Association Between High-Density Lipoprotein Cholesterol and Type 2 Diabetes Mellitus Among Chinese: The Beijing Longitudinal Study of Aging

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Research article

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Abstract

Background: Contradictory conclusions of association between high-density lipoprotein cholesterol (HDL-C) levels and type 2 diabetes mellitus (T2DM) were reported in different populations. This study aimed to clarify the effect of HDL-C on the risk of T2DM incidence using a cohort lasting for 25-year follow-up.

Methods: This study included 1462 community residents aged 55 or above, excluding subjects with diabetes at baseline. Incident cases of T2DM were ascertained by self-reported T2DM or fasting plasma glucose testing. The data were collected in nine surveys held between the years 1992 to 2017. Cox regression and the Fine-Gray model were applied to evaluate the relationship between HDL-C levels and the risk of T2DM incidence.

Results: 120 participants developed new diabetes during follow-up period. There was a significant negative association between HDL-C levels and the risk of newly on-set T2DM. The incidences of T2DM decreased with the increasing quartile ranges of HDL-C levels, which were 12.60, 9.70, 5.38 and 5.22 per 1000 person-years, respectively. The adjusted hazard ratios (HRs) and 95% confidence intervals were 0.78 (0.50-1.23), 0.51 (0.29-0.90) and 0.47 (0.26-0.84) for subjects with baseline HDL-C levels in ranges of 1.15-1.39, 1.40-1.69 and ≥ 1.70 mmol/L, compared with ones in the range of < 1.15 mmol/L. Similar decreased HRs of T2DM for elevated HDL-C levels were observed in time-dependent Cox regression and other sensitivity analyses.

Conclusion: Higher HDL-C levels were independently related to the lower risk of the newly-onset T2DM among the elderly in China.

Introduction

Diabetes mellitus is one of the most common chronic diseases with an increasing worldwide prevalence from 5.9% in 2007 to 9.3% in 2019. This percentage is expected to increase to 10.9%, in 2045, in accordance with the International Diabetes foundation and thus, representing an enormous disease burden on the world population [1, 2]. Meanwhile, the overall prevalence of diabetes among Chinese adults was 11.2% according to a nationally representative cross-sectional survey conducted in 2015 to 2017 [3]. Type 2 diabetes mellitus (T2DM), which accounts for more than 90% of the person with diabetes, has been recognized as one of the most preventable diseases over the next two decades [4]. Besides, it has also been demonstrated that DM is one of the leading causes of death, especially from cardiovascular disease (CVD) [5, 6]. Therefore, identification and intervention of these modifiable risk factors are critical to the prevention and control of T2DM [7, 8].

Low level of high-density lipoprotein cholesterol (HDL-C) is generally concomitant with hyperglycemia [9–11]. In recent decades, some studies have investigated the relationship between HDL-C level and the T2DM incidence but showed inconsistent results. Some studies have reported the low HDL-C levels were associated with the high T2DM risk among European or American populations [12–14]. However, two studies showed no relationship between HDL-C levels and the T2DM risk, respectively, in the urban and

rural Chinese populations [15, 16]. These contradictory results may be due in part to the underestimation of T2DM incidence in a long time interval between two adjacent follow-up visits. In addition, another explanation for these inconsistent findings may be due to the different ranges of HDL-C levels selected by the studies. Furthermore, most of the existing studies focused on the association between HDL-C levels and the risk of T2DM incidence based on the levels of HDL-C measured at baseline only even though the occurrence and development of T2DM is a long-term dynamic process involving complex pathophysiological changes at cellular and molecular concentrations and HDL-C levels usually fluctuate over time. As a result, conclusions inference on the relationship between the HDL-C levels and the T2DM risk may contradict or tend to be less robust due to few visits during follow-up, underestimate of T2DM incidence in a relative long time interval between two adjacent surveys, different HDL-C stratification or not considering time-varying changes of covariates in statistical analysis. For these reasons, it is necessary to conduct a prospective study with many visits during follow-up to better clarify the association between HDL-C levels and the risk ofT2DM incidence. Therefore, based on a well-designed and more representative prospective study with nine visits during 25 years of follow-up, we assessed the association between the baseline and time-dependent HDL-C levels and the risk of new-onset T2DM.

Material And Methods

Study Design and Population

Data of this investigation were form the Beijing Longitudinal Study of Aging (BLSA) of Chinese community residents aged 55 or above. The participants in the BLSA were selected by conducting a three-stage stratification-random clustering sampling procedure [17–19]. In the baseline survey of 1992, 2101 representative residents recruited from Xuanwu District, Daxing County and Huairou County completed the health examinations and were followed up periodically every several years (in 1994, 1997, 2000, 2004, 2007, 2009, 2012 and 2017). Participants underwent questionnaire interviews and anthropometric measurements at each follow-up and received clinical assessments laboratory examinations in five surveys (years of 1992, 2000, 2009, 2012 and 2017).

Among the 2101 recruited participants, 246 subjects were excluded because they reported medical history of diabetes or had fasting plasma glucose level higher than 7.0 mmol/L. We further excluded 393 individuals who didn't complete the laboratory examination or had incomplete data on HDL-C at baseline. Finally, a total of 1462 participants were incorporated into the present study. All participants provided written informed consent and this study was approved by the Ethics Committee of Capital Medical University (approval number: Z2019SY008), and followed the principles of the Declaration of Helsinki.

Measurement and data collection

We used a standard vis-à-vis questionnaire conducted by well-trained senior medical students to collect the data on demographics behavior lifestyles and previous medical history in nine surveys. Height and weight were measured by standardized stadiometer and weight-scale, with participants wearing thin clothing and no shoes. BMI (Body Mass Index) was calculated by dividing weight (kg) by height squared

(m^2). Blood pressure of the participant was measured on the right arm in the sitting position after resting at least for 5 minutes. Laboratory examinations were conducted on overnight fasting venous blood samples and fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were tested at the laboratory of Xuanwu Hospital, Capital Medical University, Beijing.

Assessments of HDL-C and confounding covariates

Based on the HDL-C levels among 1462 participants at baseline, the HDL-C levels were classified into four groups by the quartiles in the present study. Given that Daxing County and Huairou County have roughly equal economic and educational levels, the two were combined into one group (ie, rural sites). Educational levels were categorized into two groups: primary or lower and secondary or higher. Alcohol consumption was defined as any alcoholic drink greater than or equal to daily intake of 50 ml. Physical activity levels were categorized into three groups: low, moderate and high, by an average exercise time < 3, 3–10, > 10 hours per week respectively.

Assessments of T2DM incidence

Incident T2DM cases were confirmed via a self-reported medical history of T2DM or the FPG level higher than 7.0 mmol/L (126 mg/dl) [20, 21] during the nine follow-up visits since 1992. Subjects were followed up for T2DM incidence, mortality or end of follow-up from the baseline examination (August 1992) to end of follow-up (December 2017). We obtained the death data from death certificates and the interview with family members.

The time of follow-up for every participant was defined as from the baseline time to either the date of T2DM incidence, death date, or loss of follow-up, whichever came first.

Statistical analysis

Continuous variables were displayed by means ± standard deviation (SD) and categorical variables by frequency and percentages. Multivariable Cox model was incorporated to assess the association of HDL-C levels with the risk of T2DM incidence. Considering potential impact of death as competing risk events rather than the censored, we used competing-risks regression based on the Fine and Gray's proportional sub-hazards model to evaluate the association of HDL-C levels with the risk of T2DM [22, 23]. The hazard ratio (HR) or Sub-distribution hazard ratio (SHR) were computed from the Cox regression and Fine-Gray model, separately [24]. For all analysis, we built four steps forward multivariable-adjusted models to assess the relationship between HDL-C levels and the T2DM risk. Model 1 was adjusted for demographic and behavioral characteristics including age, sex, education, daily smoking consumption, daily alcohol intake, physical activity, residence. Model 2 adjusted for the additional confounders of BMI and blood pressure. Model 3 was adjusted for all the variables in Model 2, as well as TC, TG and LDL-C. Finally, we further added baseline FPG concentration (Model 4) to examine the potential effect of baseline blood glucose on the association between HDL-C and the T2DM risk. We assigned the median value to each HDL categories and considered it as a continuous variable for the liner trend testing. Kaplan–Meier

curves and survival curves adjusted for covariates in a regression model4 were generated respectively, according to the category of HDL-C levels, and the log-rank test was used to compare survival curves.

Sensitivity analysis was implemented by excluding subjects who were 75 years old or elder in 1992 in order to examine whether the correlation between HDL-C levels and T2DM risk was probably put down to the aging, Additionally, while age, smoking consumption, drinking status, physical activity, body mass index, blood pressure, TC, TG and LDL-C were time-dependent confounding variables, sex, educational level, residence and FPG measure at baseline were identified as the time-invariant variables. Besides, we used restricted cubic spline regression to explore the nonlinearity association between continuous HDL-C levels at baseline and HRs of T2DM. Analyses were performed with R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) and SAS version 9.4 (SAS Institute, Cary, NC, USA), a 2-tailed level of 0.05 was considered to be statistically significant.

Results

Characteristics of the Cohort Study

During a median follow-up of 8 years, a total of 120 participants developed T2DM, 712 participants died while the 566 subjects lost to the follow-up. At baseline, the mean age of the baseline 1462 individuals (733 men and 729 women) was 68.81 ± 8.49 years. Figure 1 shows the flow chart of this study and the number of T2DM cases at each analysis point. The characteristics of participants in the five different surveys (year of 1992, 2000, 2009, 2012) have been summarized in Table 1. Most of the populations included in the study had HDL-C and systolic pressure readings greater than the above-average of normal. Over 80% of the participants were older than 55 years and had either primary or lower level of education. During the follow-up period, a decrease in the proportion of smoking and alcohol intake was reported. During 14157.04 person-years of follow-up, the cumulative incidence of T2DM was 8.48 per 1000 person-years overall.

Table 1
Characteristics of Study Participants According to The Survey Time.

Variables	1992	2000	2009	2012
	(n = 1462)	(n = 666)	(n = 232)	(n = 122)
Age, year	68.81 ± 8.49	73.61 ± 7.18	79.47 ± 5.04	82.07 ± 4.48
Male, n (%)	733 (50.13)	317 (47.60)	100 (43.10)	52 (42.62)
Educational level, n (%)				
secondary or higher	302 (20.66)	150 (22.52)	55 (23.71)	33 (27.05)
primary or lower	1160 (79.34)	516(77.48)	177 (76.29)	89 (72.95)
Residence, no (%)				
Urban	829 (56.70)	340 (51.05)	95 (40.95)	53 (43.44)
Rural	633 (43.30)	326 (48.95)	137 (59.05)	69 (56.56)
Smoking, n(%)				
0	1010 (69.08)	517 (77.63)	200 (86.21)	106 (86.89)
1–5	104 (7.11)	46 (6.91)	9 (3.88)	3 (2.46)
> 5	348 (23.81)	103 (15.47)	23 (9.91)	13 (10.66)
Alcohol intake, n (%)				
Yes	187 (12.79)	69 (10.36)	16 (6.90)	8 (6.56)
No	1275 (87.21)	597 (89.64)	216 (93.10)	114 (93.44)
Physical activity,				
hours/week, n (%)				
< 3	592 (40.56)	237 (35.59)	56 (24.14)	36 (29.51)
3–10	605 (41.45)	258 (38.74)	96 (41.38)	52 (42.62)
>10	263 (17.99)	171 (25.68)	80 (34.48)	34 (27.87)
BMI (kg/m^2)	23.13 ± 3.86	23.77 ± 3.85	23.00 ± 3.94	22.64 ± 4.37
SBP (mmHg)	141.3 ± 25.2	142.5 ± 24.9	143.8 ± 21.7	142.6 ± 21.9
DBP (mmHg)	81.6 ± 12.5	80.1 ± 12.0	76.7 ± 11.4	75.8 ± 11.2
TC (mmol/L)	4.34 ± 1.02	5.14 ± 1.16	5.46 ± 1.18	5.27 ± 1.15
TG (mmol/L)	1.46 ± 0.75	1.52 ± 0.97	1.52 ± 0.95	1.43 ± 0.80

Variables	1992	2000	2009	2012
	(n = 1462)	(n = 666)	(n = 232)	(n = 122)
LDL-C (mmol/L)	2.98 ± 0.98	2.93 ± 0.85	2.93 ± 0.81	2.94 ± 0.86
HDL-C(mmol/L)	1.50 ± 0.53	1.65 ± 0.51	1.46 ± 0.45	1.49 ± 0.37
FPG (mmol/L)	5.17 ± 0.98	5.15 ± 0.93	5.10 ± 0.90	5.08 ± 0.95

Association Between baseline HDL-C levels and the T2DM Risk

There was a significant association between the HDL-C levels and future risk of T2DM. The incidences of T2DM decreased with the increasing HDL-C quartiles, which were 12.60, 9.70, 5.38 and 5.22 per 1000 person-years, respectively. Figure 2A shows the Kaplan–Meier unadjusted survival estimates for different HDL-C categories. A log-rank test revealed a significant difference in the four groups of HDL-C levels (*P*-values < 0.001). Compared with the lowest quartile Q1 (< 1.15 mmol/L) of HDL-C levels at baseline, higher quartiles Q3 (1.40–1.69 mmol/L) and Q4 (≥ 1.70 mmol/L) were associated with the low risk of newly-onset diabetes while Q2 (1.15–1.39 mmol/L) was not statistically associated with the diabetes incidence in Model 1 and Model 2 in both Cox regression model and competing risk model (Table 2). Moreover, there was a consistent and significant decrease in the T2DM risk for increased quartiles of HDL-C levels at baseline simultaneous adjusting for confounding variables. The adjusted HRs of T2DM incidence for participants with baseline HDL-C levels in the quartiles Q2, Q3 and Q4 were 0.78 (0.50–1.23), 0.51 (0.29–0.90) and 0.47 (0.26–0.84) compared with ones in the lowest quartile in Model 4. The risk of T2DM incidence for subjects in Q3 and Q4 decreased significantly by about 50% in comparison to the lowest quartile of HDL-C level. Figure 2B displays the significant difference in the survival probabilities and the increased trend of adjusted survival curves in the four groups of increased HDL-C levels. Although no statistically significant difference in the Q2 of HDL-C levels was observed, the trend of reduction in T2DM risk was significantly different for all the categories with elevated HDL-C levels (P_{trend}-value = 0.009). Besides, the similar results of sub-distribution hazard ratios (SHRs) were obtained (Table 2). HDL-C levels in Q3 and Q4 remained strongly associated with the risk of newly-onset diabetes, and the SHRs were 0.51 (0.30–0.86), 0.40 (0.28–0.88), respectively, in comparison to the lowest quartile Q1(Table 2).

Table 2
Risk of Type 2 Diabetes Mellitus Incidence According to HDL-C Levels at Baseline.

	HDL-C (mmol/L)				P_{trend}-value
	< 1.15	1.15–1.39	1.40–1.69	≥ 1.70	
No. of subjects	365	361	372	364	-
No. DM cases	46	35	20	19	-
Incidence/1000 person-years	12.60	9.70	5.38	5.22	-
Cox regression					
Model 1	1.00	0.79 (0.51–1.23)	0.45 (0.26–0.77)	0.41 (0.24–0.70)	0.001
Model 2	1.00	0.81 (0.52–1.26)	0.50 (0.29–0.85)	0.45 (0.26–0.78)	0.002
Model 3	1.00	0.83 (0.53–1.30)	0.56 (0.33–0.98)	0.52 (0.29–0.93)	0.020
Model 4	1.00	0.78 (0.50–1.23)	0.51 (0.29–0.90)	0.47 (0.26–0.84)	0.009
Fine-Gray model					
Model 1	1.00	0.79 (0.51–1.21)	0.44 (0.26–0.73)	0.41 (0.24–0.69)	0.001
Model 2	1.00	0.82 (0.53–1.27)	0.48 (0.29–0.81)	0.46 (0.28–0.78)	0.002
Model 3	1.00	0.85 (0.55–1.30)	0.55 (0.33–0.94)	0.54 (0.31–0.96)	0.030
Model 4	1.00	0.81 (0.52–1.25)	0.51 (0.30–0.86)	0.40 (0.28–0.88)	0.015
Model 1: Adjusted for age, sex, education, smoking, alcohol intake, physical activity, residence.					
Model 2: Multivariable model 1 plus SBP, DBP, BMI.					
Model 3: Multivariable model 2 plus TC, LDL-C, TG.					
Model 4: Multivariable model 3 plus FPG					

Sensitivity Analyses

The time-dependent HDL-C levels were also negatively associated with the future T2DM risk (Table 3). In the multivariable-adjusted models, we found that the risk of T2DM decreased with step elevated HDL-C levels. In the fully adjusted models, the hazard ratios (HRs) (95% CI) of T2DM incidence for those with HDL-C levels in the quartiles of Q2, Q3 and Q4 were 1.00 (0.64–1.61), 0.52 (0.29–0.94) and 0.47 (0.25–0.89), respectively, compared with individuals with the lowest quartile Q1 (Table 3). The results did not fundamentally alter by analysis using a competing risk model that aimed to exclude the influence of mortality case (Table 3).

Table 3
Multivariable Risk Analyses to Assess the Association of the T2DM Risk with Time-Dependent HDL-C Levels.

	HDL-C (mmol/L)				P_{trend}-value
	< 1.15	1.15–1.39	1.40–1.69	≥ 1.70	
Cox regression					
Model 1	1.00	0.98 (0.63–1.52)	0.46 (0.27–0.80)	0.38 (0.22–0.66)	< 0.001
Model 2	1.00	1.02 (0.65–1.58)	0.51 (0.30–0.89)	0.45 (0.26–0.79)	0.001
Model 3	1.00	1.08 (0.68–1.70)	0.58 (0.33–1.04)	0.53 (0.28–0.98)	0.020
Model 4	1.00	1.00 (0.64–1.61)	0.52 (0.29–0.94)	0.47 (0.25–0.89)	0.009
Fine-Gray model					
Model 1	1.00	0.96 (0.62–1.48)	0.45 (0.26–0.77)	0.40 (0.23–0.68)	< 0.001
Model 2	1.00	1.02 (0.66–1.57)	0.51 (0.29–0.87)	0.50 (0.30–0.85)	0.003
Model 3	1.00	1.05 (0.67–1.64)	0.53 (0.30–0.93)	0.47 (0.25–0.88)	0.008
Model 4	1.00	1.01 (0.64–1.59)	0.49 (0.28–0.87)	0.44 (0.23–0.81)	0.004

Moreover, the results were consistent after excluding the individuals older than 75 years at baseline (Fig. 3A). Restricted cubic spline Cox regression illustrated the non-linear negative association between baseline HDL-C levels and the T2DM risk (Fig. 3B). HRs and 95% CI at continuous HDL-C were computed with 1.15 mmol/L as the reference value after adjusting all confounding variables. We found that there were significant non-linear dose-response relationships between HDL-C levels and the T2DM risk (*P*-value = 0.005).

Discussion

This community-dwelling prospective study demonstrated that the higher HDL-C levels were independently and negatively associated with the risk of newly-onset T2DM. Notably, this adverse correlation was similar in multivariable competitive risk model when death was regarded as a competitive event. Otherwise, time-dependent HDL-C levels were significantly associated with the risk of T2DM incidence. Furthermore, there was a decreasing and non-linear dose-response relationship between the continuous HDL-C levels and the T2DM risk. All the analyses in the current study presented a robust conclusion that HDL-C levels are independent risk factors of T2DM incidence.

Previous studies have already demonstrated the relationship between HDL-C levels and the future risk of T2DM incidence after adjusting for the potential covariates [12, 14, 25–27]. The PREVENT study, based on Danish patients without diabetes at an average age of 49 years, lasted for 8 years of follow-up,

showed that high HDL-C was a protective factor for the risk of T2DM incidence with an odds ratio (OR) of 0.55 (0.47–0.64) [12]. High baseline HDL-C levels were also associated with a decreased risk of new T2DM in hypertensive patients. Moreover, 14120 participants with significant predictors of incident T2DM were enrolled in The ASCOT-BPLA trial, which reported the HR to be 0.72 (95% CI, 0.58–0.89) for each unit rise in HDL-C [25]. Consistently, a longitudinal study enrolling participants from the fifth clinic examination of the Framingham Offspring study reported a negative association between the HDL-C levels and the T2DM risk with an OR being 0.96 (95% CI, 0.95–0.98) [27]. However, two Chinese studies reported the contradictory conclusions. The multivariable-adjusted model based on a rural China cohort study, demonstrated a non-association between the T2DM risk and the HDL-C levels in the fourth quartile versus the lowest quartile with a HR being 0.92 (95% CI, 0.70–1.19) [15]. Similarly, another prospective study of Chinese people also failed to independently predict T2DM incidence (OR = 0.460; *P*-value = 0.189) [16]. In these two Chinese studies, enrolling participants with low and moderate HDL-C levels may contribute to inconsistent results with studies based on the American or European populations. In addition, in these two Chinese studies, the participants only underwent two visits to access the medical history and examination in a long period of 7 and 15 years, respectively. The underestimate of T2DM incidence in a long time interval may have an effect on the evaluation of true association between the HDL-C levels and the T2DM risk.

Most of previous studies, including Chinese studies, focused only on a single measurement, failing to adjust time-dependent variables, which may lead to inconsistent conclusions since HDL-C concentrations usually fluctuate over time. In current study, while we implied HDL-C as a time-dependent variable, other time-varying confounders that may affect the risk of our endpoint were also used to estimate the association between time-dependent HDL-C levels and the T2DM incidence accurately. In addition, we disposed death as a competitive event to reduce the bias caused by right-censored processing of non-terminal event. Moreover, the robustness of our observations that both the baseline and time-dependent HDL-C levels were significantly associated with the risk of T2DM was verified. To the best of our knowledge, it is the only prospective study in Chinese population that evaluate the impact of HDL-C levels on the T2DM risk by the multiple analysis using the baseline and time-dependent values of variables.

Several possible mechanisms based on clinical and experimental researches have been reported to explain the association between higher HDL-C and decreased risk of T2DM incidence, including increased insulin secretion, glucose uptake by peripheral muscles, and an anti-inflammatory response [28–34]. In vitro studies have shown that HDL can counteract the damage to the insulin secretion process caused by oxidized low-density lipoproteins while a random-control trial in vivo suggested that infusion of recombinant HDL promotes the activation of AMP-activated protein kinase pathway in skeletal muscles among person with diabetes [33, 35]. In double-blinded placebo experiments, the participants who received an intravenous dose of reconstituted HDL-C (rHDL-C) showed an excellent improvement in the plasma glucose. Furthermore, the apolipoprotein (apo) A-I, an important component of HDL-C, have been shown to activate the AMP-mediated protein kinase pathway (AMPK) and hence, the glucose uptake by peripheral muscles [28, 33]. Moreover, by injecting human apoA-I into an insulin-resistant mice, a sharp increase in the insulin secretion was observed and as well as the enhanced ability to eliminate the

glucose [29]. Another Study utilizing the humans and rats demonstrated that the HDL-particles could neutralize the damage caused by the oxidized LDL cholesterol to β-cell function via the JNK pathway [30]. In addition, another study on mice concluded that low HDL-C levels reduced the glucose uptake in peripheral skeletal muscles by disrupting the respiratory function of mitochondria in skeletal muscle cells [31].

There are several major strengths in this study. Firstly, our study was based on a well-designed cohort with standardized procedures and strict quality control, which may represent a sample of middle-aged and elderly people in China. The data in our study are robust and the conclusions are compelling. Secondly, we used repeated measurements of HDL-C levels as a time-variant variable to reduce the regression dilution bias and provide more accurate assessment of association between HDL-C levels and the T2DM risk. Lastly, competitive risk analysis considering death as a competing event were employed to make sure the robust conclusions of association between HDL-C levels and the T2DM risk.

We acknowledge some limitations in this study. First, lacking the 2-h post-load glucose test and fasting HbA1c might induce misclassification of T2DM cases. Therefore, some participants who were supposed to develop diabetes were not diagnosed. However, we identified diabetes according to multiple measures of fasting plasma glucose and self-report physician diagnosis in a relative short time interval, and the impact of underdiagnoses of diabetes on the observed association between HDL-C levels and the T2DM risk could be small. Second, information on dietary habits were not collected in the current study since they might have influence on the levels of HDL-C, which could confound the association between HDL-C and T2DM risk. Third, focusing on elderly population in Beijing, our study cannot fully ensure the stability of extrapolating the results to general population given the ethnic difference. Therefore, further studies based on the epidemiological and experimental methods are required to explore the pathogenesis and the mechanisms of association between the HDL-C levels and the risk of newly-onset diabetes.

Conclusions

In summary, our finding shows that the HDL-C levels were independently associated with the risk of T2DM incidence in middle aged and elderly Chinese. The elevated HDL-C levels decreased the risk of T2DM incidence. This results indicates that elevated HDL-C level might play an important role in glucose metabolism and could provide some information in T2DM prevention, Hence, lipid profiles are important indexes to predict adverse outcome and proposing certain treatment plans in clinical practice.

Abbreviations

BLSA, Beijing Longitudinal Study of Aging; BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol; SHR, sub-distribution hazard ratio; TC, total cholesterol; TG, triglyceride; T2DM, type 2 diabetes mellitus

Declarations

Ethics approval and consent to participate

The Ethics Committee of Capital Medical University approved the study (Z2019SY008).

All participants provided written informed consent in the present study.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Author of Contributions

X. C., Z. T. and D. Z. contributed to the study concept and design. Z. T., F. S., X. G. and D. Z. contributed to the acquisition of data. X. C., J. Z. and H. L. performed the statistical analysis. M. S., J. Z., X. L., C. L., Y. W., X. G. and D. Z. were involved in interpretation of the data. All authors contributed to drafting, modifying and approving the manuscript, and take responsibility for accuracy and integrity of the manuscript.

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Figures

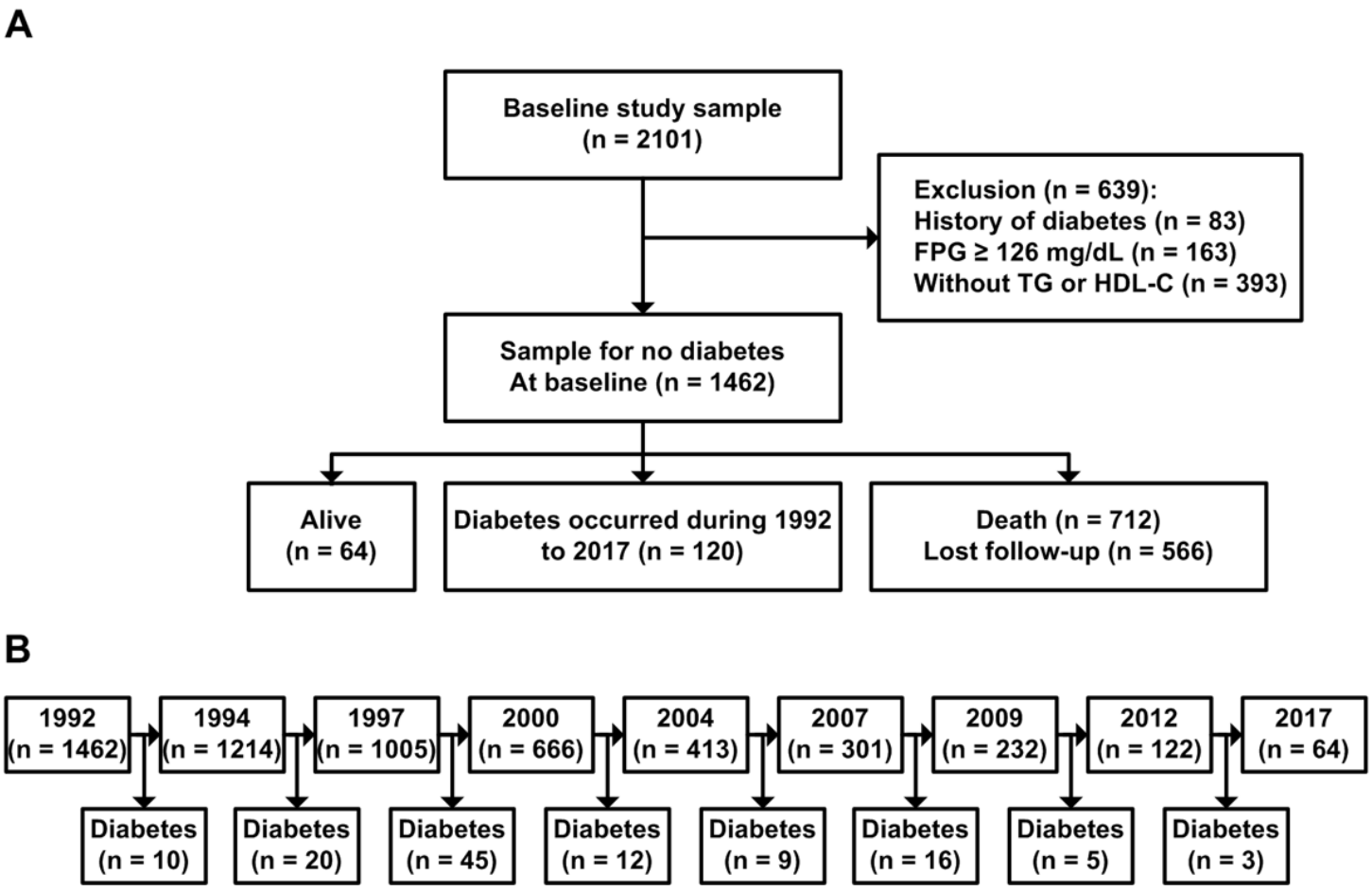

Figure 1

Flowchart of selection of study participants and incidence of T2DMduring 25-year follow-up. (Fig. 1A). Flowchart of the selection of participants in this study. (Fig. 1B). Number of T2DM incidence during nine surveys.

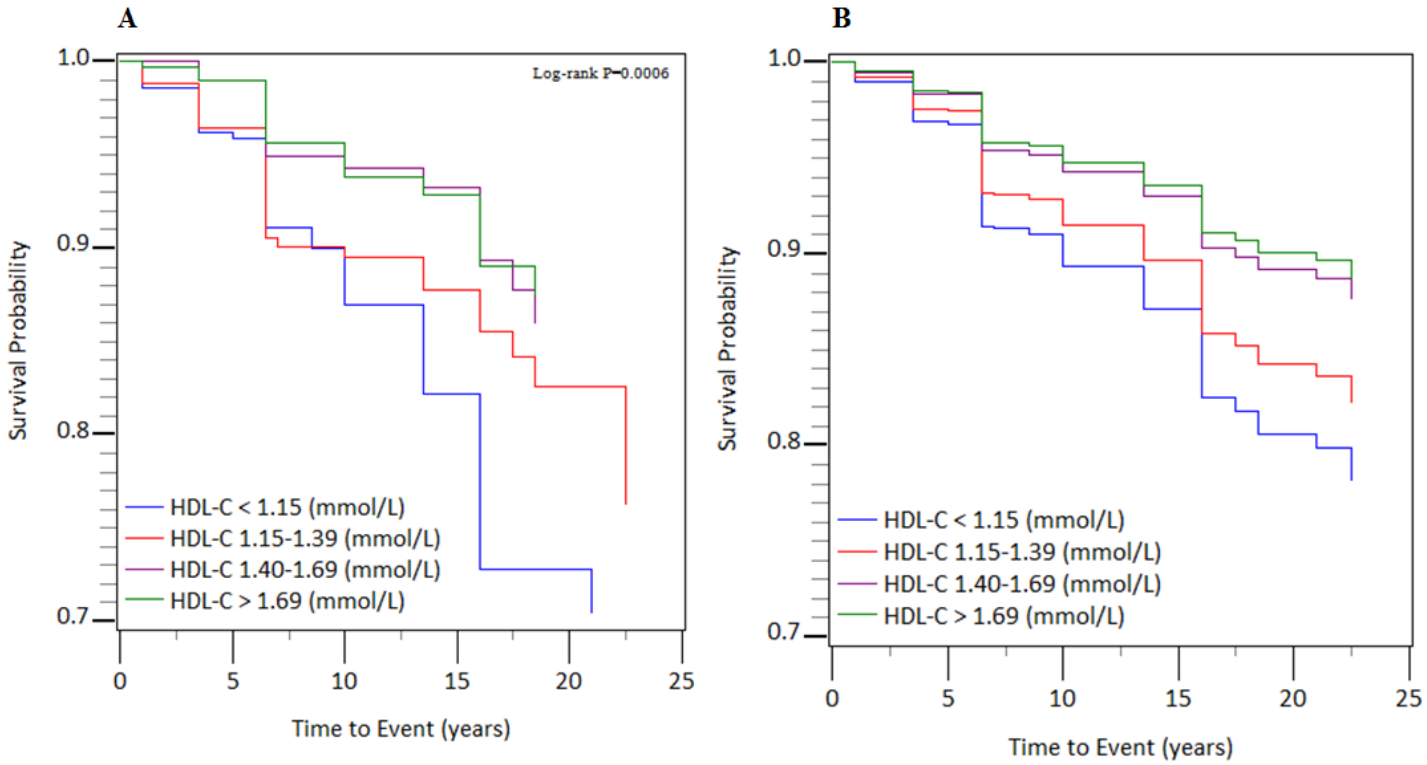

Figure 2

Survival curves for four groups of HDL-C levels. (Fig. 2A) Kaplan–Meier curve (Fig. 2B) Adjusted survival curves for Cox regression in Model 4.

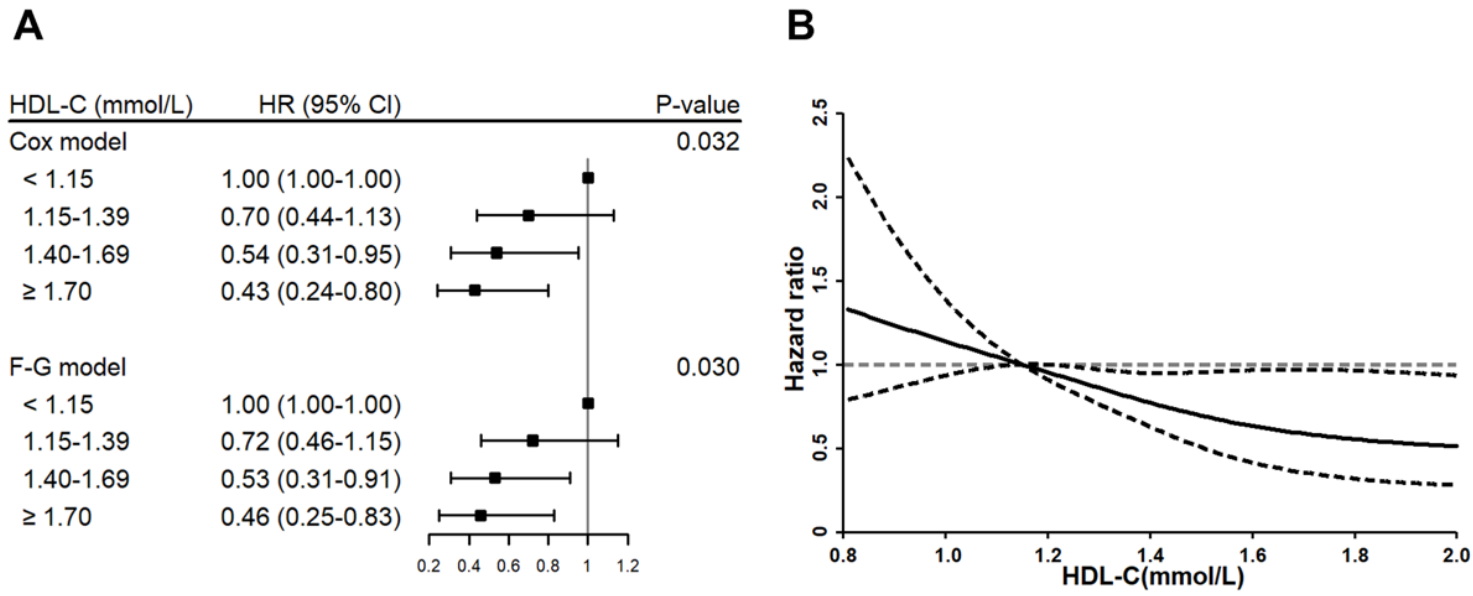

Figure 3

Sensitivity analyzes for the relationship between HDL-C levels and the risk of T2DM incidence. (Fig. 3A). Adjusted hazard ratios and sub-hazard ratios (F-G model represents Fine-Gray model) of T2DM incidence for different quartiles compared with the lowest quartile of HDL-C levels among subjects younger than 75

years old in 1992. (Fig. 3B). Dose-response relationship between continuous HDL-C levels and the risk of T2DM incidence. The estimates of HRs were displayed by solid lines, and the corresponding 95% confidence interval were shown by the dashed lines.