Elevated triglycerides and risk of myocardial infarction in HIV-positive persons

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Objectives: To explore the relationship between elevated triglyceride levels and the risk of myocardial infarction (MI) in HIV-positive persons after adjustment for total cholesterol (TC), high-density lipoprotein–cholesterol (HDL-C) and nonlipid risk factors.

Background: Although elevated triglyceride levels are commonly noted in HIV-positive individuals, it is unclear whether they represent an independent risk factor for MI.

Methods: The incidence of MI during follow-up was stratified according to the latest triglyceride level. Multivariable Poisson regression models were used to describe the independent association between the latest triglyceride level and MI risk after adjusting for TC and HDL-C, nonlipids cardiovascular disease (CVD) risk factors, HIV and treatment-related factors.

Results: The 33 308 persons included in the study from 1999 to 2008 experienced 580 MIs over 178 835 person-years. Unadjusted, the risk of MI increased by 67% [relative risk (RR) 1.67, 95% confidence interval 1.54–1.80] per doubling in triglyceride level. After adjustment for the latest TC and HDL-C level, the RR dropped to 1.33 (95% confidence interval 1.21–1.45); this effect was further attenuated by other CVD risk factors and the RR was reduced to 1.17 (95% confidence interval 1.06–1.29). In models that additionally adjusted for HIV and treatment factors, the risk was further diminished, although remained significant (RR 1.11, 95% confidence interval 1.01–1.23).

Conclusion: Higher triglyceride levels were marginally independently associated with an increased risk of MI in HIV-positive persons, although the extent of reduction in RR after taking account of latest TC, latest HDL-C and other confounders suggests that any independent effect is small.

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Introduction

Elevated triglyceride levels are common in HIV-positive persons for several reasons. First, conditions that traditionally result in elevated triglyceride, such as insulin resistance, diabetes mellitus and fatty liver, are prevalent in the HIV-positive population [1–4]. Second, the physiological distress that results from untreated HIV infection may cause lipid perturbations, particularly elevated triglyceride [5,6]. Indeed, it has been suggested that HIV-positive patients may experience increased postprandial triglyceride levels [7], this being one potential explanation for the increased risk of myocardial infarction (MI) that is seen in HIV-positive persons. The presence of increased levels of atherogenic remnant lipoproteins (chylomicron remnants and very low-density lipoprotein remnants) might be associated with increased levels of nonfasting triglycerides. These smaller triglyceride-rich lipoproteins may penetrate the endothelial cell layer in which they can contribute to the formation of foam cells, involved in early stages of atherosclerosis [8].

Finally, elevated triglyceride is a frequent side-effect of antiretroviral therapy (ART) [9–11]. Different antiretroviral drugs have different propensities to cause elevated triglyceride, with drugs not only from the protease inhibitor class but also the nonnucleoside reverse transcriptase inhibitor (NNRTI) efavirenz and some NRTI drugs [9–11], all being reported to cause elevated triglyceride. Some of these drugs have been associated with an increased risk of MI in HIV-positive patients [12,13].

The extent to which elevated triglyceride is a cause of or even an independent risk factor for cardiovascular disease (CVD) in the general population remains controversial. Some recent articles have identified elevated triglyceride as an independent risk factor for CVD after adjusting for high-density lipoprotein–cholesterol (HDL-C) and total cholesterol (TC) [14,15]. However, a recent meta-analysis concluded that there was no independent effect of elevated triglyceride on the risk of MI [16]. In HIV-positive persons, in whom the causes and clinical implications of elevated triglyceride may differ, it is particularly unclear whether triglyceride levels provide additional prognostic information regarding MI risk once TC and HDL-C are taken into account. The purpose of this analysis is, therefore, to explore the independent relationship between elevated triglyceride levels and the risk of MI in HIV-positive persons, after adjustment for cardiovascular risk factors (including TC and HDL-C), HIV and treatment-related factors.

Methods

The D:A:D study (Data Collection on Adverse Events of Anti-HIV Drugs) is a prospective, observational study formed by the collaboration of 11 cohorts following HIV-positive persons from 212 clinics in Europe, Australia and the United States. The primary objective of the study is to investigate the possible association between combination ART (cART) and the onset of MI. The D:A:D study methodology has been described in detail elsewhere [12].

Data collection

Patients are followed prospectively during visits to outpatient clinics as a part of regular medical care. At enrolment and at least every 8 months thereafter standardized data collection forms are completed at the sites providing information concerning family history of coronary heart disease, prior history of CVD and diabetes mellitus, cigarette smoking, blood pressure, lipid-lowering and antihypertensive therapy, the presence of physician-documented lipodystrophy and serum lipid levels (TC, HDL-C, triglyceride levels and information on fasting conditions), as well as HIV-related information (ART, CD4 cell counts, HIV viral loads and dates of diagnoses of all AIDS-defining diseases).

End points

All incident cases of MI are reported to the study coordinating office for validation and coding. Reported MIs are classified as definite, possible or unclassifiable according to criteria applied in the WHO MONICA (Multinational MONItoring of trends and determinants in CArdiovascular disease) study independently of knowledge of a patient's antiretroviral treatment history (with cardiologists' input). Patients who had already experienced an MI, or coronary revascularization (bypass or angioplasty), or a stroke prior to study entry were defined as having previous CVD. These events were not validated centrally. Only the first MI during prospective follow-up was included in the present analysis.

Statistical analysis

Follow-up was counted from D:A:D enrolment until the first MI event, the date of death, 1st February 2008 or 6 months after the patient's last clinic visit (whichever occurred first). Patient's follow-up period was split into a series of consecutive 1-month periods, and their covariate data was updated (if this information had changed) at the start of each month. For the purpose of this analysis, fasting status of the lipids was not taken into consideration, that is there was no requirement for triglycerides to be performed in a fasting or nonfasting state.

As an exploratory analysis, the incidence of the first MI during prospective D:A:D follow-up was calculated according to the latest (time-updated) triglyceride, TC and HDL-C level. For the purposes of these analyses, the latest measurement of each lipid was stratified into quintiles based on the distribution of levels across all measures on all people (see Table 2 for categories), with an additional category for follow-up and events in patients

in whom no measurement was available. As these analyses were time-updated, person-years of follow-up and any events that occur will be allocated to the most recently available triglyceride measurement at the time; if a new triglyceride measurement becomes available, then subsequent person-years and events are allocated to the new value. This information was used to assess the appropriateness of incorporating each measurement into a regression model as a continuous covariate.

Using Poisson regression, we analysed the relationships between the development of MI and each lipid measurement separately, followed by each pair of measurements, then all three lipids adjusted for one another in the same model. On the basis of the exploratory analyses, the latest triglyceride and TC levels were incorporated into these models as continuous time-updated covariates (with the triglyceride level being $\log_2$-transformed prior to inclusion, thus estimates are per doubling in triglyceride level), whereas the HDL-C level was incorporated as a categorical time-updated covariate (due to the higher proportion of follow-up time without a measurement available) with six levels, including category for missing HDL-C. We then repeated these analyses after adjusting for other CVD risk factors [age (continuous covariate), sex, ethnicity, mode of infection, BMI, smoking status, previous CVD event (CVD events before and after baseline, excluding MI after baseline), family history of CVD and calendar year (all categorical covariates)]. All analyses were performed using the GENMOD procedure in SAS (SAS Institute Inc., Cary, North Carolina, USA).

Several further adjusted analyses were performed. First, we re-ran the model after additionally adjusting for the latest $CD4^+$ cell count and HIV RNA level (both fitted as time-updated covariates) as well as cumulative exposure to the protease inhibitor, NRTI and NNRTI drug classes. Second, as diabetes mellitus and the use of lipid-lowering drugs may both have an impact on MI risk and may also occur more frequently in those receiving ART, we included adjustment for these in our model again as time-updated covariates, thus reflecting the changing status of an individual over time. We next additionally adjusted for blood glucose level, another factor that may lie on the causal pathway between ART and MI risk. Given the high proportion of follow-up time in which no HDL-C measurement was available, we then repeated our main analyses after using multiple imputation methods to complete the missing lipid data. Specifically, we used PROC MI in SAS to impute missing lipid measurements (triglyceride, TC and HDL) at baseline. Variables included in the model used to impute baseline lipids were baseline covariates (age, sex, ethnicity, risk group, BMI, smoking status and prior CVD) and whether the patient developed an MI over follow-up; imputed values were then carried forward until the time of the first available measurement for each individual. Five datasets were imputed and the MI procedure in SAS was used to combine the relative risk (RR) estimates from the five different datasets. To explore whether any apparent relationship between the latest triglyceride level and MI risk was being driven by a small number of individuals with particularly high triglyceride levels, we further stratified the highest triglyceride group into 3–4, 4–5 and more than 5 mmol/l. Finally, as several drugs have been reported to be associated with an increased triglyceride level, most notably lopinavir/r and ritonavir, we investigated whether there was a statistical interaction between the latest triglyceride level and ever or current receipt of these drugs. Such an interaction might indicate a different clinical relevance of raised triglyceride levels in patients receiving these drugs with those in patients not receiving them.

Results

The 33 308 patients included in the D:A:D study were followed for a total of 178 835 person-years {median 5.8 [interquartile range (IQR) 3.9–7.5] per person} over which time 580 incident MIs occurred (event rate 3.2 per 1000 person-years, 95% confidence interval 3.0–3.5). Overall, 30 703 (92.2%) patients had at least one triglyceride measurement available; these patients contributed 435 658 triglyceride measurements to the analysis [median 13 (IQR 7–18) per person]. Of these, 25.7% were known to be measured in a fasting state and 12.1% in a nonfasting state; information on fasting state was not available for the remaining 62.2% of triglyceride measures. Overall, the median (IQR) triglyceride measurement was 1.70 mmol/l (IQR 1.10–2.80) ($n=$ 435 658), the median TC measurement was 5.00 mmol/l (IQR 4.20–5.90) ($n=425\,677$) and the median HDL-C measurement was 1.18 mmol/l (IQR 0.94–1.45) ($n=303\,075$).

Most of the patients included in the analysis were male (74.1%), white (53.6%) and likely mode of HIV acquisition was through sex between men (43.2%). Around a third (34.7%) of patients were current smokers, 2.9% had diabetes mellitus and 18.8% were co-infected with hepatitis C (Table 1). A total of 3.1% had a BMI less than 18 kg/m^2, 4.5% had a BMI more than 30 kg/m^2 and 4.1% were on a lipid-lowering drug. Their latest median CD4 cell count was 408 cells/μl (IQR 249–600) and 32% of patients were virologically suppressed ($\leq$50 copies/ml) of which 97.8% were ART experienced.

Risk of myocardial infarction associated with elevated triglyceride levels

The incidence of MI increased as triglyceride levels increased, from 1.1 per 1000 person-years in those with triglyceride level of less than 1.00 mmol/l to 6.1 per 1000 person-years in those with triglyceride level of

Table 1. Characteristics of patients at entry in the D:A:D study.

Number of patients, *N* (%)	33 308 (100)
Male sex, *n* (%)	24 669 (74.1)
Race, *n* (%)	
White	17 835 (53.6)
Black	3548 (10.7)
Other	1051 (3.2)
Unknown	10 874 (32.7)
BMI (kg/m^2), *n* (%)	
<18	1038 (3.1)
18–26	22 073 (66.3)
26–30	4237 (12.7)
>30	1504 (4.5)
Unknown	4456 (13.4)
Mode of infection, *n* (%)	
Sex between men	14 388 (43.2)
Sex between men and women	10 017 (30.1)
IDU	5997 (18.0)
Other/unknown	2906 (8.7)
Smoking status, *n* (%)	
Current smoker	11 572 (34.7)
Exsmoker	6120 (18.4)
Never smoked	9014 (27.1)
Unknown	6602 (19.8)
Family history of CVD, *n* (%)	
Yes	2312 (6.9)
No	22 631 (67.9)
Unknown	8365 (25.1)
Previous CVD[a], *n* (%)	
Yes	537 (1.6)
No	32 771 (98.4)
Diabetes mellitus, *n* (%)	
Yes	976 (2.9)
No	32 322 (97.1)
Receipt of lipid-lowering drugs, *n* (%)	
Yes	1357 (4.1)
No	21 922 (65.8)
Unknown	10 029 (30.1)
Co-infected with hepatitis C virus, *n* (%)	
Yes	6257 (18.8)
No	17 520 (52.6)
Unknown	9531 (28.6)
Previous exposure to ART, *n* (%)	
PIs	19 355 (58.1)
NNRTIs	11 112 (33.4)
NRTIs	24 308 (73.0)
Median value (IQR), number of patients	
Age (years)	39 (34–45); 33 307
BMI (kg/m^2)	23 (21–25); 28 852
Log HIV-1 RNA (copies/ml)	2.7 (1.7–4.2); 32 085
CD4 counts (cells/μl)	408 (249–600); 32 442
Lipids	
HDL–cholesterol	1.1 (0.9–1.4); 15 123
Total cholesterol	4.9 (4.1–5.9); 27 656
Triglycerides	1.6 (1.0–2.6); 27 646

ART, antiretroviral therapy; CVD, cardiovascular disease; HDL, high-density lipoprotein; IQR, interquartile range; MI, myocardial infarction; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.
[a]Patients who had already experienced an MI or coronary revascularization (bypass or angioplasty) or a stroke prior to study entry.

more than 3.00 mmol/l (Table 2). Similarly, the incidence of MI increased as TC increased, from 1.8 per 1000 person-years in those with TC level of less than 4.0 mmol/l to 6.7 per 1000 person-years in those with TClevel of more than 6.1 mmol/l. In contrast, the incidence of MI decreased as HDL-C levels increased, from 4.4 per 1000 person-years in those with HDL-C level of less than 0.90 mmol/l to 1.9 per 1000 person-years in those with HDL-C level of more than 1.60 mmol/l.

Results from unadjusted analyses of the association between triglyceride level and MI mirrored the crude analyses described above. Particularly, in unadjusted analyses, each doubling in the latest triglyceride level was associated with a 67% increased risk of MI (RR 1.67, 95% confidence interval 1.54–1.80; Table 3, model 1). We next considered the impact of adjusting for the other lipid markers on the association between triglyceride and MI, but without adjusting for any other potential confounder. After adjusting for the latest HDL-C level (model 5), the RR associated with a doubling of triglyceride level did not change appreciably (RR 1.63, 95% confidence interval 1.50–1.77), but adjustment for the latest TC measurement (model 4) did lead to a reduction in the RR associated with an elevated triglyceride (RR 1.43, 95% confidence interval 1.32, 1.56). Adjustment for both the latest TC and HDL-C measurement (model 7) reduced the association further (RR 1.33, 95% confidence interval 1.21, 1.45). Of note, the latest TC and HDL-C measurements remained strongly associated with MI risk in all models (Table 3).

Figure 1 shows the association between the latest triglyceride level and MI risk after adjusting for the latest TC and HDL-C levels, as well as the results from additional adjusted analyses. Further adjustment for other CVD risk factors, as well as for HIV and treatment-related factors, reduced the association between a doubling of triglyceride and MI risk further, from 1.33 to 1.17 and 1.11, respectively. At this point, further adjustment for diabetes mellitus and the use of lipid-lowering drugs, as well as for blood glucose levels, had no additional impact on the RR associated with elevated triglyceride, although confidence intervals were widened slightly.

In models that used multiple imputation methods to impute lipid data, the association between a doubling of triglyceride and MI risk (after adjustment for other lipids as well as CVD risk factors) changed from 1.17 (95% confidence interval 1.05–1.30) to 1.18 (95% confidence interval 1.07–1.30). To exclude the possibility that the apparent residual association between a doubling of triglyceride and an increased risk of MI was being driven by a small number of patients with very high levels of triglyceride, we repeated the analyses after subdividing the highest triglyceride strata further. The results were unchanged, and continued to support a gradual increase in MI risk as the triglyceride level increased (data not shown). Although sensitivity analyses suggested that the association between raised triglyceride levels and MI risk might be slightly stronger in women (RR 1.14, 95% confidence interval 0.79–1.64) than in men (RR 1.10, 95% confidence interval 0.99, 1.23), a formal interaction test was nonsignificant ($P = 0.20$). Although the test of interaction between older age (≥40 years) and raised

Table 2. Myocardial infarction event rates (per 1000 person-years) according to the latest measurement of triglyceride, total cholesterol and high-density lipoprotein–cholesterol.

	Number of myocardial infarctions	Person-years	Event rate (per 1000 person-years)	95% confidence interval
TG (mmol/l)				
<1.0	38	33 765	1.1	0.8–1.5
1.0–1.4	80	35 942	2.2	1.7–2.7
1.4–2.0	95	31 753	3.0	2.4–3.6
2.0–3.0	136	32 623	4.2	3.5–4.9
≥3.0	206	33 984	6.1	5.2–6.9
Missing	25	10 768	2.3	1.4–3.2
TC (mmol/l)				
<4.0	56	30 943	1.8	1.3–2.3
4.0–4.7	69	37 925	1.8	1.4–2.2
4.7–5.3	82	33 019	2.5	1.9–3.0
5.3–6.1	131	34 094	3.8	3.2–4.5
>6.1	219	32 845	6.7	5.8–7.6
Missing	23	10 010	2.3	1.4–3.2
HDL-C (mmol/l)				
<0.9	123	28 194	4.4	3.6–5.1
0.9–1.1	124	28 791	4.3	3.5–5.1
1.1–1.3	99	26 461	3.7	3.0–4.5
1.3–1.6	82	26 142	3.1	2.5–3.8
≥1.6	42	22 146	1.9	1.3–2.5
Missing	110	47 102	2.3	1.9–2.8

HDL-C, high-density lipoprotein–cholesterol; TC, total cholesterol; TG, triglyceride.

Table 3. Relationships between the development of myocardial infarction and the latest measurement of each lipid.

Model number	Lipids		Relative risk	95% confidence interval	*P* value
Separate models for each lipid					
1	TG	Per $\log_2$ higher	1.67	1.54–1.80	<0.001
2	TC	Per mmol/l higher	1.29	1.26–1.33	<0.001
3	HDL-C	<0.9	2.30	1.62–3.26	<0.001
		0.9–1.1	2.27	1.60–3.22	
		1.1–1.3	1.97	1.38–2.83	
		1.3–1.6	1.65	1.14–2.40	
		≥1.6	1	–	
		Missing	1.23	0.86–1.76	
Models for each pair of lipid measurements					
4	TG	Per $\log_2$ higher	1.43	1.32–1.56	<0.001
	TC	Per mmol/l higher	1.23	1.17–1.28	<0.001
5	TG	Per $\log_2$ higher	1.63	1.50–1.77	<0.001
	HDL-C	<0.9	1.36	0.94–1.95	0.005
		0.9–1.1	1.52	1.07–2.18	
		1.1–1.3	1.47	1.02–2.11	
		1.3–1.6	1.41	0.97–2.05	
		≥1.6	1	–	
		Missing	0.96	0.66–1.39	
6	TC	Per mmol/l higher	1.32	1.28–1.36	<0.001
	HDL-C	<0.9	3.04	2.12–4.36	<0.001
		0.9–1.1	2.75	1.92–3.94	
		1.1–1.3	2.29	1.58–3.31	
		1.3–1.6	1.88	1.29–2.75	
		≥1.6	1	–	
		Missing	1.53	1.05–2.23	
Model including all three lipid measurements					
7	TG	Per $\log_2$ higher	1.33	1.21–1.45	<0.001
	TC	Per mmol/l higher	1.26	1.20–1.32	<0.001
	HDL-C	<0.9	2.02	1.39–2.95	<0.001
		0.9–1.1	2	1.38–2.88	
		1.1–1.3	1.76	1.22–2.55	
		1.3–1.6	1.59	1.09–2.32	
		≥1.6	1	–	
		Missing	1.21	0.83–1.77	

HDL-C, high-density lipoprotein–cholesterol; TC, total cholesterol; TG, triglyceride.

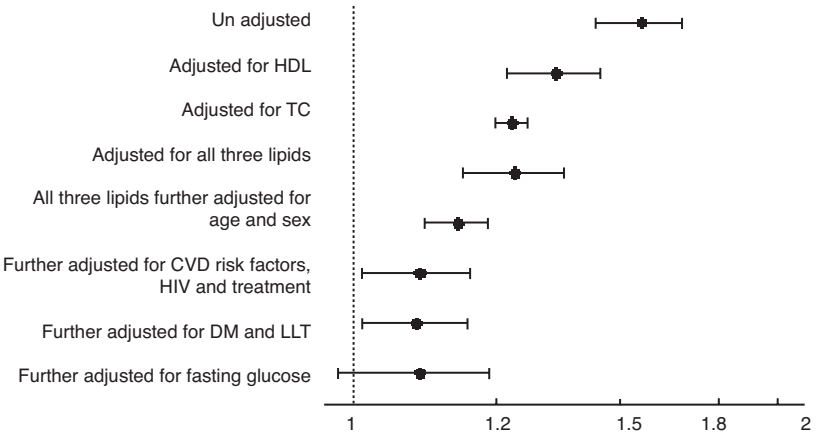

Fig. 1. Relative risk of myocardial infarction per doubling (log_2 increase) in triglyceride, additional adjustments. Cardiovascular disease (CVD) risk factors are as follows: age, sex, ethnicity, mode of infection, BMI, smoking status, previous CVD event, family history of CVD event and calendar year. HIV factors are as follows: CD4 cell count and HIV RNA levels. Treatment factors are as follows: cumulative exposure to protease inhibitor, nucleoside reverse transcriptase inhibitor (NRTI) and non-NRTI drug classes. DM, diabetes mellitus; HDL, high-density lipoprotein; LLT, lipid-lowering therapy; TC, total cholesterol.

triglyceride levels was significant ($P = 0.01$), estimates in the two age groups did not differ greatly (<40 years: RR 1.15, 95% confidence interval 0.86–1.52; ≥40 years: RR 1.11, 95% confidence interval 1.00–1.24). Finally, we explored whether the 'residual effect' of triglyceride of 11% was explained by ART-induced triglyceride changes. However, there was no such evidence or modification by exploring an interaction with drugs and triglyceride.

Discussion

Despite the fact that elevated triglyceride is a frequent side-effect of ART, the association between elevated triglyceride and the risk of MI has never yet been assessed in a study with clinical end points. In the present study, we found that higher triglyceride levels were independently associated with an increased risk of MI. However, the residual effect of elevated triglyceride levels after adjustment for TC, HDL-C and nonlipid risk factors was very small (11% per doubling in triglyceride) compared with the original unadjusted effect size of 67%. Overall, these findings suggest that MI risk stratification in HIV-positive persons should focus more on other modifiable risk factors than elevated triglyceride.

Our findings are in accordance with two recent meta-analyses based on studies conducted in the general population [16,17] in which adjustment for HDL-C led to a reduction in the RR associated with triglyceride levels from 1.37 (95% confidence interval 1.31–1.42) to 0.99 (95% confidence interval 0.94–1.05) [15], but are less concordant with findings from other studies [14,15,18–21]. One explanation for the differences between the studies may be the different CVD risk profile of the included patients: not only were patients in the D:A:D study 10–15 years younger, on average, than persons in most studies from the general population, but the average BMI at baseline is also much lower (median 23 kg/m^2, with 4.5% of patients having a BMI of more than 30 kg/m^2).

Of interest, neither the association between TC and MI risk nor that between HDL-C and MI risk changed dramatically after adjustment for other CVD or HIV-related risk factors, and both remained significant after adjustment in multivariable models. The strong and independent association between elevated TC and MI risk has also been shown in the general population [16,17,22].

It may be anticipated that drug-induced triglyceride changes might have a different impact on MI risk than 'lifestyle'-induced triglyceride changes. However, a sensitivity analysis in which we explored the interaction between triglyceride levels and use of lopinavir/r and/or ritonavir (protease inhibitor drugs that are both known to lead to rapid increase in triglyceride levels after initiation) did not indicate that this was the case.

Although our findings are based on observational cohort data, a risk of 11% of MI associated with a doubling in triglyceride levels would question whether the use of drugs to lower triglyceride levels (e.g. fibrates, nicotinic acid) would have a major impact on the incidence of MI in HIV-positive patients, particularly if these drugs have no other independent effects on MI risk. Two randomized controlled trials have demonstrated the effectiveness of fibrates in terms of lipid parameters in

HIV-positive persons [23,24]. However, no randomized controlled trial of the effect of these drugs on the risk of MI has been conducted in HIV-positive persons. Recent guidelines from the European AIDS Clinical Society (EACS) do not recommend the use of niacin and fibrates to treat elevated triglyceride [25].

Limitations

Several limitations of our study should be noted. First, information on fasting conditions was not available for all lipid measurements. Previous analysis from our study suggest that although the absolute level of triglyceride measurements differed according to whether the measurement was taken in a fasting or nonfasting condition, the association between elevated triglyceride and MI risk did not differ (D. Kamara, in preparation). Second, the lack of repeated sampling and the within-person variability of triglyceride levels may introduce bias when assessing the association with CVD, a phenomena known as regression dilution bias [26]. Although this is unlikely to have a major impact on our findings, it may mean that we have underestimated the effects of TC and HDL-C and, hence, the extent to which they attenuate the association between triglyceride and MI risk. In addition, our study does not include data on low-density lipoprotein–cholesterol, nor on insulin resistance, lipoproteins or particle size, all factors that have an impact on triglyceride [13]. The duration of elevated triglyceride might have been too short to translate into a clinical end point such as MI, so we cannot exclude the possibility that elevated triglyceride for more than 7–10 years is associated with a greater risk of MI. Finally, as this is an observational study, we cannot capture information on other changes to patient management and/or lifestyles that may have had an impact on MI risk.

The large reduction in RR from 1.67 to 1.11 suggests that a large proportion (if not all) of the effect seen in univariable analyses is due to confounding. Additional adjustments for diabetes mellitus and fasting glucose levels did not modify the RR further, but did result in wider confidence intervals and nonsignificant associations. Furthermore, a causal link between triglyceride level and MI cannot be established due to the observational nature of our study.

The importance of understanding whether high levels of triglyceride preceded or followed the presence of cardiovascular risk factors is not yet clear. As elevated triglyceride are often seen in many conditions associated with inflammation (e.g. CVD, fatty liver disease), elevated triglyceride might be a nonspecific biomarker, rather than an independent risk factor for MI or CVD and, therefore, likely more affected in HIV-positive persons in whom ongoing inflammation is not infrequent, compared with the general population.

Conclusion

Given the ageing of the HIV population, and their potential lifelong reliance on ART, it has become essential to identify patients at risk for MI and CVD, allowing preventive measures to be targeted more appropriately. On the basis of our results, we suggest that future risk stratification should be focused more closely on non-triglyceride lipids such as TC and HDL-C, and on other and modifiable CVD risk factors including smoking.

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