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Original Article

Prognosis of patients with coronary artery disease treated in different therapy units at department of cardiology: a retrospective cohort study

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Abstract: Background: Coronary artery disease (CAD) is a major health problem in global. Benefit from different care unit for various type of CAD is remaining unknown. We investigate if coronary care unit (CCU) reduces the incidence of major adverse cardiovascular events (MACEs). Method: 806 CAD patients including stable angina (SA) and acute coronary syndrome (ACS) who treated in department of cardiology were involved in the study as two groups. Each group involved two subgroups according to the therapy unit including CCU and normal unit. 12-48 months follow-up was carried out. The primary end point was all cause mortality. Results: For SA, death from any cause occurred in 1.0% of the patients in the normal group (1 of 108), as compared with 5.1% in the CCU group (3 of 59) (hazard ratio [HR], 0.164; 95% confidence interval [CI], 0.017 to 1.580; P=0.118). Kaplan-Meier survival analysis showed that there were no significant differences between the two subgroups with respect to the risk of death (P=0.074), revascularization (P=0.660), stroke (P=0.497), heart failure (P=0.658) and hemorrhage (P=0.096). For ACS, death occurred in 1.9% of the patients in the normal subgroup (5 of 267), as compared with 1.3% in the CCU subgroup (5 of 372) (HR, 1.403; 95% CI, 0.406-4.846; P=0.593). Kaplan-Meier survival analysis showed that there were no significant differences between the two subgroups with respect to the risk of death (P=0.591), revascularization (P=0.996), stroke (P=0.425), heart failure (P=0.625). Conclusion: CAD patients treated in CCU obtain little benefits compared with normal.

Keywords: Coronary artery disease, coronary care unit, outcomes

Introduction

Coronary artery disease (CAD) contributed greatly to the deaths in individuals around the world. In China, the incidence and mortality of CAD has increased every year [1, 2]. Acute coronary syndrome (ACS) is the severe type of CAD that need to be diagnosed, anti-platelet and vascularized as earlier as possible. Recently, ACC/AHA and ESC guideline have emphasized the importance of early recognition and revascularization due to the obviously benefits from early clinical treatment. Complying with the guideline strictly make for the reduction of mortality of CAD patients [3, 4].

Numbers of hospitals and clinical centers have established the coronary care unit (CCU) to cure severe CAD estimated higher probability of death, especially the ST-elevated myocardial infarction (STEMI) and non-ST elevated myocardial infarction (non-STEMI). Most of CCU have complete vital sigh monitoring including electrocardiogram (ECG), respiration, blood pressure, oxygen saturation and even invasive central venous catheter and Swan-Ganz float catheter to real time monitoring the function of left and right heart. Also, invasive hemodynamics parameter measurement was not applied in all CCU. CCU may help the doctors to handle the situation of disease in time so that to institute the therapy plan individually. However, in clinical practice, it occurs that patients with ACS accidentally are referred to normal care unit. Either, patients with chest pain that doubly ACS are referred to CCU who accurately diagnosed as SA or no CAD [5, 6]. That is may harmful to high risk ACS patients that required therapy may not performed in time [7] and waste the emergency medical resources so that numbers of CAD patients who have low risk of death have been treated in CCU due to over estimating the status of disease [8].

On account of these reasons, it is important to identify if CCU may have clinical benefits for SA patients and normal care unit may elevate the mortality of ACS patients. We examined 806 patients with SA or ACS that treated in CCU or normal unit. Clinical characters and follow-up data were collected then determined whether CAD patients benefit from CCU therapy and what type of CAD may obtain more benefits from CCU.

Method

Study design

This study was a single center, retrospectively cohort research. Trial administration, data management, and statistical analyses were performed at the department of Cardiology, Zhong Da hospital affiliated to Southeast University. The patient samples involved in this study that diagnosed as CAD was analyzed except for the patients who were accordance with exclusion criterion. The investigation conforms to the principles outlined in the Declaration of Helsinki. This trial design was approved by the Ethics Committee in Zhong Da hospital.

Patient population

Total of 960 patients with CAD diagnosed by coronary angiography (CAG) in department of Cardiology, Zhong Da hospital from December, 2008 to December, 2011. The definition of myocardial infarction was described previously [9]. Patients who have cancer, stroke, old myocardial infarction, received stent implantation before, severe kidney and/or liver dysfunction, heart failure, autoimmune diseases and infection diseases, died before discharge from hospital were excluded. Either, lack of clinical document was excluded. The patients that involved in the study were separated into two groups according to the type of CAD: SA group, and ACS group. Subgroups of each group were set up according to the therapy unit: CCU and normal unit. Patients received drug therapy according to the situation of disease based on the guideline. All patients were asked to confirm their agreement to accept the 12-48 months follow-up by providing written informed consent.

Therapy procedures

All the patients that involved in the study underwent coronary angiography and 515 patients underwent percutaneous coronary intervention (PCI); usage of platelet inhibitors or anticoagulants drugs and other symptomatic treatment was left to the discretion of the treating physician according to guideline. For patients diagnosed as myocardial infarction, clopidogrel and aspirin was administered as 600 mg and 300 mg once arrived in hospital and then immediately transferred to catheter room that CAG and PCI were performed. Clopidogrel and aspirin was administered 75 mg and 100 mg per day after PCI, respectively. Beta receptor blocker, statin, Low molecular weight heparins (LMWH) and ACEI/ARB were administered according to the patients' status and guideline. Additionally, real time monitoring of heart rate, heart rhythm, blood pressure, respiration and finger plus oxygen saturation was applied but on invasive central venous pressure and pulmonary artery wedge pressure detection in CCU. For patients who were treated in normal unit, the usage of bedside monitors was determined by physician based on the changing of patient's condition. After discharge from hospital, standard drugs therapy according to CAD therapy guideline was performed. Physicians determine and guide the therapy procedures according to the patients' situation.

End points

Major adverse cardiovascular events were recorded (MACEs). Death from any cause was defined as the primary end points which defined as death of cardiac causes or any death without another known cause. Coronary revascularization was defined as angioplasty or stenting or coronary artery bypass grafting. Stroke was defined as loss of neurologic function due to an ischemic event (hemorrhagic event was excluded). Heart failure was defined as NT-proBNP was at least one value above the 5* 99th percentile upper reference limit. Hemorrhagic was defined as TIMI criteria (major). MACEs were verified by hospital medical records and telephone.

Statistical analysis

The data were analyzed using the statistical software package of SPSS (SPSS Inc., Chicago, IL, USA, Version 17.0). Numerical variables were expressed as mean ± standard deviation and categorical variables as percentages. Continuous variables between groups were

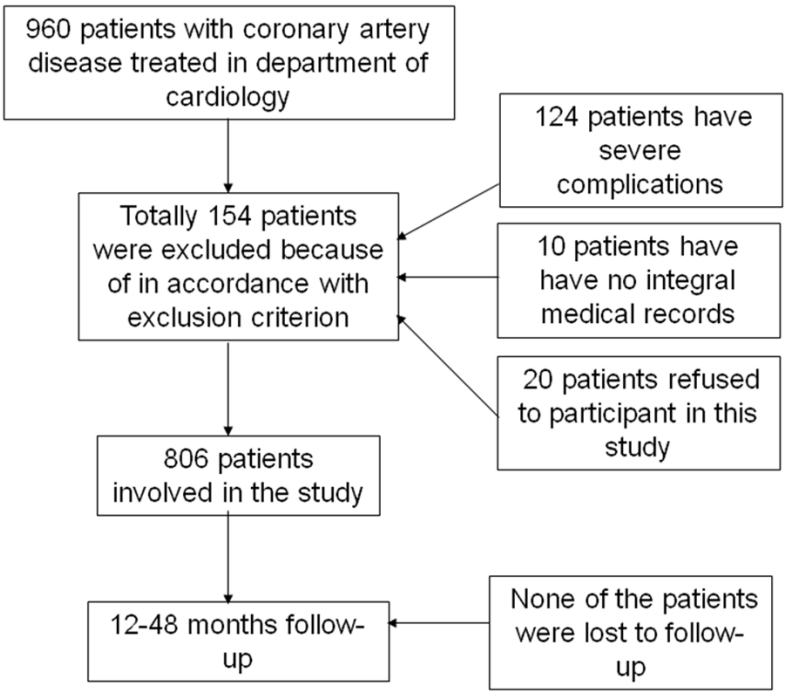

Figure 1. The flow diagram of this study.

compared by unpaired Student's t test. Categorical variables were compared by Chi-square test. Kaplan-meier survival analysis was performed. Hazard ratio (HR) and 95% confidence intervals (CI) were calculated by Cox proportional hazard model. Two-tailed *P* values < 0.05 were considered significant.

Results

Study population

Among the 960 patients, 154 patients were excluded because of accordance with exclusion criterion. 124 patients have severe complications described above, 10 patients have no integral medical records and 20 patients refused to participant in this study. 806 patients involved in this study after exclusion. The flow diagram is shown in **Figure 1**. There were 167 patients involved in SA group, 59 and 108 patients in CCU and Normal subgroups respectively. 60 patients underwent PCI; 639 patients involved in ACS group; 372 and 267 patients involved in CCU and normal subgroups respectively. 455 patients underwent PCI. The baseline clinical characters and biochemical data, lesion coronary artery, complications and therapy were listed in **Table 1**. Estimate glomerular filtration rate (e GFR) was calculated by MDRD formula. None of the patients were lost to follow-up with respect to the end point.

Long term clinical outcomes SA group

4 patients died during 12-48 months follow-up, 3 in CCU subgroup and 1 in normal care subgroup, respectively (HR, 0.164; 95% CI, 0.017-1.580; P=0.118). 21 patients have revascularization while 8 patients in CCU subgroup and 13 patients in normal subgroup, respectively (HR, 0.821; 95% CI, 0.340-1.983; P= 0.662). Stroke occurred in 9 patients, 4 in CCU subgroup and 5 in normal subgroup, respectively (HR, 0.636; 95% CI, 0.171-2.372; P=0.501). Heart failure occurred in 21 patients, 8 in CCU subgroup and 13 in normal subgroup, respectively (HR, 0.820; 95% CI, 0.340-1.980; P=0.659). Hemorrhage occurred in 4 patients, 3 in CCU subgroup and 1 in normal care subgroup, respectively (HR, 0.182; 95% CI, 0.019-1.748; P=0.140) (**Table 2**). Kaplan-meier survival analysis showed that the cumulative hazard of all cause death (P=0.074), revascularization (P=0.660), stroke (P=0.497), heart failure (P=0.658) and hemorrhage (P=0.096) were no difference between two subgroups (**Figure 2**).

ACS group

10 patients died during 12-48 months follow-up, 5 in CCU subgroup and 5 in normal care subgroup, respectively (HR, 1.403; 95% CI, 0.406-4.846; P=0.593). 145 patients underwent revascularization, 84 in CCU subgroup and 61 in normal subgroup, respectively (HR, 0.999; 95% CI, 0.719-1.390; P=0.996). Stroke occurred in 22 patients, 11 in CCU subgroup and 11 in normal subgroup, respectively (HR, 1.402; 95% CI, 0.608-3.253; P=0.428). Heart failure occurred in 58 patients, 32 in CCU subgroup and 26 in normal subgroup, respectively (HR, 1.137; 95% CI, 0.678-1.908; P=0.626).

Table 1. Baseline Characteristics of the Patients with CAD of all subgroups

	SA (n=167)			ACS (n=639)		
	CCU (n=59)	Normal (n=108)	P	CCU (n=372)	Normal (n=267)	*P*
Sex, M/F	27/32	76/32	0.002	271/101	209/58	0.118
Age, y	69.7±10.1	65.2±10.5	0.009	67.8±12.2	67.2±11.1	0.542
WBC	7.2±2.9	6.5±1.7	0.073	8.0±3.2	7.7±3.2	0.199
cTnI	0.03±0.01	0.02±0.01	0.954	16.6±2.0	24.2±3.7	0.870
TC	4.2±1.2	4.3±1.2	0.636	4.4±1.1	4.4±1.0	0.829
TG	1.1±0.5	1.4±1.2	0.082	1.5±0.9	1.4±0.8	0.509
LDL	2.6±0.9	2.6±0.9	0.777	2.7±0.9	2.7±0.8	0.727
HDL	1.1±0.3	1.0±0.3	0.025	1.1±0.3	1.1±0.3	0.766
eGFR	79±26	77±28	0.624	81±28	83±30	0.408
Smoking, n (%)	14 (23.7)	35 (32.4)	0.239	111 (29.8)	75 (28.1)	0.631
HP, n (%)	46 (78.0)	82 (75.9)	0.766	272 (73.1)	199 (74.5)	0.689
DM, n (%)	17 (28.8)	21 (19.4)	0.167	94 (25.3)	77 (28.8)	0.315
LM, n (%)	3 (5.1)	5 (4.6)	0.895	19 (5.1)	21 (7.9)	0.156
LAD, n (%)	24 (40.7)	79 (73.1)	0.559	263 (70.7)	190 (71.2)	0.899
LCX, n (%)	19 (32.2)	30 (27.8)	0.548	174 (46.8)	124 (46.4)	0.934
RCA, n (%)	14 (23.7)	22 (20.4)	0.614	205 (55.1)	136 (50.9)	0.297
PCI, n (%)	23 (39.0)	37 (34.3)	0.543	264 (71.0)	191 (71.5)	0.876
Aspirin, n (%)	53 (89.8)	97 (89.8)	0.997	361(97.0)	260 (97.4)	0.801
Betaloc, n (%)	40 (67.8)	80 (74.1)	0.389	277 (74.5)	193 (72.3)	0.538
ACEI/ARB, n (%)	31 (52.5)	46 (42.6)	0.218	210 (56.5)	153 (57.3)	0.830
Statin, n (%)	50 (84.7)	85 (78.7)	0.343	336 (90.3)	248 (92.9)	0.255
LMWH, n (%)	13 (22.0)	26 (24.1)	0.766	223 (59.9)	175 (65.5)	0.150
Clopidogrel, n (%)	24 (40.7)	43 (39.8)	0.913	280 (75.3)	201 (75.3)	0.997
Nitrate, n (%)	36 (61.0)	62 (57.4)	0.651	174 (46.8)	138 (51.7)	0.221

*WBC: White blood cell, $\times 10^9$/L; cTnI: Cardiac troponin I, ng/mL. TC: Total cholesterol, mmol/L. TG: Triglyceride, mmol/L. LDL: Low density lipoprotein, mmol/L. HDL: High density lipoprotein, mmol/L. e GFR: estimate glomerular filtration rate, mL/min/1.73 m^2. HP: Hypertension. DM: Diabetes mellitus. LM: Left Main Artery. LAD: Left anterior descending branch. LCX: Left Circumflex Artery. RCA: Right coronary artery. LMWH: Low molecular weight heparins.

Hemorrhage occurred in 3 patients and none of patients in normal subgroup (**Table 3**). Kaplan-meier survival analysis showed that the cumulative hazard of all cause death (P=0.591), revascularization (P=0.996), stroke (P=0.425), heart failure (P=0.625) were no difference between two subgroups (**Figure 3**).

Discussion

This trial showed that the benefits from treated in CCU or normal unit for CAD patients include SA and ACS were no significantly different, especially for patients with SA. For ACS patients, the cumulative hazard of MACEs during follow-up had no differences between the two subgroups, although the obvious trend decreasing of MACEs were detected.

In recent years, a great number of researches have focused on the therapy procedures to reduce the mortality of CAD, especially the ACS. Early diagnosis of ACS according to the serum myocardial injury biomarkers plays a major role in ACS therapy. Hassan [10] reported that point-of-care testing of cardiac markers take a leading role in management of ACS patients. Point-of-care testing provided a quick method to determine the serum myocardial injury biomarkers that can early identified myocardial infarction. In CCU, highly doubted myocardial infarction patients can receive post-of-care testing of myocardial injury biomarkers to identified myocardial infarction in time and clinical pathway of myocardial infarction will established effectively. Invasive hemodynamic measurement is a widely used cardiac function monitor that can indicate the action of left

Table 2. Rate of MACEs according to two subgroups of SA patients

	SA (n=167)			
	CCU (n=59)	Normal (n=108)	Hazard Ratio (95% CI)	P
Death, no./total no. (%)	3/59 (5.1)	1/108 (1.0)	0.164 (0.017-1.580)	0.118
Revascularization, no./total no. (%)	8/59 (13.6)	13/108 (12.0)	0.821 (0.340-1.983)	0.662
Stroke, no./total no. (%)	4/59 (6.8)	5/108 (4.6)	0.636 (0.171-2.372)	0.501
Heart failure, no./total no. (%)	8/59 (13.6)	13/108 (12.0)	0.820 (0.340-1.980)	0.659
Hemorrhage, no./total no. (%)	3/59 (5.1)	1/108 (1.0)	0.182 (0.019-1.748)	0.140

HR was calculated as CCU subgroup was control group.

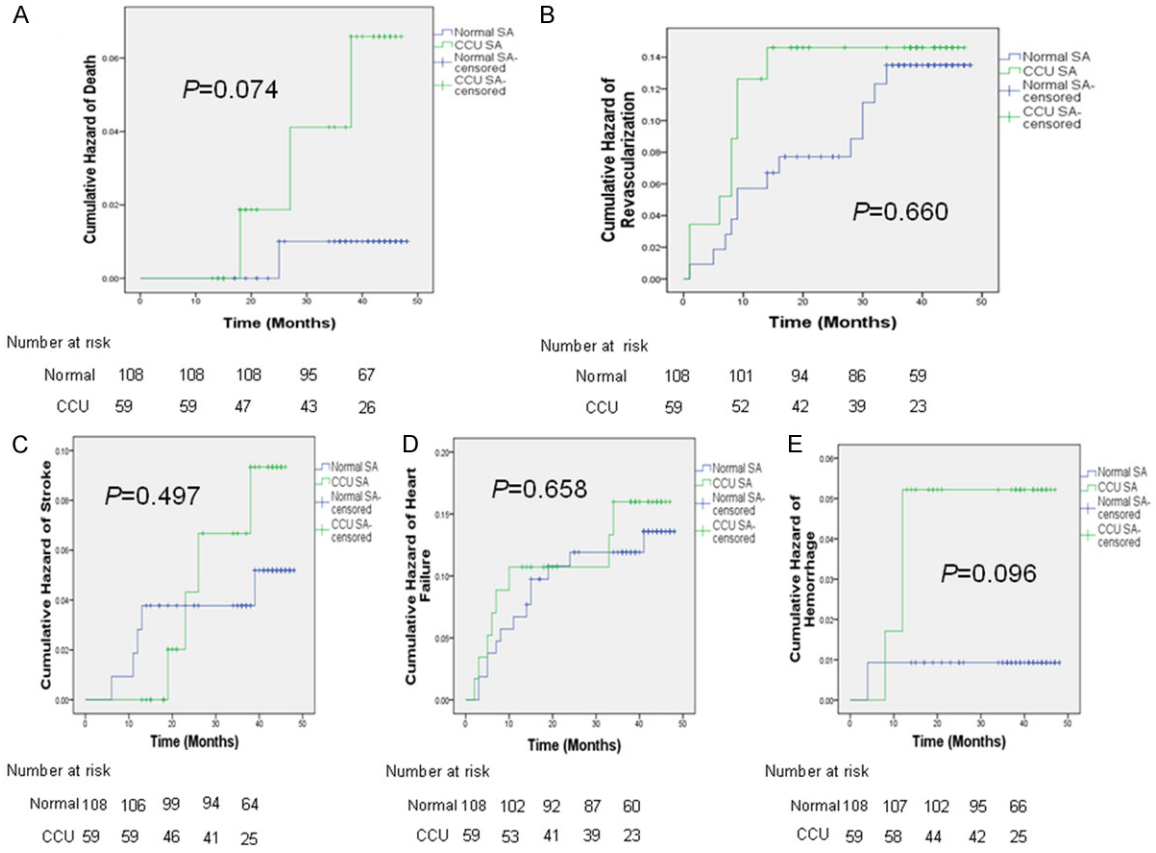

Figure 2. Kaplan-Meier Curves for MACEs of SA patients. A: Cumulative hazard ratio of death between two groups. B: Cumulative hazard ratio of revasclarization between two groups. C: Cumulative hazard ratio of stroke between two groups. D: Cumulative hazard ratio of heart failure between two groups. E: Cumulative hazard ratio of hemorrhage between two groups.

heart and right heart especially for cardiac shock. Previous research reported that central venous pressure and pulmonary capillary wedge pressure measurement may have potential benefit for patients who underwent coronary artery by-pass [11]. For ACS patients, invasive measurement of hemodynamic may predict the response to volume administration in the setting of acute left ventricular myocardial infarction [12]. Our trial showed that in CCU patients with ACS, no significant clinical benefits were obtained, although long time cumulative hazard of MACEs was lower than patients treated in normal unit. These results have further justified that intensive care without invasive hemodynamic measurement for ACS in case of equal drug therapy failed to give patients benefits. CCU either failed to improve mortality and long term rate of MACEs in SA patients which indicated that early recognition

Table 3. Rate of MACEs according to two subgroups of ACS patients

	ACS (n=639)			
	CCU (n=372)	Normal (n=267)	Hazard Ratio (95% CI)	P
Death, no./total no. (%)	5/372 (1.3)	5/267 (1.9)	1.403 (0.406-4.846)	0.593
Revascularization, no./total no. (%)	84/372 (22.6)	61/267 (22.8)	0.999 (0.719-1.390)	0.996
Stroke, no./total no. (%)	11/372 (3.0)	11/267 (4.1)	1.402 (0.608-3.253)	0.428
Heart failure, no./total no. (%)	32/372 (8.6)	26/267 (9.7)	1.137 (0.678-1.908)	0.626
Hemorrhage, no./total no. (%)	3/372 (0.8)	0/267 (0)	//	/

HR was calculated as CCU subgroup was control group.

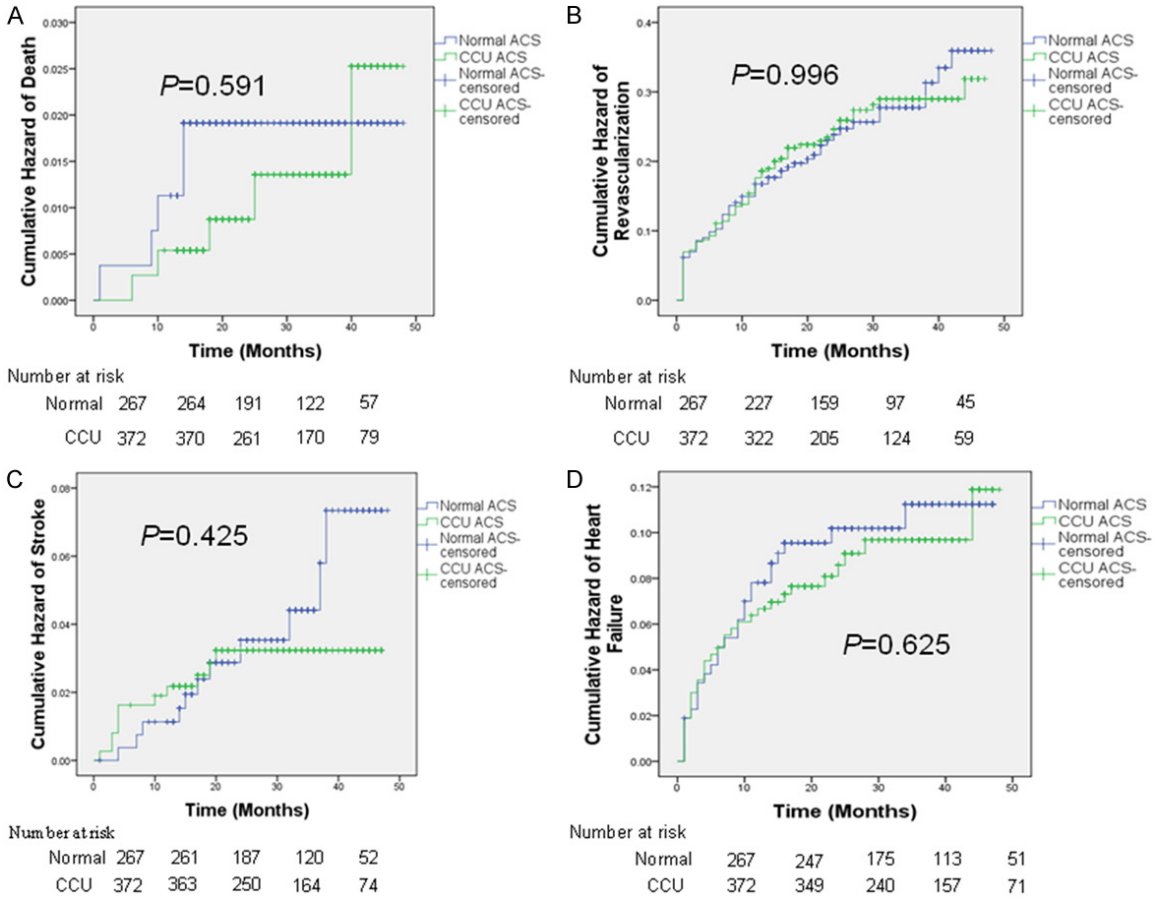

Figure 3. Kaplan-Meier Curves for MACEs of ACS patients. A: Cumulative hazard ratio of death between two groups. B: Cumulative hazard ratio of revasclarization between two groups. C: Cumulative hazard ratio of stroke between two groups. D: Cumulative hazard ratio of heart failure between two groups.

of SA and ACS patients may influence the waste of medical resources.

Vital monitoring was a effective method that can real time monitor the vital sigh to guide the therapy procedures according to the changing of diseases condition, especially for the patients of ACS that have high risk of death. Hervás [13] has found that monitoring can prevent cardiovascular disease better. Electrocardio-monitoring have efficiency to found fatal arrhythmia promptly that save patients from death. However, lack of clinical evidence demonstrated if the vital monitoring can reduce the rate of death for ACS patients. Our results have shown that CCU monitoring method have little clinical benefit for ACS patients and equally no profit for SA patients. The rationality of monitoring application for SA patients is doubted according to our trial data.

Anti-platelets, anti-coagulation and lowing cholesterol were the three major methods for curing CAD patients [4, 14]. For the chest pain patients that have high probability of CAD or ACS, CCU may strongly recommend early usage of anti-platelets, anti-coagulation and statin therapy before conclusive diagnosis was determined. Strongly anti-platelets, anti-coagulation and lowing cholesterol therapy may be applied as soon as possible. Early standard therapy of myocardial infarction and ACS obtained more benefits for ACS patients [15-17], but for SA patients is uncertain. Although Ortega-Gil has reported that early using aggressive medical therapy including statin and anti-platelets before reperfusion have advantage for CAD patients [18], our research indicated that high rate of complication occurred. A recent retrospective trial has showed that only low percentage of doubted ACS patients treated in intensive care unit were definitive CAD [8]. The guideline of SA did not recommend the jacobinical anti-platelets and anti-coagulation [19]. The incorrect diagnosis of SA that identified as ACS may bring high risk of hemorrhage because of intensive anti-platelets and anti-coagulation. The unnecessary application of dual anti-platelets and anti-coagulation usually result in low ratio of benefit/risk. With regard to the patients who had been diagnosed as ACS yet but poor compliance was used to refuse to be treated in CCU. Standard therapy of ACS also utilized but vital monitoring was not applied. This may limit the efficiency of therapy. Our study has confirmed that receive standard therapy in CCU for SA patients have no trend of decreasing the cumulative hazard of MACEs during 12-48 months follow-up but increasing ratio of complications was observed. Patients with ACS either have no significant low rate of MACEs although trend of decreasing cumulative hazard of MACEs have found. These results may indicate that CCU may have limited advantages for healing CAD patients in condition of equal standard therapy was utilized.

Furthermore, statin therapy that lowing LDL have widely used in CAD patients whatever ACS or not. Both in CCU and normal unit, statin have seldom absent. Previous study have demonstrated that statin have various protective effort that can reduce mortality [20-22]. Our study has not detected evidence that identical statin therapy in different care unit may influence the mortality and ratio of MACEs. Further study may proceed to demonstrated if the protective of statin besides lowing LDL can influence the prognosis of CAD patients in different care unit.

β-blocker and ACEI/ARB can prove the long term prognosis of ACS that have been proved by researches [23, 24]. However, the usage in SA patients was controversy [25]. In our study, the usage of β-blocker and ACEI/ARB was no significant differences between subgroups which were accordance with present guideline no matter the type of care unit. These finding may partly indicate that CCU have little effort to reduce the mortality and incidence of MACEs without invasive homodynamic measurement. Basic real time vital monitoring seemed useless to prove the prognosis of CAD include ACS.

Conclusion

The standard therapy of CAD in CCU and normal care unit was nearly coincidental. Patients with ACS treated in CCU obtain little benefits than in normal unit, although the risk of MACEs reduced. No clinical benefits were observed for SA patients treated in CCU and even elevated rate of MACEs was revealed.

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Disclosure of conflict of interest

None.

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