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Review Article

Amiodarone is superior to lidocaine in treating arrhythmia caused by coronary heart disease

Shuangying Zha[1*], Mingcheng Zhou[2*], Hongman Huang[3], Liuliu Feng[3], Xinbing Liu[3], Tianhua Liu[3]

[1]Heart Special Inspection Department, Shanghai Shidong Hospital, Shanghai, China; [2]Department of Cardiovascular Medicine, Shanghai First Rehabilitation Hospital, Shanghai, China; [3]Department of Cardiovascular Medicine, Shanghai Shidong Hospital, Shanghai, China. [*]Equal contributors.

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Abstract: Coronary heart disease is the most common cardiovascular disease, which may cause arrhythmia, and in severe cases, may cause death, posing a threat to human health. In this study, amiodarone showed better efficacy than lidocaine in the treatment of arrhythmia caused by coronary heart disease. The therapeutic advantages of amiodarone lie in its higher response rate and safety, better quality of life, more distinct improvement in cardiac function, and sharper reduction in myocardial enzymes. In summary, amiodarone is more effective in treating arrhythmia caused by coronary heart disease compared with lidocaine.

Keywords: Lidocaine, amiodarone, arrhythmia caused coronary heart disease, efficacy, cardiac rhythm recovery

Introduction

Arrhythmia refers to an irregular heartbeat caused by cardiac electrical impulse conduction disorder [1]. Atrial fibrillation in patients with arrhythmia can seriously endanger patients' lives and may lead to poor prognoses such as stroke or sudden cardiac death [2]. There are several causes of arrhythmia, including hypertension, cardiomyopathy, congenital heart disease, coronary artery disease, cardiovascular disease, etc. [3-5]. Cardiovascular disease is the leading cause of human death in both low and middle-income countries and high-income countries [6]. Coronary heart disease, a common cardiovascular disease induced by atherosclerosis, imposes a great economic burden on patients and society [7, 8]. Existing treatment methods for arrhythmia in patients with coronary heart disease include stereotactic ablation radiotherapy, pacemaker implantation, and drug treatment. Among them, drug treatment is a common method for patients with arrhythmia [9, 10]. Therefore, the exploration of drug treatment for arrhythmia caused by coronary heart disease is crucial for reducing the economic stress and the risk of death.

Lidocaine is an aminoamide anesthetic agent to treat arrhythmia. Its underlying mechanism of action is to inhibit voltage-gated sodium channels and thereby change neuronal signaling [11]. In a previous study [12], lidocaine showed a certain analgesic effect in patients with neuropathic pain without causing serious adverse events, suggesting that lidocaine is clinically safe and can be used for analgesia. However, the widespread use of lidocaine is restrained due to its possible risk of causing cardiac events [13]. Amiodarone is an effective drug for various types of arrhythmia that can inhibit adrenalin [14]. However, amiodarone may lead to toxic and side effects due to the long circulation time in the body and the cumulative off-target effect [15]. Amiodarone and lidocaine can also be used in patients with cardiac arrest, superior to placebo in enhancing the survival rate of patients after hospital admission, but neither leads to a great improvement of the long-term prognosis [16].

Few studies have been made to compare between lidocaine and amiodarone in the efficacy for treating arrhythmia caused by coronary heart disease. Here we explored the efficacy of either drug in patients, aiming to guide the drug treatment strategies.

Table 1. Baseline data of patients [n (%), mean ± SD]

Factors	n	Control group (n=88)	Intervention group (n=95)	χ^2/t	P
Sex				0.080	0.777
Male	102	50 (56.82)	52 (54.74)		
Female	81	38 (43.18)	43 (45.26)		
Age (year)				0.309	0.578
< 55	98	49 (55.68)	49 (51.58)		
≥ 55	85	39 (44.32)	46 (48.42)		
Average age (year)	183	54.16 ± 7.54	54.88 ± 8.02	0.624	0.533
Cardiac function classification				0.896	0.639
I	37	16 (18.18)	21 (22.11)		
II	79	41 (46.59)	38 (40.00)		
III	67	31 (35.23)	36 (37.89)		
Disease type				2.628	0.105
Supraventricular arrhythmia	62	35 (39.77)	27 (28.42)		
Ventricular arrhythmia	121	53 (60.23)	68 (71.58)		
Coronary heart disease				2.245	0.134
No	138	62 (70.45)	76 (80.00)		
Yes	45	26 (29.55)	19 (20.00)		
Hypertension				0.175	0.676
No	122	60 (68.18)	62 (65.26)		
Yes	61	28 (31.82)	33 (34.74)		
Diabetes				1.314	0.252
No	128	58 (65.91)	70 (73.68)		
Yes	55	30 (34.09)	25 (26.32)		
Drinking				0.730	0.393
No	70	32 (36.36)	38 (40.00)		
Yes	113	56 (63.64)	57 (60.00)		
Smoking				0.730	0.393
No	67	35 (39.77)	32 (33.68)		
Yes	116	53 (60.23)	63 (66.32)		
Place of residence				0.406	0.524
Rural area	44	23 (26.14)	21 (22.11)		
Urban area	139	65 (73.86)	74 (77.89)		

Materials and methods

Basic information

We randomly assigned 183 patients with arrhythmia caused by coronary heart disease admitted to Shanghai Shidong Hospital from December 2017 to December 2019 to receive lidocaine (the control group, CG, 88 patients) or to receive amiodarone (the intervention group, IG, 95 patients). CG comprised 50 males and 38 females, aged 30 to 78 years, with an average age of 54.16 ± 7.54 years. IG comprised 52 males and 43 females, aged 32 to 79 years, with an average age of 54.88 ± 8.02 years. This study was approved by the ethics committee of Shanghai Shidong Hospital. All the research participants and their guardians signed the written informed consent. Inclusion criteria: Patients with coronary heart disease as their primary disease; patients meeting the diagnostic criteria for arrhythmia [17]; patients meeting the criteria for cardiac function classification [18]; patients at least 30 years old; patients with no previous treatment. Exclusion criteria: Patients with comorbid malignant tumors or severe organ dysfunction; patients with mental illness or communication impairment; patients with infectious diseases; patients who have taken drugs that have a potential impact on the

Table 2. Comparison of clinical efficacy [n (%)]

Group	n	Marked response	Moderate response	No response	Total effective rate
Control group	88	23 (26.14)	43 (48.86)	22 (25.00)	75.00
Intervention group	95	48 (50.53)	44 (4.32)	3 (3.15)	96.84
χ^2	-	-	-	-	18.478
P	-	-	-	-	< 0.001

Table 3. Comparison of the incidence of toxic and side effects [n (%)]

Factors	Control group (n=88)	Intervention group (n=95)	χ^2	P
Phlebitis	0 (0.00)	5 (5.26)	-	-
Sinus bradycardia	0 (0.00)	2 (2.11)	-	-
Nausea and vomiting	9 (10.23)	0 (0.00)	-	-
Discomfort in the head	6 (6.82)	0 (0.00)	-	-
Total	15 (17.05)	7 (7.37)	4.045	0.044

indicators of this study within the past six months. The inclusion criteria applied to both groups of patients.

Treatment methods

Patients from both groups received routine treatment: CG: An intravenous injection of 50 mg lidocaine (Caiyou Industrial Co., Ltd., Shanghai, China, 137-58-6) plus 20 ml of 20% glucose (Yuanmu Biotechnology Co., Ltd., Shanghai, China, YM552B), 3 times a day for two weeks.

IG: An intravenous injection of 150 mg of amiodarone (Shanghai Rongweida Industrial Co., Ltd., Shanghai, China, HY-14187) at a rate of 0.5-1.0 mg/min, and an additional oral administration of amiodarone 3 times a day (the dosage of oral amiodarone was 0.2 g/time if the treatment lasted for 2-3 days and 0.4 g/time if the treatment lasted for a week).

Efficacy evaluation

A marked response referred to disappeared arrhythmia within 2 hours, decreased ventricular premature beats by at least 90%, and enhanced cardiac function (degree I or above). A moderate response referred to relieved arrhythmia within 2 hours, decreased ventricular premature beats by at least 50%, enhanced cardiac function (degree I or below), and improved clinical symptoms. No response referred to persisting arrhythmia within 2 hours and no change in clinical symptoms. Overall response rate = (case number of marked response + case number of moderate response)/total number of cases × 100%.

Outcome measures

The two groups were compared in the overall response rate, the incidence of adverse clinical symptoms and toxic and side effects, quality of life, heart rate (HR), rate-corrected Q-T interval (QTc), Q-T dispersion (QTd), aspartate transaminase (AST), lactate dehydrogenase (LDH), and creatine kinase-MB (CK-MB). The quality of life was assessed by the MOS 36-item short-form health survey (SF-36) [19]. AST and LDH levels were determined by the rate method in strict accordance with the instructions of AST and LDH kits (Shanghai Yuduo Biotechnology Co., Ltd., Shanghai, China, YDLC-16409, YDLC-12781). CK-MB level was determined by the immunosuppressive method in strict accordance with the instructions of the CK-MB kit (Yagi Biotechnology Co., Ltd., Shanghai, China, E006).

Statistical analysis

Data visualization was performed using GraphPad Prism 6 (GraphPad Software Inc., San Diego, USA). Count data were expressed by the case number/percentage (n/%) and its intergroup comparison was analyzed by the chi-square test. The correction for continuity was used when the theoretical frequency in the chi-square test was less than 5. Measurement data were expressed by the mean ± SD and its intergroup comparison was analyzed by the independent sample t-test, its intragroup comparison by the paired t-test. Multivariate logistic regression analysis was performed using SPSS22.0 (Beijing Baiao Yijie Technology Co., Ltd., China) to analyze the risk factors affecting the treatment effectiveness in patients with arrhythmia caused by coronary heart disease. The difference was statistically significant when $P < 0.05$.

Table 4. Comparison of adverse clinical symptoms after treatment

Factors	Control group (n=88)	Intervention group (n=95)	χ^2	P
Frequent atrial premature beats	21 (23.86)	9 (9.47)	6.902	0.009
Paroxysmal supraventricular tachycardia	5 (5.68)	2 (2.11)	1.588	0.208
Multiple ventricular premature beats	18 (20.45)	10 (10.53)	3.475	0.062
Atrioventricular block	8 (9.09)	4 (4.21)	1.776	0.183
Atrial fibrillation	2 (2.27)	0 (0.00)	2.183	0.140

Results

Baseline data

The two groups of patients were not significantly different in sex ratio, age, average age, cardiac function classification, disease type, coronary heart disease, hypertension, diabetes, drinking, smoking, and place of residence ($P > 0.05$). More details are shown in **Table 1**.

Amiodarone showed superior clinical efficacy to lidocaine

IG had a markedly higher overall response rate than CG (96.84% vs. 75.00%, $P < 0.05$). More details are shown in **Table 2**.

Amiodarone showed a greater safety

The incidence of toxic and side effects (phlebitis, sinus bradycardia, nausea, vomiting, and discomfort in the head) was markedly lower in IG than in CG ($P > 0.05$). More details are shown in **Table 3**.

Amiodarone relieved clinical symptoms and improved the quality of life of patients

IG had a lower incidence of frequent atrial premature beats, paroxysmal supraventricular tachycardia, multiple ventricular premature beats, atrioventricular block, and atrial fibrillation than CG. But only the difference in frequent atrial premature beats was statistically significant ($P > 0.05$). IG had markedly higher scores of quality of life than CG in terms of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health ($P < 0.05$). More details are shown in **Table 4** and **Figure 1**.

Amiodarone enhanced the cardiac function and decreased myocardial enzymes

There were no notable differences between the two groups before treatment in the indicators for cardiac function (HR, QTc, QTd) and myocardial enzymes (AST, LDH, CK-MB) ($P > 0.05$). The expression of HR, QTd, AST, LDH, and CK-MB showed a marked decrease in both groups after treatment, while QTc expression showed a marked increase after treatment. IG had markedly reduced HR, lower expression of HR, QTd, AST, LDH, and CK-MB, and markedly higher expression of QTc than CG ($P < 0.05$) (**Figure 2**).

The treatment method was one of the risk factors affecting the efficacy in patients with arrhythmia caused by coronary heart disease

Totally 25 patients showed no response to the treatment. The comparison between patients with no response and patients with a marked or moderate response showed no significant difference in sex ratio, age, average age, cardiac function classification, disease type, diabetes, drinking, smoking, place of residence, HR, QTc, QTd, AST, LDH, CK-MB ($P > 0.05$), but revealed statistical differences in the history of coronary heart disease, hypertension, and the treatment method ($P < 0.05$). Factors showing differences were subjected to multivariate logistic regression analysis. The history of coronary heart disease ($P=0.015$), hypertension ($P=0.020$), and treatment method ($P=0.003$) were independent risk factors affecting the treatment efficacy for arrhythmia caused by coronary heart disease. Patients with a lidocaine treatment and a history of coronary heart disease and hypertension had a higher risk of showing no response to the treatment. More details are shown in **Tables 5-7**.

Discussion

Arrhythmia is a possible complication of coronary heart disease and the most common cause of involuntary admission to the hospital for patients with coronary heart disease [20]. According to epidemiological data, nearly 102 deaths are reported per 100,000 coronary heart disease patients, with a lifetime risk of

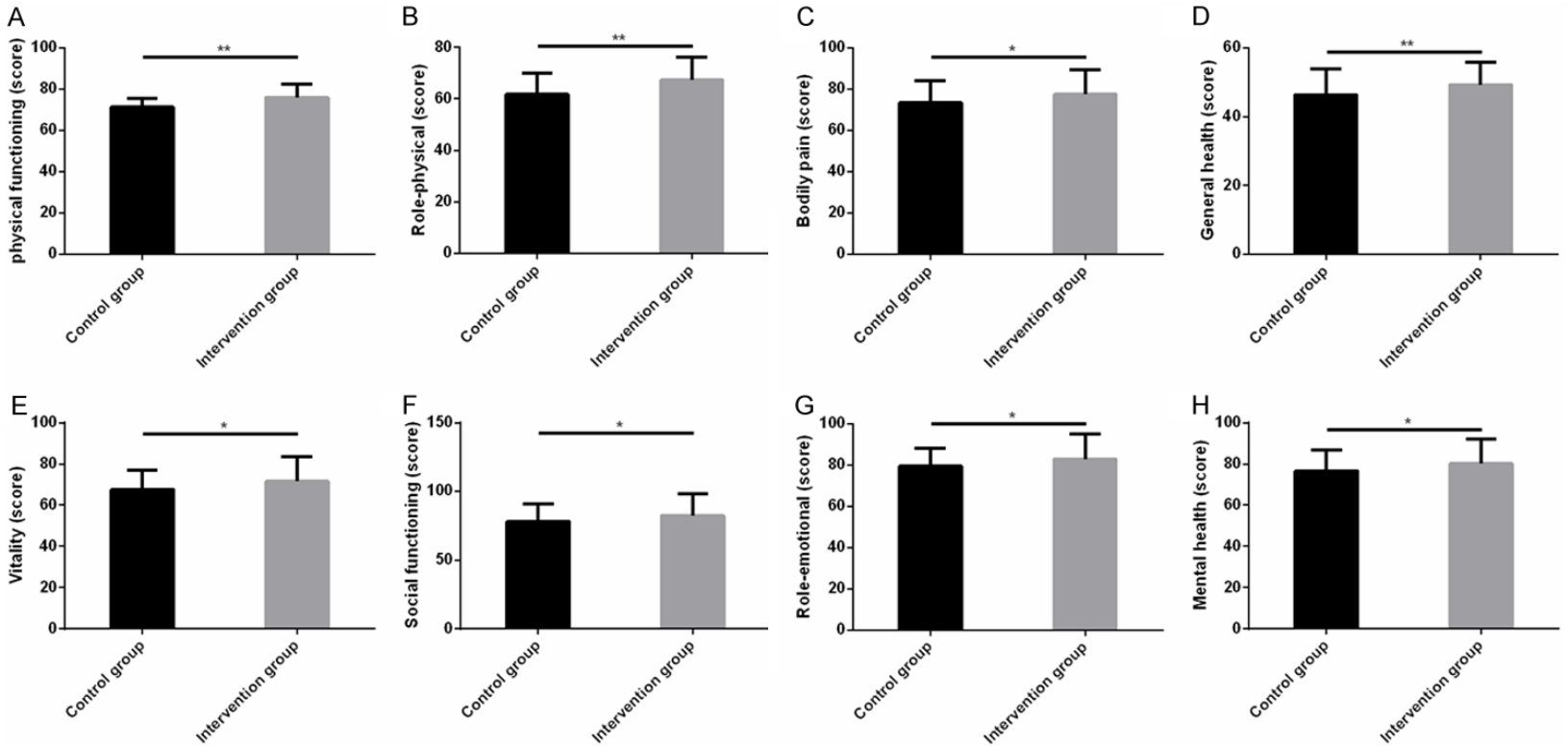

Figure 1. Comparison of the quality of life of patients after treatment. A: The score of physical functioning was higher in IG than in CG. B: The score of role-physical was higher in IG than in CG. C: The score of bodily pain was higher in IG than in CG. D: The score of general health was higher in IG than in CG. E: The score of vitality was higher in IG than in CG. F: The score of social functioning was higher in IG than in CG. G: The score of role-emotional was higher in IG than in CG. H: The score of mental health was higher in IG than in CG. Note: *P < 0.05, **P < 0.01.

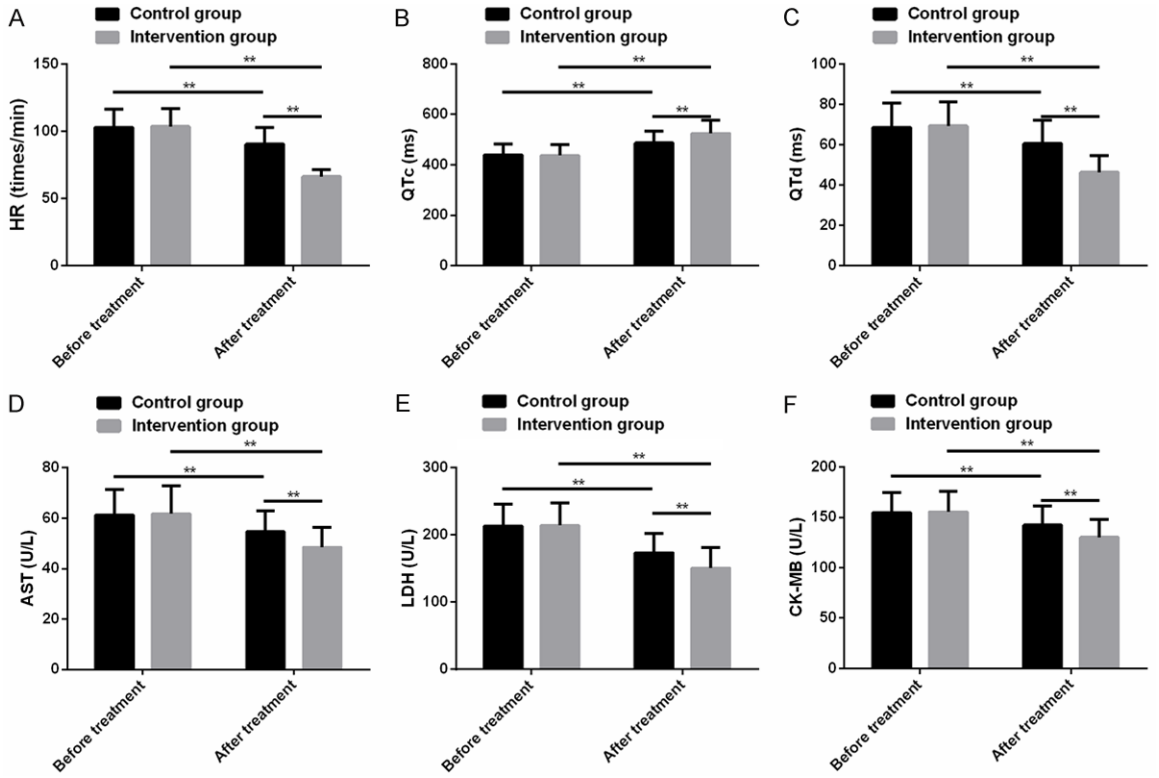

Figure 2. Comparison of indicators for cardiac function and myocardial enzymes. A: HR level was notably reduced after treatment in IG, markedly lower than in CG. B: QTc level was notably increased after treatment in IG, markedly higher than in CG. C: QTd level was notably reduced after treatment in IG, markedly lower than in CG. D: AST level was notably reduced after treatment in IG, markedly lower than in CG. E: LDH level was notably reduced after treatment in IG, markedly lower than in CG. F: CK-MB level was notably reduced after treatment in IG, markedly lower than in CG. Note: **P < 0.01.

37.5% for men and 18.3% for women [21]. The investigation into the treatment of arrhythmia caused by coronary heart disease is of great value in reducing the mortality of patients.

A growing number of scholars have been interested in the treatment of arrhythmia and gained some achievement. As in the study by Hong and others [22], tetrodotoxin combined with lidocaine showed superior efficacy for severe arrhythmia to the single use of either, indicating that the combination of the two may integrate their effectiveness and presents as a new potential treatment for severe arrhythmia. The study by Huang et al. [23] reported that amiodarone can improve the prognosis of hepatocellular carcinoma patients with arrhythmia through the autophagy degradation mechanism, which shows that amiodarone is also effective for hepatocellular carcinoma patients with arrhythmia. Here we mainly compared between lidocaine and amiodarone in the efficacy for treating arrhythmia caused by coronary heart disease. Patients from IG who were treated with amiodarone had a higher overall response rate, suggesting that aminiodine is more effective in patients with arrhythmia caused by coronary heart disease. IG had a lower incidence of adverse clinical symptoms, but only the difference in frequent atrial premature beats was statistically significant. Patients in IG mainly suffered from phlebitis and sinus bradycardia, while patients in CG mainly suffered from nausea, vomiting, and discomfort in the head. The total incidence of toxic and side effects was markedly lower in IG than in CG, suggesting that amiodarone is more safe and effective in relieving frequent atrial premature in patients with arrhythmia caused by coronary heart disease than lidocaine. The report of Sossalla and others [24] concluded that arrhythmia manifests as frequent atrial early, paroxysmal supraventricular tachycardia, multiple ventricular premature beats, atrioventricular block, and atrial fibrillation. Despite such toxic and side effects as phlebitis and sinus

Table 5. Clinical parameters and indicators of patients with arrhythmia caused by coronary heart disease and their relationship with efficacy [n (%)]

Factors	n	No response (n=25)	Marked or moderate response (n=158)	χ^2/t	P
Sex				0.164	0.686
Male	102	13 (52.00)	89 (56.33)		
Female	81	12 (48.00)	69 (43.67)		
Age (year)				0.070	0.792
< 55	98	14 (56.00)	84 (53.16)		
≥ 55	85	11 (44.00)	74 (46.84)		
Average age (year)	183	54.93 ± 8.21	54.13 ± 7.65	0.624	0.533
Cardiac function classification				0.350	0.839
I	37	4 (16.00)	33 (20.89)		
II	79	11 (44.00)	68 (43.04)		
III	67	10 (40.00)	57 (36.07)		
Disease type				2.577	0.108
Supraventricular arrhythmia	62	12 (48.00)	50 (46.30)		
Ventricular arrhythmia	121	13 (52.00)	108 (53.70)		
Coronary heart disease				8.557	0.003
No	138	13 (52.00)	125 (79.11)		
Yes	45	12 (48.00)	33 (20.89)		
Hypertension				6.695	0.010
No	122	11 (44.00)	111 (70.25)		
Yes	61	14 (56.00)	47 (29.75)		
Diabetes				0.505	0.477
No	128	19 (76.00)	109 (68.99)		
Yes	55	6 (24.00)	49 (31.01)		
Drinking				0.165	0.280
No	70	12 (48.00)	58 (36.71)		
Yes	113	13 (52.00)	100 (63.29)		
Smoking				0.143	0.705
No	67	10 (40.00)	57 (36.08)		
Yes	116	15 (60.00)	101 (63.92)		
Place of residence				0.259	0.611
Rural area	44	5 (20.00)	39 (24.68)		
Urban area	139	20 (80.00)	119 (75.32)		
Treatment method				15.106	< 0.001
Amiodarone treatment	95	22 (88.00)	73 (46.20)		
Lidocaine treatment	88	3 (12.00)	85 (53.80)		
HR (beat/min)	183	92.63 ± 10.09	89.85 ± 8.94	1.419	0.158
QTc (ms)	183	472.52 ± 42.86	491.36 ± 48.69	1.825	0.070
QTd (ms)	183	61.48 ± 10.03	58.21 ± 8.28	1.780	0.077
AST (U/L)	183	56.06 ± 8.10	53.25 ± 7.12	1.799	0.074
LDH (U/L)	183	174.82 ± 32.78	170.75 ± 34.21	0.556	0.579
CK-MB (U/L)	183	146.86 ± 25.64	139.64 ± 21.35	1.527	0.129

bradycardia caused by amiodarone in the treatment of arrhythmia, amiodarone is still a prominent drug for arrhythmia with excellent short-term efficacy and safety [25, 26].

Arrhythmia is related to ECG parameters such as HR, QTc, and QTd: HR is associated with respiratory sinus arrhythmia, QTc with ventricular arrhythmia, and QTd with complex ventricu-

Table 6. Assignment for multivariate logistic regression analysis

Factors	Variables	Assignment
Coronary heart disease	X1	No=0, Yes=1
Hypertension	X2	No=0, Yes=1
Treatment method	X3	Radial access for PCI=0, femoral access for PCI=1

Table 7. Multivariate logistic regression analysis of factors affecting the efficacy for arrhythmia caused by coronary heart disease

Variables	B	S.E	Wals	P	OR	95% CI
Coronary heart disease	2.195	0.478	5.460	0.015	1.769	1.253-4.028
Hypertension	4.356	0.607	6.296	0.020	1.903	1.248-4.537
Treatment method	1.329	0.612	4.198	0.003	2.436	1.125-5.121

lar arrhythmia [27, 28]. We monitored the changes in these three indicators before and after treatment. The results showed that IG had markedly more favoring profiles of HR, QTc, and QTd than IG, indicating that amiodarone is superior to lidocaine in improving the cardiac function of patients with arrhythmia caused by coronary heart disease. Extremely high levels of myocardial enzyme indexes such as AST, LDH, and CK-MB can induce malignant arrhythmias [29]. In the present study, the levels of AST, LDH, and CK-MB after treatment were lower in IG than in CG, which suggests that amiodarone can better relieve symptoms of arrhythmia. According to the results of SF-36 in this study, the quality of life of patients was notably higher in IG than in CG, implying that amiodarone leads to a sharper improvement in the quality of life. Multivariate Logistic regression analysis demonstrated that the history of coronary heart disease, hypertension, and the treatment method were independent risk factors swaying the efficacy for arrhythmia caused by coronary heart disease, which means that patients with a history of coronary heart disease and hypertension and treated with lidocaine have a higher risk of showing no response to the treatment.

In summary, amiodarone shows superior efficacy to lidocaine in treating arrhythmia caused by coronary heart disease, with a more distinct improvement in cardiac function, a sharper reduction in myocardial enzymes, and a better postoperative quality of life of patients. So amiodarone deserves a clinical promotion. However, there is still room for improvement in this study. First, we should prolong the follow-up time to analyze whether amiodarone and lidocaine have a positive effect on the long-term survival of patients with arrhythmia caused by coronary heart disease. Besides, we should conduct basic experiments to further compare the pathological regulation mechanism of the two drugs.

Disclosure of conflict of interest

None.

Address correspondence to: Shuangying Zha, Heart Special Inspection Department, Shanghai Shidong Hospital, Shanghai, China. E-mail: w1sg1ax@163.com; Mingcheng Zhou, Department of Cardiovascular Medicine, Shanghai First Rehabilitation Hospital, Shanghai, China. E-mail: wen882515881474714@163.com

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