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Long-term benefits of high-intensity atorvastatin therapy in Chinese acute coronary syndrome patients undergoing percutaneous coronary intervention

A retrospective study

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Abstract

There is lack of long-term data on high-intensity statin therapy of Chinese acute coronary syndrome (ACS) patients scheduled to undergo percutaneous coronary intervention (PCI). In this retrospective study, we compared the long-term efficacy and safety of high-intensity and conventional atorvastatin therapy in reducing low-density lipoprotein cholesterol (LDL-C) and plaque size, and improving cardiac function of ACS patients who underwent PCI.

We retrospectively analyzed the clinical records of 120 consecutive ACS patients who underwent PCI at our hospital. Group I received a loading dose of atorvastatin (80 mg/day) prior to PCI, followed by a maintenance dose of 40 mg/day for 3 months post-PCI. Group II received a regular dose of atorvastatin (20 mg/day) from the date of admission until 1 year post-PCI. The composite primary efficacy end point was the mean percent change in calculated LDL-C from baseline to week 48 in both groups and percentage of patients achieving the LDL-C target of $\leq$1.81 mmol/L.

Group I had significantly higher mean baseline LDL-C than group II. Moreover, 8.3% of group I patients had an LDL-C $\leq$1.81 mmol/L versus 43.3% for group II. At week 24, 75.0% and 90.0% of group I and II patients, respectively, achieved the LDL-C target. At week 48, 85.0% and 96.7% of group I and II patients, respectively, achieved the LDL-C target. Additionally, the mean percent changes at week 4 from baseline in LDL-C were $-33.6\% \pm 20.0\%$ for group I versus $-12.8\% \pm 19.6\%$ for group II, and $-47.0\% \pm 25.5\%$ at week 48 for group I versus $-36.4\% \pm 20.2\%$ for group II. Meanwhile, significant reduction in plaque size and marked improvement in cardiac function were seen in patients receiving high-intensity atorvastatin therapy.

Compared to conventional therapy, high-intensity statin therapy is more effective in reducing LDL-C and improving cardiac function of ACS patients, with a general benign safety profile over a period of 48 weeks. Our findings support the use of high-intensity statin therapy for Chinese ACS patients to improve the proportion of patients attaining the LDL-C target and reduction in plaque size and improvement cardiac function.

Abbreviations: ACS = acute coronary syndrome, CK = creatine kinase, cTNI = cardiac troponin I, HDL-C = high-density lipoprotein cholesterol, hs-CRP = high-sensitivity C-reactive protein, LDL-C = low-density lipoprotein cholesterol, PCI = percutaneous coronary intervention, TG = triglycerides.

Keywords: acute coronary syndrome, atorvastatin, cardiac function, cystatin C, high intensity, hs-CRP, LDL-C, percutaneous coronary intervention, plaque size

1. Introduction

Cardiovascular diseases pose a serious global heath burden; in China alone, there are approximately 250 million persons suffering from cardiovascular diseases. Among cardiovascular diseases, acute coronary syndrome (ACS) is considered a very complex disorder with pathologies encompassing tissue remodeling, necrosis, thrombosis, and inflammation. ACS contains a wide spectrum of diseases due to acute myocardial ischemia and/or necrosis secondary to a reduction in coronary blood flow as a result of unstable angina, non-ST-elevation myocardial infarction, or ST-elevation myocardial infarction.

Patients with ACS experience high rates of recurrent coronary events, particularly, early in their presentation. Lipid interventions after ACS have focused primarily on lowering low-density lipoprotein cholesterol (LDL-C) or raising high-density lipoprotein cholesterol (HDL-C) to reduce the risk of recurrent cardiovascular events among the patients. The latest guidelines recommend that the target LDL-C for patients with ACS should

Editor: Ovidiu Constantin Baltatu.

HL and AD are co-first authors.

Clinical registration number: ChiCTR-IOR-17012291.

The authors have no conflicts of interest to disclose.

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Medicine (2018) 97:42(e12687)

Received: 2 January 2018 / Accepted: 13 September 2018

http://dx.doi.org/10.1097/MD.0000000000012687

be ≤1.81 mmol/L after percutaneous coronary intervention (PCI).[1] However, a sizable proportion of Chinese ACS patients failed to attain the LDL-C target. The DYSIS-China study showed that only 61.5% patients attained the LDL-C target, and a markedly lower proportion of high risk patients such as those with metabolic syndrome achieved the LDL-C target.[2] Zhang et al retrospectively studied 633 consecutive prospectively enrolled ACS patients who were treated with PCI and statins (atorvastatin 20 mg/day, rosuvastatin 10 mg/day, pravastatin 40 mg/day, fluvastatin 80 mg/day, or simvastatin 20 mg/day) for 1 year and found that after 1 year of therapy, close to half of the patients (48%) failed to attain the LDL-C target.[3]

The 2013 American College of Cardiology/American Heart Association cholesterol management guidelines replaced LDL-C targets with a risk assessment model to guide statin therapy[4] and advised physicians to tailor high-intensity statin after ACS instead of titration of statin to reach LDL-C targets. Liu et al[5] investigated 798 Chinese patients with stable angina or ACS who were randomized to receive high-intensity atorvastatin (80 mg/day before PCI and 40 mg/day thereafter for 1 year) or moderate-intensity atorvastatin (20 mg/day for 1 year) and found that the 1-year major adverse cardiovascular event (MACE) rate was significantly higher in the moderate- than in the high-intensity atorvastatin group (16.8% vs 10.1%, $P = .021$; adjusted hazards ratio = 1.71, 95% CI = 1.08–2.77, $P = .021$). In the current retrospective study, we compared the long-term efficacy and safety of high-intensity and conventional low-intensity atorvastatin therapy in reducing LDL-C of ACS patients who underwent PCI.

2. Patients and methods

2.1. Patients

We retrospectively analyzed the clinical records of consecutive ACS patients who underwent PCI at our hospital between April 2015 and April 2016. ACS was defined as the presence of an acute myocardial infarction, with or without ST-segment elevation on electrocardiography, or high-risk unstable angina.

The study protocol was approved by the local institutional review board at the authors' affiliated institution (No. 201503-015), and patient consent was not required because of the retrospective nature of this study.

2.2. Therapeutic protocol

PCI was performed in all the patients as routinely done. All patients received aspirin (100–300 mg/day) and clopidogrel (300–600 mg) at least 2 hours before PCI. Glycoprotein IIb/IIIa inhibitors were used at the surgeon's discretion. Aspirin was prescribed at a dose of 300 mg/day for 1 to 3 months, followed by 100 mg/day for lifelong medication. Clopidogrel (75 mg/day) was given for at least 1 year after PCI. In addition, group I received a loading dose of atorvastatin (80 mg) prior to PCI, followed by a maintenance dose of 40 mg/day for 3 months post-PCI. Group II received a low dose of atorvastatin (20 mg/day) from the date of admission until 1 year post-PCI. Atorvastatin dose in group I was adjusted to the conventional low dose if AST or ALT abnormality developed within 3 months of treatment.

2.3. Laboratory studies

Serum samples were prepared immediately after blood sampling and stored frozen at −70 °C until laboratory assessment. Serum levels of total cholesterol (TC), LDL-C, HDL-C, and triglycerides (TG) were collected at admission and at week 4, 12, 24, 36, and 48 of treatment. Serum cystatin C content was measured by using the Human Cystatin C ELISA kit as instructed by the manufacturer (Elabscience Biotechnology Co., Ltd, Wuhan, Hubei, China). A turbidimetric immunoassay Wako CRP-HS (Wako Chemicals, Germany) was used for quantitative determination of high-sensitivity C-reactive protein (hs-CRP) with ADVIA 1650 biochemical analyzer (Siemens, GRE). The plasma concentration of cardiac troponin I (cTNI) was measured using the Troponin I Ultra assay on an ADVIA Centaur CP Immunoassay System (Siemens Healthcare GmbH; Eschborn, Germany) with a detection limit of 6 pg/mL, a 99th percentile at 40 pg/mL, and a coefficient of variation of less than 10% at 30 pg/mL, as specified by the manufacturer.

2.4. Ultrasonography

Bilateral B-mode ultrasound examination of the carotid artery was undertaken by an experienced sonographer using a 12-MHz linear matrix array transducer (GE Vivid-7 ultrasound scanner; GE Vingmed Ultrasound). Images from the baseline assessment were used as a reference for subsequent visits at week 4, 12, 24, 36, and 48. Plaque length and width measurements were read offline by an experienced cardiologist. Carotid plaque length and width were measured from the leading edge at the maximum height of the plaque to the leading edge of the adventitia in the longitudinal view and the horizontal view.

Global left ventricular systolic functions were assessed in all patients by transthoracic echocardiography using a Vivid 7 cardiac ultrasonography system (GE VingMed Ultrasound AS; Horten, Norway) equipped with harmonic imaging capabilities. Left ventricular ejection fraction was recorded by the modified Simpson method. Views were acquired and analyzed upon admission and at week 4, 12, 24, 36, and 48 of treatment by a single echocardiographer using the software program of the echocardiography machine.

2.5. Study end points

The composite primary efficacy end point was the mean percent change in calculated LDL-C from baseline to week 48 in patients treated with high-intensity atorvastatin therapy and conventional low-intensity atorvastatin therapy and percentage of patients achieving the LDL-C goal of ≤1.81 mmol/L according to the 2007 Chinese adult Dyslipidemia Prevention Guidelines.[6] Secondary efficacy end points included the percent change from baseline to week 48 in TC, TG, HDL-C, plaque size, ejection fraction, cTNI, cystatin C, and hs-CRP.

Safety assessments included clinical laboratory tests for AST, ALT, serum creatinine, and blood urea nitrogen.

2.6. Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation or median with interquartile range for continuous variables and as frequency and percentages for nominal variables. Differences in baseline characteristics between women and men were assessed by χ^2-test for categorical variables and Student t test or Wilcoxon rank sum test for continuous variables, as appropriate.

3. Results

3.1. Patient demographic and baseline characteristics

The study flowchart is shown in Figure 1. Totally 120 patients with ACS were included in the current study. The demographic

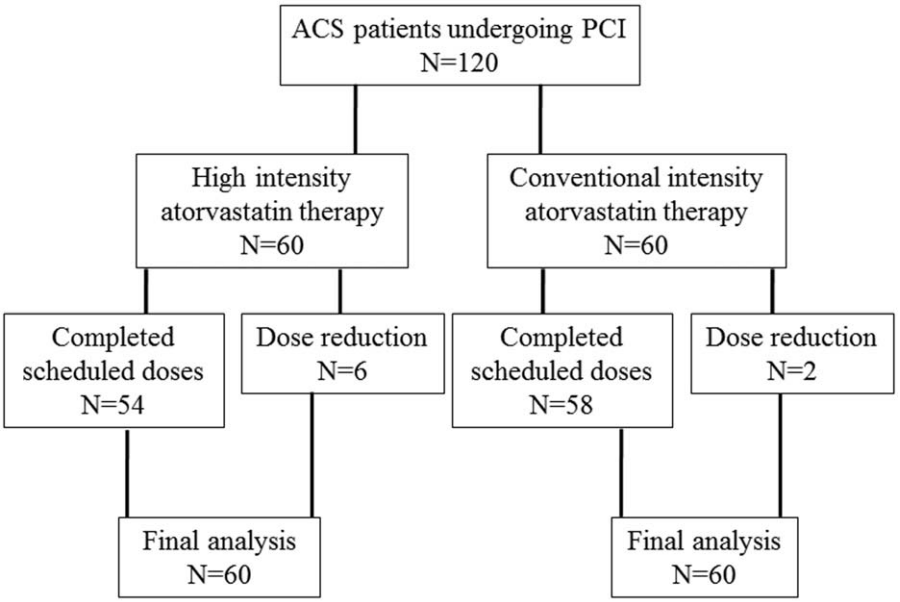

Figure 1. The study flowchart.

and baseline data of the study subjects are shown in Table 1. Their mean age was 60.3 ± 11.2 years (range 34–80 years) and 75% of the patients were men. Thirty-seven (30.8%) patients had STEMI followed by STEMI (25.8%) and non ST-segment elevation myocardial infarction (16.7%). Ninety-six (90.6 80%) patients were of TIMI III. Forty-six (38.3%) patients had a history of dyslipidemia and 46 (29.2%) patients used statin. Fifty-four (45%) patients showed abnormality on carotid ultrasound.

A significantly higher proportion of ACS patients in group II and STEMI (51.7% vs group I, 25.0%) while a significantly higher proportion of ACS patients in group I had STIMI (61.7% vs group II, 0%) (Fisher exact, $P < .0001$). In this study, 31 patients (51.7%) in group I had STEMI, compared with 37 patients (61.7%) in group II. Moreover, 20 patients (16.7%) in group I had (NSTEMI), compared with 8 patients (6.7%) in group II. In addition, significantly more patients in group II had previous dyslipidemia (51.7% vs group I 25.0%; Chi-square = 9.0247, $P = .0027$). Abnormality on carotid ultrasound was found in 45% of patients in group II (vs group I, 40%; Fisher exact, $P = .0036$).

Table 1

Demographic and baseline characteristics of the study population*.

	All	High intensity	Low intensity	*P* value
N (%)	120 (100)	60 (50)	60 (50)	
Mean age (SD), y	61.48 ± 11.25	60.33 ± 11.22	62.62 ± 11.27	T = −1.11, $P = .2681$
Male gender, N (%)	90 (75.0)	44 (73.3)	46 (76.7)	Chi-square = 0.1778, $P = .6733$
ACS stage, N (%)				Fisher exact, $P < .0001$
NSTEMI	28 (23.3)	20 (33.3)	8 (13.3)	
STEMI	68 (56.7)	31 (51.7)	37 (61.7)	
STEMI (after thrombolysis)	7 (5.8)	7 (11.7)	0 (-)	
UA	17 (14.2)	2 (3.3)	15 (25.0)	
TIMI stage, N (%)				Fisher exact, $P = .5160$
II	4 (3.3)	3 (5.00)	1 (1.7)	
II+	20 (16.7)	11 (18.3)	9 (15.0)	
III	96 (80.0)	46 (76.7)	50 (83.3)	
Previous dyslipidemia				Chi-square = 9.0247, $P = .0027$
Yes	46 (38.3)	31 (51.7)	15 (25.0)	
Statin use				Chi-square = 1.0084, $P = .3153$
Yes	35 (29.2)	20 (33.3)	15 (25.0)	
Carotid ultrasound, N (%)				Fisher exact, $P = .0036$
No	7 (5.8)	7 (11.7)	0 (–)	
Normal	59 (49.2)	23 (38.3)	36 (60.0)	
Abnormal	54 (45.0)	30 (50.0)	24 (40.0)	

ACS = acute coronary syndrome, NSTEMI = non ST-segment elevation myocardial infarction, SD = standard deviation, STEMI = ST-segment elevation myocardial infarction, TIMI = thrombolysis in myocardial infarction, UA = unstable angina.

* Data were expressed as N (%) unless otherwise indicated.

Table 2

Mean (±SD%) percent changes from baseline of lipid parameters.

	Week 4		Week 12		Week 24		Week 36		Week 48	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
LDL-C, mmol/L	−33.6±20.0	−12.8±19.6	−39.5±21.6	−19.7±18.5	−44.4±18.9	−26.7±17.7	−47.0±21.9	−30.7±18.2	−47.0±25.5	−36.4±20.2
HDL-C, mmol/L	20.5±37.7	11.8±19.6	26.3±36.7	21.2±19.2	41.2±60.6	27.7±24.3	50.6±58.8	43.1±28.6	66.0±70.5	46.6±29.3
TC, mmol/L	−25.5±16.3	−8.3±16.6	−28.6±16.6	−2.4±100.3	−32.6±17.0	−18.5±13.0	−35.8±18.2	−20.6±16.7	−35.0±20.8	−23.6±17.4
TG, mmol/L	−13.4±33.9	−6.0±45.9	−18.3±33.8	−12.0±45.6	−20.8±39.1	−14.8±46.7	−22.5±42.3	−18.4±45.2	−21.3±58.5	−23.1±42.9

HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, SD = standard deviation, TC = total cholesterol, TG = triglycerides.

3.2. Changes in the lipid profile with high- and conventional low-intensity atorvastatin therapy

Group I patients had significantly higher mean LDL-C (3.13 ± 0.96 mmol/L) at baseline than group II patients (2.00 ± 0.70 mmol/L; T = 7.40, $P = .0000$). Moreover, 8.3% of group I patients had an LDL-C ≤1.81 mmol/L versus 43.3% for group II patients. At week 24, 75.0% of group I patients and 90.0% of group II patients achieved the LDL-C target ≤1.81 mmol/L. At week 48, 85.0% of group I patients and 96.7% of group II patients achieved the LDL-C target ≤1.81 mmol/L. In addition, the mean percent changes at week 4 from baseline in LDL-C were −33.6% ± 20.0% with high-intensity atorvastatin therapy versus −12.8% ± 19.6% with conventional low-intensity atorvastatin therapy (T = −5.76, $P < .0001$), and −47.0% ± 25.5% at week 48 with high-intensity atorvastatin therapy versus −36.4% ± 20.2% with conventional low-intensity atorvastatin therapy (T = −2.52, $P = 0.0131$) (Table 2).

Moreover, a significant mean percent reduction in TC was observed with high-intensity atorvastatin therapy from week 4 (−25.5% ± 16.3% vs conventional low-intensity atorvastatin therapy −8.3% ± 16.6%; T = −5.71, $P < .0001$) to week 48 (−35.0% ± 20.1% vs conventional low-intensity atorvastatin therapy −23.6% ± 17.4%; T = −5.71, $P < .0001$). A comparable mean percent reduction in TG was noted with high-intensity and conventional low-intensity atorvastatin therapy with a −21.3% ± 58.5% change from baseline at week 48 for group I and a −23.1% ± 42.9% change from baseline at week 48 for group II (T = 0.19, $P = .8528$). In addition, both high-intensity and conventional low-intensity atorvastatin therapy caused a significant rise in HDL-C from baseline at week 48 (T = 1.97, $P = .0513$), but no significant difference was observed for mean percent change in TG between group I and II (T = 0.19, $P = .8528$).

3.3. Changes in plaque size with high- and conventional low-intensity atorvastatin therapy

No apparent difference was observed in the baseline levels of plaque length (group I 10.66 ± 15.48 vs group II 11.07 ± 2.6; T = .17, $P = .8660$) and width (group I 7.71 ± 1.98 vs group II 8.14 ± 1.62; T = −1.06, $P = .2945$ (Table 3). A dramatic reduction was seen in plaque size with both high-intensity atorvastatin therapy at week 12 and conventional low-intensity atorvastatin therapy (length: group I: 7.92 ± 2.96 vs group II: 10.13 ± 2.52; T = 4.87, $P = .0001$; width: group I: 6.83 ± 1.73 vs group II: 7.50 ± 1.60; T = 1.84, $P = .0070$). The difference lasted for the 48 week (length: group I: 5.32 ± 2.25 vs group II: 7.71 ± 2.25; T = 4.38, $P = .0001$; width: group I: 4.94 ± 1.70 vs group II: 5.78 ± 1.47; T = −2.38, $P = .00196$). The total atheroma value at baseline was markedly larger in group II than group I (F = 22.20, $P < .0001$) (Table 3). A significant −39.8% ± 18.3% reduction in plaque length and a marked −35.9% ± 20.1% reduction in plaque width at week 48 were observed in group I (T = −11.58, $P < .0001$ for length; T = −9.72, $P < .0001$ for width, respectively). This percentage reduction at week 48 was significantly higher than that in group II (T = −2.37, $P = .0203$ for length; T = −2.03, $P = .0461$ for width).

3.4. Changes in cardiac biomarkers with high- and conventional low-intensity atorvastatin therapy

No apparent difference was observed in the baseline levels of cTNI between group I (3.45 ± 2.86) and group II (3.59 ± 3.55; T = −.23, $P = .8168$) (Table 4). A dramatic reduction was seen in plasma cTNI content with both high-intensity atorvastatin therapy at week 4 and conventional low-intensity atorvastatin therapy (group I: 0.05 ± 0.03 vs group II: 0.04 ± 0.02; T = 1.39, $P = .1668$). This effect was maintained at week 48 in both groups

Table 3

Changes in plaque size with high and conventional atorvastatin therapy (mean ± SD).

	Plaque length, mm			Plaque width, mm		
	Group 1	Group 2	*P*	Group 1	Group 2	*P*
Baseline	10.66±15.48	11.09±2.63	$t = 0.17$ $P = .8660$	7.71±1.99	8.12±1.63	$t = -1.06$ $P = .2945$
Week 12	7.92±2.96	10.15±2.52	$t = 4.87$ $P = .0001$	6.76±1.71	7.48±1.61	$t = 1.84$ $P = .0700$
Week 24	6.56±2.83	9.39±2.45	$t = 4.76$ $P = .0001$	6.25±1.72	6.83±1.58	$t = 1.58$ $P = .1189$
Week 48	5.32±2.61	7.78±2.23	$t = 4.38$ $P = .0001$	4.96±1.72	5.78±1.41	$t = -2.38$ $P = .0196$

SD = standard deviation.

Table 4

Changes in cardiac biomarkers with high and conventional atorvastatin therapy (mean ± SD).

	cTNI, U/L			Cystatin-c, μmol/L			hs-CRP, mg/L			CK-MB, U/L		
	Group I	Group II	P	Group I	Group II	P	Group I	Group II	P	Group I	Group II	P
Baseline	3.45 ± 2.86	3.59 ± 3.55	T = −0.23, P = .8168	1.23 ± 0.45	1.24 ± 0.36	T = −0.15, P = .8845	6.54 ± 4.45	6.53 ± 6.79	T = 0.01, P = .9916	143.26 ± 131.84	101.03 ± 118.33	T = 1.85, P = .0674
Week 4	0.05 ± 0.03	0.04 ± 0.02	T = 1.39, P = .1668	1.00 ± 0.23	1.04 ± 0.23	T = −0.98, P = .3312	3.01 ± 2.02	3.18 ± 2.64	T = −0.46, P = .6447	19.17 ± 4.83	18.78 ± 4.21	T = 0.46, P = .6442
Week 12	0.05 ± 0.02	0.05 ± 0.03	T = −0.20, P = .8455	0.98 ± 0.23	0.99 ± 0.21	T = −0.32, P = .7458	1.72 ± 1.02	3.19 ± 2.85	T = −3.77, P = .000	16.01 ± 12.95	16.17 ± 4.35	T = −.09, P = .9272
Week 24	0.04 ± 0.02	0.05 ± 0.02	T = −3.7, P = .0003	0.93 ± 0.18	0.91 ± 0.20	T = 0.79, P = .4298	1.67 ± 0.99	4.82 ± 11.06	T = −2.20, P = .0298	16.38 ± 3.62	15.15 ± 3.98	T = 1.78, P = .0784
Week 36	0.03 ± 0.02	0.04 ± 0.02	T = −1.3, P = .1842	0.89 ± 0.32	0.94 ± 0.24	T = −0.83, P = .4062	1.51 ± 1.02	2.72 ± 2.26	T = −3.78, P = .0003	16.65 ± 8.02	13.23 ± 4.59	T = 2.86, P = .0052
Week 48	0.04 ± 0.02	0.04 ± 0.02	T = −0.98, P = .3270	0.84 ± 0.22	0.96 ± 0.29	T = −2.6, P = .0121	1.49 ± 0.81	2.73 ± 3.43	T = −2.73, P = .00073	13.33 ± 4.18	12.25 ± 4.53	T = 1.36, P = .1763

CK-MB = creatine kinase-MB, cTNI = cardiac troponin I, hs-CRP = high-sensitivity C-reactive protein, SD = standard deviation.

(group I: 0.04 ± 0.02; group II: 0.04 ± 0.02; T = −.98, P = .327). The baseline plasma cystatin C content was comparable between group I and II (T = −.15, P = .8845). A significantly greater magnitude of reduction in cystatin C content at week 48 from baseline was observed in group I (24% ± 31%) versus group II (18% ± 30%; T = −1.2, P = .2354). In addition, both high-intensity and conventional low-intensity atorvastatin therapy were associated with a significant reduction in creatine kinase (CK) or CK-MB levels from week 4 to week 48 versus baseline. No apparent difference was observed in the baseline levels of hs-CRP between group I (6.54 ± 4.45) and group II (6.53 ± 6.79; T = .01, P = .9916). At week 12, a significantly greater magnitude of reduction in hs-CRP content from baseline was observed in group I (1.72% ± 1.02%) versus group II (3.19% ± 2.85%; T = 3.77, P = .0000). This effect was maintained at week 48 in group I (group I: 1.49 ± 0.81; group II: 2.73 ± 3.43; T = 2.73, P = .00073). High-intensity atorvastatin therapy caused a 71.0% reduction in hs-CPR from baseline versus a 38.6% reduction with conventional low-intensity atorvastatin therapy (T = 2.48, P = .0160).

3.5. Changes in cardiac function with high- and conventional low-intensity atorvastatin therapy

The LVEF at baseline was comparable between group I and II (T = 1.09, P = .2787) (Table 5). A modest but significant increase (7.1% ± 15.2% over baseline; T = −3.32, P = .0015) in EF was observed at week 48 with high-intensity atorvastatin therapy while virtually no significant increase (9.3% ± 22.8% over baseline; T = −1.74 P = .0871) in LVEF was noted with conventional low-intensity atorvastatin therapy (group I vs group II: T = −0.61, P = .5442).

3.6. Safety profile

Treatment-related side effects were not observed in this study. No patients showed an increase in ALT greater than 3 times the upper limit of normal (ULN) or AST greater than 5 times the ULN (Table 6). Hepatitis or jaundice was not observed. No patient complained of myopathy-associated symptoms, and no patient showed greater than 5 times elevations of CK levels.

4. Discussion

Current data is lacking on long-term efficacy of high-intensity atorvastatin therapy for Chinese ACS patients receiving PCI. This current study demonstrates that high-intensity atorvastatin therapy was associated with a more significant reduction in LDL-C versus conventional low-intensity atorvastatin therapy at week 48. Moreover, the baseline LDL-C level of group I was significantly higher than group II, and 85.0% patients attained the LDL-C target after 48 weeks of high-intensity atorvastatin therapy versus 96.7% patients who reached the LDL-C target with conventional low-intensity atorvastatin therapy. However, the mean percent changes at week 4 from baseline in LDL-C were −33.6% ± 20.0% with high-intensity atorvastatin therapy versus −12.8% ± 19.6% with conventional low-intensity atorvastatin therapy, and −47.0% ± 25.5% at week 48 with high-intensity atorvastatin therapy versus −36.4% ± 20.2% with conventional low-intensity atorvastatin therapy. This suggests that high-intensity statin therapy is more effective in reducing LDL-C than conventional low-intensity atorvastatin therapy.

Liu et al[5] reported the 1-year MACE rate of a Chinese population of stable angina or ACS receiving high-intensity statin

Table 5

Changes in ejection fraction with high and conventional atorvastatin therapy (mean ± SD).

	Baseline	Week 12	Week 24	Week 48
Group I	0.49 ± 0.14	0.51 ± 0.10	0.52 ± 0.09	0.54 ± 0.09
Group II	0.51 ± 0.10	0.47 ± 0.12	0.48 ± 0.10	0.51 ± 0.10
P value	T = 1.09, P = .2787	T = 2.11, P = .0371	T = 2.20, P = .0296	T = 1.84, P = .0690

SD = standard deviation.

Table 6

Changes of hepatic and renal function with high and conventional atorvastatin therapy (mean ± SD).

	Baseline			Week 12			Week 24			Week 48		
	Group I	Group II	P	Group I	Group II	P	Group I	Group II	P	Group I	Group II	P
ALT	55.65 ± 45.63	46.55 ± 50.25	T = 1.04, P = .3012	55.43 ± 39.07	27.63 ± 15.81	T = 5.11, P = .0000	30.20 ± 15.35	27.65 ± 12.91	T = 0.98, P = .3267	28.00 ± 15.45	25.85 ± 11.00	T = 0.88, P = .3819
AST	146.52 ± 145.02	93.07 ± 98.15	T = 2.36, P = .0199	39.58 ± 27.10	28.50 ± 14.65	T = 2.79, P = .0065	30.22 ± 12.16	26.83 ± 10.27	T = 1.65, P = .1024	30.80 ± 13.03	27.18 ± 8.61	T = 1.79, P = .0757
BUN	5.76 ± 1.97	5.93 ± 1.72	T = −.49, P = .6262	5.08 ± 1.25	5.06 ± 0.93	T = 0.10, P = .9169	5.26 ± 1.34	4.94 ± 1.00	T = 1.47, P = .1450	5.32 ± 1.67	4.99 ± 0.92	T = 1.17, P = .2462
Cr	72.96 ± 24.06	70.46 ± 14.54	T = 0.69, P = .4919	46.45 ± 30.44	62.80 ± 11.81	T = −3.9, P = .0002	66.79 ± 15.04	60.81 ± 11.82	T = 2.42, P = .0171	64.71 ± 14.81	61.59 ± 9.83	T = 1.36, P = .1769

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BUN = blood urea nitrogen, Cr = creatinine, SD = standard deviation.

therapy and found that high-intensity statin therapy was superior to conventional low-intensity statin therapy in ACS patients. Although we did not analyze data on MACE in our study population, our findings indicated that high-intensity atorvastatin therapy was more effective in reducing LDL-C than conventional low-intensity atorvastatin therapy and the reduction in LDL-C was significant and observable after 4 weeks of treatment and maintained at week 48. We noticed a higher percentage of patients on conventional low-intensity atorvastatin therapy attained the LDL-C target at week 48 (96.7% vs high-intensity atorvastatin therapy 85.0%). This may be related to the fact that patients on high-intensity atorvastatin therapy had significantly higher baseline LDL-C than patients on conventional low-intensity atorvastatin therapy. Consistent with our finding that high-intensity atorvastatin therapy was associated with a reduction in LDL-C to a greater extent than conventional low-intensity atorvastatin therapy, Dohi et al found that higher LDL-C at baseline was associated with a lower risk of MACCE at 1 year (OR, 0.25; 95% CI, 0.05–0.83; $P = .035$).[7] High-intensity atorvastatin therapy also caused a greater percentage reduction in TG and TC versus conventional low-intensity atorvastatin therapy while the latter caused a greater percentage increase in HDL-C.

Consistent with the favorable changes in the lipid profile, high-intensity atorvastatin therapy brought about a significantly greater percentage reduction in plaque length and width than conventional low-intensity atorvastatin therapy. A recent meta-analysis demonstrated that high-intensity atorvastatin therapy was more effective in causing plaque regression in ACS patients than conventional low-intensity atorvastatin therapy and plaque volume reduction was sustained after 12 months. Our study indicated that plaque regression occurred as early as at week 12 and was sustained until 48 weeks. Shehata et al showed that high-intensity atorvastatin therapy (a 160 mg loading dose followed by an intensified 80 mg daily dose) significantly improved LVEF non-ST-segment-elevation ACS patients who were scheduled for PCI while conventional low-intensity atorvastatin therapy (20-mg daily dose) did not.[8] We also observed a significant increase in LVEF at week 48 in ACS patients with high-intensity atorvastatin therapy while conventional low-intensity atorvastatin therapy caused virtually no change in LVEF. The above findings suggest that high-intensity atorvastatin therapy is more effective than conventional low-intensity atorvastatin therapy in reducing plaque size and improving cardiac function by causing more favorable changes in the lipid profile.

One limitation of the current study is that we did not analyze data on MACE of the study population. However, we observed a dramatic reduction in plasma cTNI contents with both high-intensity atorvastatin therapy and conventional low-intensity atorvastatin therapy from weeks 4 to 48. A recent study suggested that elevated concentrations of cTNI were associated with an increased risk of incident heart failure in coronary syndrome patients. Ford et al also demonstrated a 5-fold greater reduction in coronary events when cTNI concentrations decreased by more than a quarter and statin therapy reduced cTNI concentrations.[9] The mechanisms whereby statins exert their actions are probably related to the pleiotropic effects of statins, one of which involves reducing low grade inflammation. Cystatin C is a cysteine protease inhibitor and recently it has been suggested that high cystatin C content is directly related to atherosclerosis[10] and inflammation. We observed a 24% reduction in cystatin C content at week 48 with high-intensity atorvastatin therapy versus 18% with conventional low-intensity atorvastatin therapy. We also observed a reduction in hs-CRP content at week 48 with high-intensity atorvastatin therapy versus with conventional low-intensity atorvastatin therapy. A recent study revealed a positive correlation between cystatin C levels and plaque burden in patients with angiographically documented coronary artery disease.[11]

Several studies suggest that a sizable proportion of ACS patients failed to attain the LDL-C target.[2,3] A recent real world study found that only 15.0% of the study population initiated therapy with a high-intensity statin, and 22.5% of these high-intensity statin initiators switched to a moderate- to low-intensity regimen during the follow-up period.[12] One concern hampering the use of high-intensity statin therapy is safety. In the current study, we did not observe noticeable abnormalities in hepatic and renal function over 48 weeks.

In conclusion, our retrospective study has demonstrated that compared to conventional low-intensity statin therapy, high-intensity statin therapy is more effective in reducing LDL-C, TC, plaque length and width, cystatin-C, and hs-CRP while improving cardiac function and HDL-C of ACS patients, with a general benign safety profile over a period of 48 weeks. Our findings support the use of high-intensity statin therapy for Chinese ACS patients to improve the proportion of patients attaining the LDL-C target and provide a better direction for the treatment of ACS.

Author contributions

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