Immune checkpoint inhibitor (ICI) therapy has restructured cancer treatment paradigms while also triggering a broad spectrum of immune-related adverse events (irAEs). Commonly prescribed ICIs include ipilimumab for cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) blockade, pembrolizumab and nivolumab for programmed cell death protein 1 (PD-1) blockade, and atezolizumab, avelumab, and durvalumab for programmed death-ligand 1 (PD-L1) blockade. Blockade of signaling pathways through ICIs enables the activation of the immune system to destroy cancer cells, allowing for clinical applications for cancer therapy. However, blockade of PD-1/PD-L1 signaling has been reported to activate and cause proliferation of autoreactive cluster of differentiation (CD) 8+ T-cells targeting self antigen-presenting

Highly active antiretroviral therapy in adult HIV-infected patients with heart failure: A 7-year prospective cohort study

Kevin Sheng-Kai Ma
Center for Global Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
(Email: kevinskma@gmail.com)

Introduction

HAART has been proposed to result in coronary artery diseases and metabolic syndromes (MetS) in HIV-infected patients. We determined whether patients with heart failure (HF) undergoing HAART were at high risk of subsequent cardiovascular complications and MetS, compared with HIV-infected patients without HF.

Materials and Methods

A prospective cohort study that recruited 172 HIV-infected patients was conducted at a medical center since 2014. Patients underwent follow-ups, with demographic and medical records including: weight, BMI, waist, blood pressure, history, status and drug use for DM, CVDs, and MetS, HAART regimens, Data Collection on Adverse Effects of Anti-HIV Drugs (D:A:D) CVD risk scores, CKD risk score and GFR, plasma viral load (PVL) of HIV, CD4 cell count, being recorded. Blood and urine samples were also collected and analyzed. Changes following HAART from baseline were compared for patients with HF versus age- and gender-matched patients without HF, using linear and logistic regression (R ver 4.0.1).

Paired t-test

Pre-HAART outcome	Post-HAART outcome	Mean of differences	95% confidence interval	R squared	two-tailed P value	P value summary	t, df
Baseline height (cm)	Last F/U height (cm)	0.0218	-0.1222 to 0.1657	0.0005	0.7674	ns	t=0.2963 df=169
Baseline weight (kg)	Last F/U weight (kg)	-3.463	-4.391 to -2.534	0.2402	< 0.0001	***	t=7.310 df=169
Baseline BMI	Last F/U BMI	-2.246	-4.311 to -0.1803	0.0262	0.0345	*	t=2.131 df=169
Baseline circumference	Last F/U circumference	-3.891	-5.281 to -2.501	0.1512	< 0.0001	***	t=5.487 df=169
Baseline DM (1=yes; 0=no)	Last F/U DM (1=yes; 0=no)	-0.0355	-0.06349 to -0.007521	0.0355	0.0139	*	t=2.487 df=168
Baseline smoking (1=yes; 0=no)	Last F/U smoking (1=yes; 0=no)	0.071	0.02573 to 0.1163	0.0533	0.0025	**	t=3.074 df=168
Baseline exercise (1=yes; 0=no)	Last F/U exercise (1=yes; 0=no)	0.027	-0.1198 to 0.1739	0.0039	0.7109	ns	t=0.3735 df=36
Baseline MetS (1=yes; 0=no)	Last F/U MetS (1=yes; 0=no)	-0.1353	-0.2046 to -0.06602	0.0798	0.0002	***	t=3.828 df=169
Baseline D:A:D (R) CVD 5 year	Last F/U D:A:D (R) CVD 5 year	-3.519	-4.666 to -2.372	0.177	< 0.0001	***	t=6.012 df=168
Baseline D:A:D (R) CVD 10 yea	Last F/U D:A:D (R) CVD 10 year	-5.654	-7.014 to -4.293	0.2842	< 0.0001	***	t=8.144 df=167
Baseline D:A:D (F) CVD 5 year	Last F/U D:A:D (F) CVD 5 year	-4.345	-5.790 to -2.900	0.1713	< 0.0001	***	t=5.893 df=168
Baseline D:A:D (F) CVD 10 year	Last F/U D:A:D (F) CVD 10 year	-6.82	-8.517 to -5.122	0.2695	< 0.0001	***	t=7.873 df=168
Baseline HIV PVL	HIV PVL at year 4	-32430	-187100 to 122300	0.0046	0.6738	ns	t=0.4242 df=39
Baseline HIV PVL	HIV PVL at year 5	50630	-3038 to 104300	0.1264	0.0634	ns	t=1.940 df=26
Baseline CD4	CD4 count at year 1	-95.34	-129.9 to -60.82	0.159	< 0.0001	***	t=5.414 df=155
Baseline CD4	CD4 count at year 2	-127.2	-165.2 to -89.19	0.2325	< 0.0001	***	t=6.558 df=142
Baseline CD4	CD4 count at year 3	-138.9	-176.6 to -101.2	0.159	< 0.0001	***	t=7.219 df=137
Baseline CD4	CD4 count at year 4	-166.9	-207.1 to -126.6	0.3254	< 0.0001	***	t=8.128 df=137
Baseline CD4	CD4 count at year 5	-184.7	-242.8 to -126.6	0.3313	< 0.0001	***	t=6.335 df=81
Baseline HbA1C	HbA1C at year 3	0.25	-10.55 to 11.05	0.0796	0.8179	ns	t=0.2941 df=1
Baseline HbA1C	HbA1C at year 4	-0.45	-4.897 to 3.997	0.6231	0.4208	ns	t=1.286 df=1
Baseline blood sugar	Blood sugar at year 4	-1.593	-4.247 to 1.061	0.0102	0.2414	ns	t=1.177 df=134
Baseline blood sugar	Blood sugar at year 5	-13.17	-27.24 to 0.8979	0.0444	0.0657	ns	t=1.868 df=75
Baseline TG	TG at year 3	9.242	-7.554 to 26.04	0.0091	0.2829	ns	t=1.078 df=127
Baseline TG	TG at year 4	-5.492	-26.58 to 15.60	0.0022	0.6071	ns	t=0.5156 df=119
Baseline TG	TG at year 5	11.79	-15.78 to 39.36	0.0119	0.3958	ns	t=0.8553 df=61
Baseline CHO	CHO at year 2	-0.5736	-7.058 to 5.911	0.0002	0.8626	ns	t=0.1734 df=128
Baseline CHO	CHO at year 3	-2.188	-8.514 to 4.139	0.0036	0.4992	ns	t=0.6778 df=127
Baseline CHO	CHO at year 4	-8.75	-16.35 to -1.147	0.0418	0.0244	*	t=2.279 df=119
Baseline CHO	CHO at year 5	-23.56	-32.71 to -14.42	0.3033	< 0.0001	***	t=5.153 df=61
Baseline LDL	LDL at year 1	-1.217	-4.961 to 2.527	0.0028	0.5252	ns	t=0.6370 df=142
Baseline LDL	LDL at year 2	1.009	-4.439 to 6.457	0.0012	0.7141	ns	t=0.3672 df=111
Baseline LDL	LDL at year 3	-6.307	-11.08 to -1.532	0.0572	0.01	*	t=2.618 df=113
Baseline LDL	LDL at year 4	-7.009	-12.85 to -1.169	0.0469	0.019	*	t=2.378 df=115
Baseline LDL	LDL at year 5	-17.44	-24.65 to -10.24	0.2743	< 0.0001	***	t=4.841 df=62
Baseline HDL	HDL at year 1	-4.737	-8.498 to -0.9766	0.0406	0.0147	*	t=2.469 df=144
Baseline HDL	HDL at year 2	-3.965	-6.236 to -1.695	0.0975	0.0008	***	t=3.463 df=111
Baseline HDL	HDL at year 3	-3.632	-5.662 to -1.602	0.0994	0.0006	***	t=3.547 df=114
Baseline HDL	HDL at year 4	-4.751	-6.964 to -2.538	0.136	< 0.0001	***	t=4.254 df=115
Baseline HDL	HDL at year 5	-7.716	-10.61 to -4.819	0.3139	< 0.0001	***	t=5.326 df=62

Results

HAART was effective for both HIV-infected patients with or without HF, with a similar viral load (r=0.001, P=0.69) and an insignificantly compromised CD4 count improvement for patients with HF at three years of follow-up (r=-0.06, P=0.48). HAART did not increase the risk of CVDs for patients with HF, with D:A:D (R) (r=0.002, P=0.97) and D:A:D (F) (r=0.04, P=0.62) CVD risk scores being similar. However, patients with HF presented with significantly higher risk of developing DM (r = 0.24, P=0.01), increasing total cholesterol (CHO) at two (r=0.23, P=0.006), three (r=0.20, P=0.02), and four (r=0.20, P=0.02) years of follow-up, all compared to baseline. Moreover, patients with HF presented with significantly higher risk of increasing LDL (r=0.18, P=0.04) at four years of follow-up. On the other hand, uric acid was increased significantly more in patients with HF at 48 (r=0.27, P=0.002) and at 96 (r=0.35, P=0.004) weeks of follow-up

Conclusion

HAART was equally effective for HIV management in patients with HF, and did not result in more subsequent CVDs or renal toxicities, when compared with patients without HF; however, increased risk of DM and increased levels of CHO, LDL, and uric acid during follow-ups, were observed.