Kobe J. Med. Sci., Vol. 57, No. 1, pp. E17-E25, 2011

Actual Situation Regarding Cardiac Etiology Determined by Clinical Diagnosis of and Medical Examiner's Postmortem Findings on Witnessed Out-of-hospital Cardiac Arrest Cases

TAKESHI YOSHIDA*[1], HIROYUKI NAKAO[1], YUSUKE ITAGAKI[1], TAKAYUKI KATO[1], TAKAHISA KAWASHIMA[1], NOBORU ISHII[1], YASUSHI NAGASAKI[2], and AKIRA IMAMURA[3]

[1]*Division of Disaster and Emergency Medicine, Kobe University Graduate School of Medicine,* [2]*Medical Examiner's Office of Hyogo Prefecture,* [3]*Kobe City Fire Department*

Received 12 January 2011/ Accepted 18 January 2011

Key Words: Utstein Style, diagnosis by exclusion, ventricular fibrillation, cardiac troponin T, out-of-hospital cardiac arrest

ABSTRACT

Aim: To examine indicators that may assist in the diagnosis of cardiac etiology using simple tests in witnessed cardiac etiology out-of-hospital cardiac arrest cases, which is emphasized in the Utstein Style.

Method: The subjects were 165 witnessed cardiac etiology out-of-hospital cardiac arrest cases, which were transported to Kobe University Hospital during the five-year period between January 1, 2005 and December 31, 2009. A comparative study was conducted into whether there were any significant differences in the initial electrocardiogram (ECG) and the various early diagnostic markers of acute myocardial infarction between the group who were finally diagnosed as being of cardiac etiology and the group who were finally diagnosed as being of non-cardiac etiology.

Results: Of the 165 witnessed cardiac etiological cases, 69 cases were finally re-classified as non-cardiac etiological cases on the basis of scrutiny after admission or postmortem findings by the Medical Examiner. Ventricular fibrillation shown in the initial ECG and Qualitative cardiac troponin T test positive were significantly higher in the final diagnosis cardiac group than in the final diagnosis non-cardiac group. Ventricular fibrillation and troponin T positive can be seen as significant indicators in determining whether a case was cardiac or non-cardiac, and the model χ^2 test result of $p < 0.01$ in the multiple logistic regression analysis was significant, and the determining predictive value was 65.4%.

Conclusion: The indicators which should be noted in simple tests to improve the precision of discrimination of cardiac etiology in out-of-hospital cardiac arrests are ventricular fibrillation in the initial ECG and the qualitative test of cardiac troponin T.

INTRODUCTION

The Utstein Style was proposed in 1990 as a set of guidelines for standardizing the definitions of the terminology used and the data recording methods regarding resuscitation of cardiac arrest cases. These guidelines have now been broadly adopted, both in Japan and

Phone: +81-78-411-0252 Fax: +81-78-411-0252 E-mail: takeyoshi4789@ybb.ne.jp

overseas, as the standard protocol for recording and analyzing out-of-hospital cardiac arrest data [1-5]. The emphasis in the Utstein Style is on evaluating pre-hospital medical treatment, post-hospital arrival medical treatment, prognosis and so on in cardiac arrest cases with cardiac etiology. However, when the etiology is unknown, based on diagnosis by exclusion, the case is classified as cardiac, thus, it has been said that the rate of cases classified as being of cardiac etiology tends to be an overestimation [6].

On the other hand, since the Ministry of Internal Affairs and Communications began keeping a national registry of out-of-hospital cardiac arrest data in 2005, approximately 100,000 cardiac arrest cases have been reported annually of which 55% were cardiac [7]. While in-hospital mortality rates of patients with ischemic heart disease have greatly declined due to improved medical care in recent years, it is reported that most (around two-thirds) of the deaths due to ischemic heart disease in North America and Europe are due to out-of-hospital cardiac arrest [8]. In Japan, ischemic heart disease is the second highest cause of adult deaths and is on an upward trend. However, there is no research that has looked at how many cases out of the total number of cases determined to be cardiac were determined to be cardiac etiological cases based on diagnosis by exclusion. Little research has been done looking at the prognosis for heart disease patients focusing on out-of-hospital sudden ischemic deaths, and the actual sudden death incidence and fatality rates remain unclear [9-10].

On the other hand, while the Medical Examiner system is designed to identify the cause of death, in reality its operation is limited to within the following three cities; the 23 wards of Tokyo, Osaka, and Kobe. Within the metropolitan Kobe City area, postmortems on unusual deaths are carried out chiefly by the Medical Examiner of the Medical Examiner's Office of Hyogo Prefecture. Assessment according to the Utstein Style has been performed in the metropolitan Kobe City area since 1999, mainly driven by the city's fire department, the Kobe City Medical Center General Hospital and Kobe University Hospital in conjunction with the city's secondary emergency medical services. According to a report by Nakao et al., the 2002 data for Kobe City was notable for the city's autopsy rate, which at 665 autopsies out of an annual death toll of 8,858 is 7.5%, higher than that of other areas where there is a Medical Examiner's system (Osaka City 5.1%, Tokyo Metropolis 4.3%) [11]. Thus, in the metropolitan Kobe City area, the systems exist to allow out-of-hospital cardiac arrest cases to be subject to both clinical diagnosis and postmortem by the Medical Examiner.

The aim of this study was to investigate the actual situation regarding witnessed cardiac arrest cases of cardiac etiology, which are emphasized in the Utstein Style, by examining both the clinical diagnosis and the Medical Examiner's postmortem findings on cases within the metropolitan Kobe City area. From those results, we examined whether simple tests may also assist in the diagnosis of cardiac etiological cases where there is no Medical Examiner system.

SUBJECTS AND METHOD

A retrospective study was conducted using patient clinical records of out-of-hospital cardiac arrest cases, excluding trauma cases, where the patient was transported to Kobe University Hospital during the five-year period between January 1, 2005 and December 31, 2009. Of the 704 out-of-hospital cardiac arrest cases, 571 cases were endogenous and 133 cases were exogenous. A postmortem was performed by the Medical Examiner in 400 of the 704 cases, which equates to 56.8%, and an autopsy was performed in 248 of those 400 cases, which equates to 62%. In the postmortem, the diagnosis of ischemic heart disease was made based on whether or not there were findings of narrowing or obstruction of coronary arteries and fibrosis of myocardial tissue. Of the total 377 cardiac etiological cases in accordance

with the Utstein Style, 165 cases were witnessed cases, which are emphasized under the Utstein Style, and these 165 cases were the subjects of this study (Figure 1).

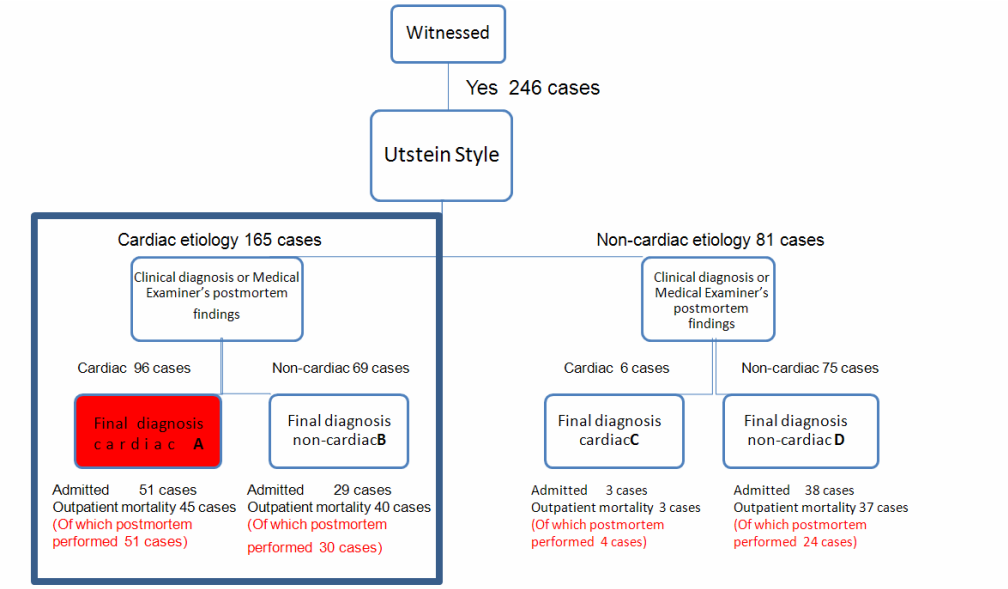

Figure 1. Composition of Witnessed Out-of-hospital Cardiac Arrest Cases Transported to Kobe University Hospital.

(1) A comparative study was conducted between the admitted group and the outpatient mortality group looking at whether there was ventricular fibrillation shown in the initial ECG, as well as the various early diagnostic markers of acute myocardial infarction, namely H-FABP, troponin T, CK, CK-MB, WBC, AST, and LD. (2) A similar comparative study was also conducted between the group who were finally diagnosed as being of cardiac etiology based on clinical or Medical Examiner's postmortem findings (hereafter referred to as the final diagnosis cardiac group) and the group who were finally diagnosed as being of non-cardiac etiology (hereafter referred to as the final diagnosis non-cardiac group).

SPSS 16.0J was employed in the statistical examination, and the χ^2 test, the t test, and multiple logistic regression analysis were performed and it was determined that there was a significant difference of $p<0.05$.

This study was conducted in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, revised in 1983.

RESULTS

Of the 165 witnessed cardiac arrest cases that were diagnosed in the emergency department as being of cardiac etiology in line with the Utstein Style, 96 cases were subsequently determined to be cardiac etiological cases and 69 cases were re-classified as non-cardiac etiological cases on the basis of scrutiny after admission or postmortem findings by the Medical Examiner. Of the 96 cardiac etiological cases, 51 cases were admitted to hospital and 45 cases were confirmed deceased in the outpatient department. Of the 69 non-cardiac etiological cases, 29 cases were admitted to hospital and 40 cases were

confirmed deceased in the outpatient department. The breakdown of the etiology of the latter, the non-cardiac etiological cases was; respiratory disease 14 cases, aortic disease 10 cases, malignant tumor 10 cases, aggravated chronic renal failure (CRF) 7 cases, electrolyte abnormality 5 cases, cerebrovascular disorder (CVD) 4 cases, old age 4 cases, peritonitis 3 cases, pulmonary thromboembolism (PTE) 2 cases, other 3 cases, and unknown 6 cases. (Table I)

Table I. Breakdown by cause of Witnessed Cardiac Arrest Cases Diagnosed as Non-cardiac etiology as Result of Clinical Diagnosis or Medical Examiner's Postmortem Findings.

	Admitted	Outpatient Mortality	Sub-total
Electrolyte	4	1	5
CRF	6	1	7
CVD	4		4
Aortic	2	8	10
Tumor	3	7	10
Respiratory	4	10	14
Peritonitis		3	3
PTE		2	2
Old age	1	3	4
Unknown	2	4	6
Other	3	1	3
Total	29	40	69

Table II. Comparison between Admitted Group and Outpatient Mortality Group of Witnessed Cases Initially Diagnosed as Cardiac Etiological Cases.

Witnessed Cardiac 165	Admitted Group 80	Outpatient Mortality Group 85	P
Initial ECG:vf	31/79(39)	7/79(9)	$1.858 \times 10^{-5*}$
H-FABP positive	52/66(79)	59/69(86)	0.307
TROP-T positive	18/67(27)	16/72(22)	0.524
			Top row χ^2 test Bottom row t test
CK↑(>248)	17/79(22) (283.14±417.53)	18/79(23) (333.18±622.96)	0.143
CK-MB↑(>25)	39/72(54) (34.83±27.58)	36/76(47) (40.84±63.06)	0.11
WBC↑(>85)	57/79(72) (107.27±34.46)	51/78(65) (106.51±45.88)	0.015*
AST↑(>31)	62/79(78) (115.35±158.59)	61/78(78) (244.38±587.41)	0.473
LD↑(>217)	72/79(91) (455.05±468.41)	71/78(91) (793.99±1498.93)	0.191

In (1), the number of cases in which there was ventricular fibrillation in the initial ECG was 31 cases in the admitted group and 7 cases in the outpatient mortality group, thus the number was significantly higher in the admitted group. No significant difference was found in H-FABP, troponin-T, CK, CK-MB, AST, or LD. The admitted group tended to have to elevated WBCs. (Table II)

In (2), 31 cases in the final diagnosis cardiac group had ventricular fibrillation in the initial ECG, which was a significantly higher number of cases compared to the 7 cases in the final diagnosis non-cardiac group. The 28 cases in the final diagnosis cardiac group that were qualitative troponin-T test positive was a significantly higher number of cases compared to the 7 cases in the final diagnosis non-cardiac group. In regards to early diagnostic markers, AST and LD were significantly low in the final diagnosis cardiac group. (Table III)

Table III. Comparison of Final Diagnosis of Witnessed Cases Initially Diagnosed as Cardiac Etiological Cases.

Witnessed Cardiac 165	Final Cardiac 96	Final Non-cardiac 69	P
Initial ECG:vf	31/96(32)	7/69(10)	0.002*
H-FABP positive	70/85(82)	43/54(80)	0.688
TROP-T positive	28/88(32)	7/55(13)	0.017*
			Top row χ^2 test Bottom row t test
CK↑(>248)	19/95(20) (318.73±346.13)	16/64(25) (289.63±503.04)	0.25
CK-MB↑(>25)	48/90(53) (41.02±53.0)	27/58(47) (32.67±42.11)	0.288
WBC↑(>85)	68/94(72) (104.87±31.1)	40/64(63) (108.73±51.79)	0.208
AST↑(>31)	73/95(77) (168.68±449.81)	51/63(81) (200.76±406.2)	0.028*
LD↑(>217)	85/95(89) (589.25±1224.57)	59/63(94) (696.95±943.59)	0.024*

The results of performing multiple logistic regression analysis using the step-up procedure using the likelihood ratio on these initial results are shown (Table IV).

The model χ^2 test result of $p<0.01$ was significant. When cardiac etiology was suspected and when finally determining whether a case was cardiac or non-cardiac, ventricular fibrillation in the initial ECG and qualitative troponin-T test positive could be seen as significant indicators, while H-FABP, CK, CK-MB, WBC, AST, and LD could not. The prediction formula used for calculation was Score = 0.088 – 1.566 × vf (0 = no, 1 = yes) – 1.143 × troponin-T (0 = negative, 1 = positive), and p = 1/(1 + exp(-1 x score)) was used to find the predictive probability p for each case, with cases with $p>0.5$ classified as non-cardiac and cases with $p<0.5$ classified as cardiac. The determining predictive value was 65.4%.

Table IV. Results of Multiple Logistic Regression Analysis used to Diagnose Witnessed Cardiac Arrests as Cardiac Etiological Cases

	Regression Coefficient	Probability		Lower Limit	95% Confidence Interval
Vf (0: no, 1: yes)	-1.566	0.004	0.209	0.073	0.599
Troponin T (0: no, 1: yes)	-1.143	0.019	0.319	0.123	0.829
Constant	0.088	0.709			

Model χ^2 test $p<0.01$ (Cardiac: 0, Non-cardiac: 1)
Determining predictive value 65.4%

DISCUSSION:

As shown in Figure 1, of the 165 cases, 69 cases were re-classified from cardiac to non-cardiac, which is 41.8%. Since there were few cases , 6 out of 81 cases, in which the determinations were revised from non-cardiac to cardiac, they could not be processed statistically. In the report by Istepan et al., the initial diagnosis was cause unclear in 4% of cases and the final diagnosis matched the initial diagnosis in 89% of cases [12]. This result is considerably higher than that of our study, however, it can be envisaged that, because the Istepan et al. results included in-hospital cardiac arrests (28%), in which the patients' medical history was known, accurate initial diagnosis was possible. Also, according to the Istepan et al. report, initial diagnosis in the emergency department had an accuracy rate of 96% (in cardiac etiological cases specificity 76.5%, sensitivity 94.8%). In contrast, cardiac initial diagnosis is difficult in cardiac arrest cases, and in the Utstein Style the rule is that if exogenous or other endogenous cannot be diagnosed, then diagnosis by exclusion shall be performed and the case classified as cardiac. However, the Istepan et al. report does not state the reasons why they were able to obtain such a high rate of accurate initial diagnosis. Also, despite it being stated in that report that the patient's medical history is important in initial diagnosis, this is inconsistent with the fact that there was no statistical difference in the initial diagnosis error rates between the in-hospital cardiac arrest group with known patient medical histories and the out-of-hospital cardiac arrest group for whom patient medical histories tend to be mostly unknown. While our study was of postmortems conducted within a few days of the cardiac arrest occurring in witnessed cardiac arrest cases with an initial diagnosis, the Istepan et al. report was of postmortem investigations performed within six months after the cardiac arrest episode. Thus, we do not think that their postmortem results can be said to accurately indicate the cause of cardiac arrest. Therefore, it can be conjectured that the results in our study better reflect realistic conditions than the result described in their report of a low re-classification rate of diagnosis.

In our investigations, there were more outpatient mortality cases in the final non-cardiac group than in the final cardiac group and the cause of death was predominantly chest disease with some cases of asphyxiation, pneumonia, aortic disease, CRF and so on. In the Czech group's report, postmortems were performed on 31.3% of the total, with 34.1% being

non-cardiac and 16.2% being revised from cardiac to non-cardiac [13]. According to this report, similar to our study results, many of the cases in this revised group had chest disease. Chest disease may be easy to misjudge as it can be difficult to distinguish in a physical examination or from diagnostic imaging. While our diagnostic performance cannot be said to be good compared with reports from North America and Europe [12-13], when the different circumstances, such as differences in emergency medical service systems, lifestyle habits, and diseases associated with groups of differing racial backgrounds are considered, there may be limits to making blanket comparisons using the Utstein Style.

We listed the following study items as possible indicators of acute myocardial infarction, which is the typical type of ischemic heart disease, which accounts for the majority of the cardiac etiological cases. *a:* ventricular fibrillation in initial ECG, *b:* H-FABP, *c:* troponin-T, *d:* CK, *e:* CK-MB, *f:* WBC, *g:* AST, *h:* LD. We eliminated the independent quantitative variables *d* through *h* from the multiple logistic regression analysis results this time and ascertained that whether there is ventricular fibrillation in the initial ECG and whether there is a troponin-T qualitative reaction are independent qualitative variables when finally determining whether a case is cardiac or non-cardiac. A test of independence ($\chi 2$ test) showed no mutual association and that they were independent factors. In the Istepan et al. report, ventricular fibrillation was seen in 50% of all cases and the diagnosis was revised in 3.9% of ventricular fibrillation cases that were initially diagnosed as cardiac etiological cases [12]. The Istepan et al. report states that taking the patient's pre-arrest medical history is important as cardiac etiology is not easy to diagnose based on the patient's present status, monitoring data, lab work, and echocardiographic data. Also, the report by Arore et al. noted a history of diabetes, a history of ischemic heart disease, having a cardiac arrest in a public place, ventricular fibrillation in the initial ECG, and ST segment depression in the initial ECG as predictive factors for positive coronary angiography in out-of hospital cardiac arrest cases, however ST segment elevation was eliminated as a factor [14]. Our results also indicated that taking a pre-arrest medical history is important in order to improve the survival rate of cardiac arrest cases, and finding new independent quantitative variables is the next challenge. We envisage that it is possible that finding out the cause of cardiac arrest from these indicators will lead to early appropriate medical treatment.

Individual observation of the study items revealed that the characteristics related to *a* were a high hospitalization rate compared with other initial ECG cases and that many cases were finally diagnosed as being of cardiac etiology, however, there were fewer of these cases compared with other initial ECGs and in many cases a postmortem was not performed. However, this is consistent with results supporting the efficacy of early defibrillation in cases where there is ventricular fibrillation [15]. The characteristics related to *b* were high cardiac specificity and also rapid deviation to the blood after myocardial damage, it is said to be a useful early diagnostic marker of acute myocardial infarction and in some cases rises within 1-2 hours [16], however it also generated false positives in non-cardiac etiological cases, such as aortic dissection, skeletal muscle damage and compromised renal function [17], and had a lower specificity than *c*. The results were similar in our study results. While *b* is used in routine diagnosis of ischemic heart disease, we do not think it is a useful marker in out-of-hospital cardiac arrest cases. The characteristics related to *c* are that while it is said to be of great diagnostic significance in acute myocardial infarction, it rises 3-4 hours after onset and sometimes shows negative in the initial test, thus it has low sensitivity and is said to be less useful diagnostically in the hyperacute phase [18]. However, we think that *c* has clinical usefulness in the diagnosis of cardiac etiology, as even in witnessed cases, the final cardiac etiological group had a significantly higher number of positives compared to the final

non-cardiac etiological group. The characteristics related to *d* and *e* are that they are said to be of great diagnostic significance in acute myocardial infarction, however, because they rise 3-4 hours after onset [19], in our results each had a lot of variability and there was a high rate of positives even in the non-cardiac etiological group. The characteristics related to *f* were low specificity as although WBC rises in the comparatively early phase 2-3 hours after onset, it also tends to rise with other conditions such as hemodyscrasia and inflammation. The characteristics related to *g* were that AST also tends to rise with other conditions such as hemolysis and hepatic disorders, and that it has low cardiac specificity, and little diagnostic value on its own. The characteristics related to *h* were heart-derived LD as LDH_1 has high specificity in isozyme analysis, and because it rises 6 hours after onset, as well as staying at an abnormal level for a comparatively long period of time, in some cases it is useful as a late-phase diagnostic marker [20]. However, there is no mention in the guidelines on medical care for acute myocardial infarction of the usefulness of clinical testing of *f*, *g*, and *h* [21].

The prognosis for out-of-hospital cardiac arrest cases of cardiac etiology in Japan is still poor [22]. Most cardiac arrests of cardiac etiology occur out-of-hospital, much is still uncertain about them, and more accurate cause-of-death statistics are necessary in order to improve prognosis in future. Thus, at Kobe University Hospital ,the general rule is that the Medical Examiner be requested to perform a postmortem, unless the cause of death is clear, or there is a primary care doctor, or the case occurred outside the Medical Examiner system's jurisdiction (Kita Ward, Nishi Ward, Kobe City). We also hold a cardiac etiological case review meeting once a week, exchange opinions with the Medical Examiner, and examine cases where the clinical diagnosis of cardiac etiology is at odds with the Medical Examiner's postmortem findings in order to facilitate more accurate diagnosis in future.

From the above considerations, we arrived at the following conclusion. In improving the precision of discrimination of cardiac etiology in out-of-hospital cardiac arrests even in areas where there is no Medical Examiner system, in addition to medical history taking, physical findings and image diagnosis, it should be noted that ventricular fibrillation in the initial ECG and the qualitative test of cardiac troponin T are positive indicator. In the future, we expect to contribute to the improvement of the prognosis of cases of cardiac etiology out-of-hospital cardiac arrest in Japan by gaining further findings on indicators for discriminating cardiac etiology.

REFERENCES

1. **Cummins RO,Chamberlain DA,Abramson NS,et al**:Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest:the Utstein Style.A statement for health professionals from a task force of the American Heart Association,the European Resuscitation Council,the Heart and Stroke Foundation of Canada,and the Australian Resuscitation Council.Circulation 1991;**84:**960-75
2. **McR Meyer AD,Cameron PA,Smith KL,et al**:Out-of-hospital cardiac arrest.Med J Aust 2000;**172:**73-6
3. **Donoghue AJ,Nadkarni V,Berg RA,et al**:Out-of-hospital pediatric cardiac arrest:an epidemiologic review and assessment of current knowledge.Ann Emerg Med 2005;**46:**512-22
4. **Hayashi Y,Hiraide A,Morita H,et al**:Three year longitudinal study for out-of-hospital cardiac arrest in Osaka Prefecture.Resuscitation 2004;**63:**161-6
5. **Jacobs I, Nadkarni V.** The ILCOR task force on cardiac arrest and cardiopulmonary resuscitation outcomes: cardiac arrest and cardiopulmonary resuscitation outcome reports. Circulation 2004;**20:**861-874

6. **Morita H** : Sudden cardiac death:out-of-hospital care and improving survival,JPN.J.ELECTROCARDIOLOGY Vol.26No.2 2006
7. **Nonogi H** : The State and Prevention of Ischemic Sudden Death in Japan, Diagnosis and Treatment Vol.96-No.10 2008:162-6
8. **Myerburg RJ,Castellanos A**:Cardiac arrest and sudden cardiac death.Heart disease;a textbook of cardiovascular medicine.5th ed(ed Eugene Braunwald WB).Saunders,Philadelphia.1997.pp742-779
9. Health and Welfare Statistics Association : The Trend of National Hygiene, The Indicator of Health and Welfare ,Vol.53,iss.9, 2006
10. **Iwami T, Hiraide A,** : The Prognosis of cardiogenic out-of-hospital cardiac arrest cases-from the Utstein Osaka Project:Japanese Circulation Society,Vol.12iss.2 2004,277-84
11. **Nakao H,Yoshida T,et al** : Statistical analysis of unknown causes of deaths using postmortem findings by medical examination, JJAAM2007 ; **18 :** 39-46
12. **Istepan Kurkciyan et al**:Accuracy and Impact of Presumed Cause in Patients with Cardiac Arrest,Circulation 1998;**98:**766-771
13. Miloslav Pleskot:Characteristics and short-term survival of individuals with out-of-hospital cardiac arrests in the East Bohemian region,Resuscitation(2006)68,209-220
14. Arore A, Jabre P, Margenet A, Lecarpentier E, Combes X. Predictive factors for positive coronary angiography in out-of hospital cardiac arrest patients. Eur J Emerg Med. 2010;20:
15. American Heart Association Guidelines 2005 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care.112,2005
16. **McCann CJ,Glover BM,Menown IB,et al:**Novel biomarkers in early diagnosis of Acute myocardial infarction compared with cardiac troponinT.Eur Heart J29;2843-2850.2008
17. **Seino Y,Ogata K,Takano T,et al.**Use of a whole blood rapid panel test for heart-type fatty acid-binding protein in patients with acute chest pain:comparison with rapid troponin T and myoglobin tests.Am J Med 2003;**115:**185-190
18. **Sakamoto K, Ogawa H:**Biochemical Test of Acute Coronary Syndrome, The Journal of the Japanese Society of Internal Medicine, **98:**248-254, 2009
19. **Halkin A,Stone GW,Grines CL,et al.**Prognostic implications of creatine kinase elevation after primary percutaneous coronary intervention for acute myocardial infarction.J Am Coll Cardiol 2006;**47:**951-961
20. **Sugawara S,Itoh T,et al:**Biomarkers Derived from Myocardial Cytoplasm,ICU & CCU, 31, 8, 565-569, 2007 ; 08
21. Guidelines for the management of patients with ST-elevation myocardial Infarction,Circ J **72:**1347-1442,2008
22. **Iwami T,Nonoki H,et al :** Epidemiological characteristics of out-of-hospital cardiac arrests and quality of emergency medical service system in Japan compared with international regions , Heart View Vol.9,No,13,2005,1363-67