE 1
Linkage disequilibrium (LD) plots containing three polymorphisms from MIR31HG. Block 1 includes rs72703442, rs2025327, and rs55683539. The numbers inside the diamonds indicate the D’ for pairwise analyses.
revealed that rs10965059 was the best single locus model to prediction the ONFH susceptibility (testing accuracy=0.581, CVC=10/10, \( p < 0.0001 \)).

**FPRP analysis**

As shown in Supplemental Table 2, all significant results of rs10965059 remained noteworthy, at the prior probability of 0.001 and FPRP threshold of 0.2.

**Discussion**

We illustrated the relationship of MIR31HG polymorphisms with alcoholic ONFH susceptibility in this study. Results of our research indicated that MIR31HG-rs10965059 decreased the susceptibility of alcoholic ONFH overall. In the age stratification, we also observed that rs10965059 and rs10965064 had protective effect on alcoholic ONFH occurrence older than 40 years old. Besides, rs10965059 could reduce the alcoholic bilateral ONFH risk. These data underline the importance of MIR31HG in alcoholic ONFH occurrence and may serve as a new biomarker for the early prevention and treatment of alcoholic ONFH.

MIR31HG is located at the chromosomal locus 9q21.3 in humans. It has been described to participant in cell proliferation, differentiation in many diseases (20–22). In recent years, the functional role of MIR31HG in bone-related diseases has been studied. For example, Sun et al. found that MIR31HG was higher in tissues of osteosarcoma patients compared with healthy controls and it could regulate osteosarcoma cell growth and migration via miR-361 (23). Ma et al. have shown that MIR31HG was elevated in chordoma patients and MIR31HG silence repressed the migration, growth, and invasion of chordoma cells (24). Besides, suppression of MIR31HG could facilitate the differentiation of osteoblast in human adipose-derived stem cell (16). Moreover, a genome-wide association studies uncovered that MIR31HG polymorphism was related to radius bone density and content in children (25). These evidences led us to hypothesize that MIR31HG may have pathogenic significance in alcoholic ONFH. Here, we firstly observed the contribution of MIR31HG polymorphisms to alcoholic ONFH susceptibility. Rs10965059 exerted a protective role in alcoholic ONFH occurrence in both overall and stratified analysis.

Rs10965059 polymorphism is in the intron region of MIR31HG. Zhao et al. confirmed that the common intronic WDFY4 rs877819 affects the expression of WDFY4 gene by affecting YY1 binding (26). Choi et al. also found that intronic...
SNP (rs2280964) significantly correlated with reduced the expression of CXCR3 gene, which resulted in changes of immune cell responses to chemokine-cytokine signaling in ex vivo and vitro (27). Based on the above studies, we speculated that rs10965059 may affect the susceptibility of alcoholic ONFH by altering the expression of MIR31HG gene. In follow-up studies, we will explore the functional consequence of intronic SNP rs10965059 in vitro and ex vivo to support our hypothesis.

Inevitably, there are some limitations to this study. First, we did not conduct a functional analysis, which is essential to understand the role of MIR31HG in alcoholic ONFH. Second, the subjects were all Chinese Han population, and there may be a certain selection bias. Therefore, we needed animal or cell experiments and more ethnic groups to verify our findings.

Conclusions

To sum up, we confirmed that MIR31HG variants have a significant correlation with the occurrence of alcoholic ONFH in a Chinese Han male population. This may provide new ideas for the prevention and diagnosis of alcoholic ONFH.

Author contributions

JX designed this study protocol; WL drafted the manuscript; XW performed the DNA extraction and genotyping; JC performed the data analysis; FZ performed the sample collection and information recording. JX conceived and supervised the study. All authors read and approved the final manuscript.

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Conflict of interest

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fendo.2022.976165/full#supplementary-material

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