Does the Effect of Supervised Cardiac Rehabilitation Programs on Body Fat Distribution Remained Long Time?

Mehdi Nalini1, Bahieh Moradi2*, Maryam Esmaeilzadeh2, Majid Maleki2

1Department of Prevention and Cardiac Rehabilitation, Kermanshah University of Medical Sciences, Kermanshah, Iran
2Echocardiography Research Center, Shaheed Rajaee Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

**ABSTRACT**

**Introduction:** An increased accumulation of fat in the intra-abdominal cavity is highly correlated with adverse coronary risk profiles. Cardiac rehabilitation (CR) produces a host of health benefits related to modifiable cardiovascular risk factors. Further research is needed to define better program for weight loss and risk improvement in coronary patients. The aim of this study was to determine the effect of supervised and unsupervised cardiac rehabilitation program on body composition and body fat distribution in a population with coronary artery disease.

**Methods:** The study investigated 167 patients with coronary artery disease (73% males; mean age = 52.67±9.11 years) before and after a supervised protocol cardiac rehabilitation program, and 12-months later. Target variables included body fat distribution indices (waist and hip circumference and waist to hip ratio), weight and body mass index.

**Results:** Weight, waist circumference, waist to hip ratio and body mass index significantly decreased with 2 month supervised program (P<0.001), but hip circumference was not significantly changed. Males improved to a greater extent than the female patients. All of measurements relatively returned to baseline at the end of program (after 12 months).

**Conclusion:** Supervised cardiac rehabilitation program results in improvements in body composition and body fat distribution. The effects of non-supervised program were minimal and the program needed to be reviewed.

**Introduction**

Obesity affects 33% of the general population in the United States, with more than 60% categorized as overweight. Coronary populations display a higher prevalence of obesity than is observed in non-coronary population. From 1996 to 2006, the mean body mass index (BMI) for Coronary Heart Disease (CHD) patients increased from 28.5 to 30.1 kg/m². Currently, more than 80% of CHD patients are overweight (BMI> 25 kg/m²), the prevalence of obesity (BMI> 30 kg/m²) is 40%, and 50% have insulin resistance manifest as metabolic syndrome. General overweight and general and abdominal obesity are independently associated with an increased risk of death, recurrent events and HF. It can interact with or amplify the effects of other cardiovascular risk factors such as hypertension, dyslipidemia, insulin resistance, and hyperinsulinemia. Low fitness and central obesity are independently and cumulatively associated with increased mortality and morbidity in CHD patients. The association of BMI with mortality is complex and altered by fitness levels. Nowadays, cardiac rehabilitation (CR) is defined as an effective non-pharmacological modality to reduce coronary risk profiles including total cholesterol, body fat, systolic blood pressure, metabolic syndrome and can improve peak aerobic capacity. Peak aerobic capacity, measured as peak oxygen consumption, is corrected for total body weight and is reported in milliliter
per kilogram of body weight per each minute.\textsuperscript{22,23} Weight loss in CR has been linked to diminished cardiovascular events.\textsuperscript{19} Unfortunately, the current CR protocols not only result in little weight loss\textsuperscript{1} during the program but also overweightness remains a prevalent and persistent risk factor after CR.\textsuperscript{24} Failure to weight reduction may be due to low energy expenditure in rehabilitation or the relatively short duration of the program.\textsuperscript{25} Monitoring weight loss after program completion is important to observe the effect of CR on long-term outcomes. The purpose of this study was to determine the effects of a 12-month (supervised and unsupervised) CR program on body composition and fat distribution in patients with coronary heart disease.

Methods

The study population consisted of 167 coronary patients who were referred for CR and exercise training program from 2009 since 2011. Subjects were clinically stable and all patients entered the program 8±3 weeks after a major coronary event including coronary artery bypass grafting surgery, acute MI or unstable angina, and catheter revascularization for acute coronary syndrome. Each subject read and signed an informed consent form. Descriptive characteristics, personal history, medications and other data were collected at the baseline. Subjects maintained their normal medication throughout the course of the study. Height, weight, waist and hip circumference were measured in the fasting state in the morning by two nurses before entering the program. Weight measurements, using a balance machine, Seca 900946 model, were performed to evaluate BMI. Measurements were taken in duplicate and the average was used, waist to hip ratio was measured using a metal tape with measurements taken at the level of the umbilicus and the greatest protrusion of the buttocks, as recommended by Lohman. Each patient was evaluated by a dietician who prescribed a phase I diet AHA. Furthermore, if the patient was found to be obese, further calorific restriction was recommended. Patients with significant hypercholesterolemia and obesity were periodically followed up by the dietician during 2 month program to ensure compliance with and understanding of the prescribed therapy. All patients participated in six classroom (25 minutes each) teaching sessions on a heart-healthy diet with a dietician, and also in a dietary motivation session with a physician. The CR protocol consisted of two phases: supervised and unsupervised program. In this study patients, first participated in supervised exercise program, which lasted approximately 8 weeks and generally included 24 exercise training sessions over 2 months. Each session consisted of approximately 5 to 10 minutes of warm up and light exercise (stretching) followed by 35 to 40 minutes of aerobic exercise including walking (treadmill), bicycling and rowing, then approximately 10 minutes of resistance training exercise; 3 exercises of 10 repetitions for upper and lower body, (Both aerobic endurance and strength training programs improve cardiovascular health in obese adults specially in heart failure patients\textsuperscript{26-29}) and finally 10 minutes cool down period (stretching). Exercise intensity was prescribed individually so that the patient heart rate reached to approximately 60% to 80% (gradually increased) of the maximum heart rate calculated after exercise stress test. Before entering the program, patients underwent exercise testing and we estimated exercise capacity.

In second phase, unsupervised exercise program, we encouraged patients to perform approximately 3 to 4 exercise sessions per week at home and control their heart rate during exercise. Physicians frequently encouraged patients to comply with both the exercise and dietary portions of rehabilitation program. After two months and again at the end of 6th and 12th months of study, several measurements: weight, BMI, waist and hip circumference and WHR were obtained by two nurses who were blinded to the previous anthropometrical data.

Statistical Analysis

The results were expressed as mean±SD. For statistical analysis we used chi-square test, analysis of variance, and paired \(t\)-tests to assess differences among patients before and after rehabilitation, analysis of variance with repeated measures in 6 and 12 months after supervised rehabilitation program. The SPSS 15 (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis and \(P\)-value of 0.05 is considered significant.

Results

Coronary artery disease patients (n=167; age= 52.67±9.11 years; 73% males) were revascularized by percutaneous coronary intervention (37%), coronary artery bypass graft (CABG) surgery (43%) or received medical treatment after acute coronary syndrome (20%). Age mean in female and male groups was not of significant difference. Medical record documentation revealed a previous acute myocardial infarction (AMI) in 18%, a previous CABG in 8%, and a previous percutaneous coronary intervention (PCI) in 21% of participants. They were taking evidence-based medications, including beta-blockers (78%), lipid-lowering agents (92%), aspirin (88%), clopidogrel (67%), and angiotensin-converting enzyme inhibitors (32%). They were attended to the phase II rehabilitation program 8±3 weeks after an event, and they did not have any previous CR course. Before initiation of rehabilitation program, mean of patients’ weight was 72.38±9.8 kg being more in male than female patients. Mean BMI was 26.19±3.05 Kg/m\(^2\) in all patients and was more in female than male patients. Both WC and hip circumference means were more in female than male patients but WHR was less in females significantly (Table 1).

At the end of supervised CR program, WC, weight and Hip circumference (HC) were significantly reduced (\(P<\)
The reduction of BMI in males was more than females and this change was statistically significant at the end of second month ($P<0.001$). The reduction of WC and WHR was significant totally, whereas there was no change in the female group (Table 2). The weight loss was more prominent in female group and its standard deviation was less. At the end of 12th month, not only measured body indices did not show any significant improvement compared to baseline but also the mean of weight and WC showed insignificant increases in measures. BMI in females increased after 12 months. The results showed the improvements in body indices were decreased during the time (Tables 3 and 4).

**The trend of changes**

**Weight:** The mean weight significantly reduced at the end of the first, second and 6th months of CR participation; however, the most reduction (by averaged $1.37 \pm 2.80$ Kg weight loss and by 2% reduction in BMI) was seen during the first 2 months of program. The least weight loss was seen between third to 6th months ($0.17\pm 2.86$ Kg). Not only the mean of weight at the end of 12th months did not show significant changes compared to baseline, but also this variable increased in female group.

**BMI:** Initially the changes in BMI trended to be decreasing; however, this decrease was more prominent during the first six months and was negligible during the second six months by averaged $0.86\pm 1.68$ Kg/m$^2$. The BMI had increasing trend to achieve the base values in females during the second half of study ($P=0.078$). The most reduction in BMI was seen during the first 3 months that was more prominent in males ($P<0.001$).

**WC:** The changes in WC, similar to BMI, trended to be decreasing; however this decrease was more significant during the first six months, and was not statistically significant in female group during the second half of study course.

**WHR:** This index had significant reduction in all patients after 2, 6 and 12 months ($P<0.001$); however, this improvement was more prominent at the end of supervised CR program. Males showed more reduction in WHR in compared to females ($P<0.001$). Table 4 shows the mean±SD of the changes of body indices at the end of each phase.

**Discussion**

At the initiation of the study, weight mean and WHR

| Table 1. The baseline body indices of patients as mean± SD
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Male</th>
<th>Female</th>
<th>Test</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>74.40±9.4</td>
<td>66.46±8.3</td>
<td>S</td>
<td>72.38±9.8</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>94.4±7.2</td>
<td>96.8±8.4</td>
<td>NS</td>
<td>95.02±7.5</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>95.12±5.5</td>
<td>99.78±8.08</td>
<td>NS</td>
<td>96.32±6.5</td>
</tr>
<tr>
<td>WHR</td>
<td>0.98±0.048</td>
<td>0.97±0.070</td>
<td>S</td>
<td>0.98±0.054</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>26.76±2.81</td>
<td>27.15±3.60</td>
<td>S</td>
<td>26.19±3.05</td>
</tr>
</tbody>
</table>

| Table 2. The mean± SD of body indices and changes at the end of supervised CR program
<table>
<thead>
<tr>
<th>Body index and its change (mean± SD)</th>
<th>Male</th>
<th>Female</th>
<th>Test</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>72.93 ± 9.2 $^{*}(1.43 \pm 8.20)$</td>
<td>65.25±8.2 $^{*}(1.19 \pm 2.8)$</td>
<td>S</td>
<td>70.92±9.6 $^{*}(1.37 \pm 2.80)$</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>91.43±6.8 $^{*}(2.74 \pm 3.2)$</td>
<td>94.78±7.8 $^{*}(1.98 \pm 5.4)$</td>
<td>S</td>
<td>92.35±7.2 $^{*}(2.53 \pm 3.9)$</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>94.81±5.8 $^{*}(0.22 \pm 2.45)$</td>
<td>98.01±6.7 $^{*}(1.76 \pm 6.5)$</td>
<td>S</td>
<td>95.62±6.2 $^{*}(0.63 \pm 4.4)$</td>
</tr>
<tr>
<td>WHR</td>
<td>0.98±0.040 $^{*}(0.02 \pm 2.9)$</td>
<td>0.97±0.079 $^{*}(0.00 \pm 0.04)$</td>
<td>S</td>
<td>0.96±0.052 $^{*}(0.02 \pm 4.47)$</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>25.24±2.6 $^{*}(0.51 \pm 1)$</td>
<td>26.85±3.50 $^{*}(0.49 \pm 1.13)$</td>
<td>S</td>
<td>25.64±2.98 $^{*}(0.51 \pm 1.03)$</td>
</tr>
</tbody>
</table>

*statistically significant

| Table 3. The body indices of patients at the end of 12th month as mean± SD
<table>
<thead>
<tr>
<th>Body index</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>76.28±8.7</td>
<td>71.21±6.4</td>
<td>72.92±8.03</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>95.68±6.8</td>
<td>99.71±7.4</td>
<td>96.91±6.7</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>98.20±3.7</td>
<td>102.00±5.4</td>
<td>96.37±6.5</td>
</tr>
<tr>
<td>WHR</td>
<td>0.94±0.058</td>
<td>0.97±0.070</td>
<td>0.95±0.062</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>25.17±2.4</td>
<td>26.69±2.6</td>
<td>26.05±2.90</td>
</tr>
</tbody>
</table>

Copyright © 2013 by Tabriz University of Medical Sciences

vascular disease and must be treated promptly.35 cm and triglyceride≥2 mmol/lit are at increased risk for BMI is high risk for cardiovascular diseases. It has ≥30 as obese. Furthermore, in people more than 18 years, BMI ≤30 is unanimously accepted as overweight and BMI classifications have been presented for BMI, in Lavie’s study about heart rehabilitation in BMI> 27.8 kg/m2 in 11 patients was more than 1 (WHR≥ 1). In our study WHR in 47.5% of patients (42 males and 14 females), was more than 1 that shows the fat distribution in their body was not balanced. 16.5% of participants were diabetic; WHR in 11 patients was more than 1 (WHR≥ 1). In our study, WC in 24 patients (22.9 %) was less than 100 cm (≤100) and including 8 females and 16 males. Various classifications have been presented for BMI, in Lavie’s study about heart rehabilitation in BMI> 27.8 kg/m2 in females was obese; however, 20 <BMI <25 in ideal, 25 ≤ BMI ≤30 is unanimously accepted as overweight and BMI ≥30 as obese. Furthermore, in people more than 18 years, 25 <BMI is high risk for cardiovascular diseases. It has also been suggested that, people with BMI ≥25, WC ≥90 cm and triglyceride≥2 mmol/lit are at increased risk for vascular disease and must be treated promptly.35

Before rehabilitation, 52% of patients were overweight. After two months, this rate decreased to 42% and obesity from 12% to 10.2%. Our results suggested that the mean reduction of weight and BMI was approximately 2% and was more prominent in overweight patients in contrast to Milani’s study in which the rate was 3% and more frequent in obese patients.36

Similar to the study of Buenmann et al., these changes in males and young people of our study were more frequent than females and old people. Lavie has observed that body composition changes in young people was better than old peoples.3

were higher in males than females but BMI, WC and hip circumference were higher in females. In a study by Rasulinejad et al., baseline BMI in female coronary patients was shown to be more than males.30 According to Mccannel et al., mean weight was more in males than females but the fat percentage was more in females. Mean weight in their study was 73.5 kg and 85.5 kg in females and males respectively. However, in our study, female mean weight was about 66.5 kg and 74.5 kg in females and males respectively; about 10kg less than that of Mccannel’s study.31 Although in our study females were more obese, fat distribution in males was more unsuitable. WHR more than 0.85 in females and more than 1 in males is accompanied by abnormalities in lipoprotein metabolism and insulin-glucose responses.2 WHR more than 0.9 and WC more than 100 cm in males and WHR more than 0.8 and WC more than 90 cm in females have been reported as the risk factors in cardiovascular disease.32,33 In our study WHR, in 47.5% of patients (42 males and 14 females), was more than 1 that shows the fat distribution in their body was not balanced. 16.5% of participants were diabetic; WHR in 11 patients was more than 1 (WHR≥ 1). In our study, WC in 24 patients (22.9 %) was less than 100 cm (≤100) and including 8 females and 16 males. Various classifications have been presented for BMI, in Lavie’s study about heart rehabilitation in BMI> 27.8 kg/m2 in females was obese; however, 20 <BMI <25 in ideal, 25 ≤ BMI ≤30 is unanimously accepted as overweight and BMI ≥30 as obese. Furthermore, in people more than 18 years, 25 <BMI is high risk for cardiovascular diseases. It has also been suggested that, people with BMI ≥25, WC ≥90 cm and triglyceride≥2 mmol/lit are at increased risk for vascular disease and must be treated promptly.35

Before rehabilitation, 52% of patients were overweight. After two months, this rate decreased to 42% and obesity from 12% to 10.2%. Our results suggested that the mean reduction of weight and BMI was approximately 2% and was more prominent in overweight patients in contrast to Milani’s study in which the rate was 3% and more frequent in obese patients.36

Similar to the study of Buenmann et al., these changes in males and young people of our study were more frequent than females and old people. Lavie has observed that body composition changes in young people was better than old peoples.3

In 1997, Lavie in another study on 588 coronary patients after three months supervised CR, showed a 2% reduction in BMI which even reached to 5% in obese patients.37 It was then strongly suggested that supervised CR program could modify risk profile especially in more obese patients. Attention to this note is very important that even very tiny changes in body competition can affect other cardiac risk factors such as hypertension, hyperglycemia and blood lipides significantly.10-14 Also 1% improvement in body indices up to 12% has positive effect on weight adjusted peak aerobic capacity.2 Results of rehabilitation and patient responses have been reported to be the same in surveyed programs and programs without surveillance; in order to decrease cost and resources, patients can be rehabilitated in their homes.38,39 In another study, patients in two separate groups took rehabilitation at home and hospital, rehabilitation in home had a better progress in health-related quality of life than group who had been rehabilitated in hospital. Later, it was suggested that low risk patients with coroner surgery can have better rehabilitation at home.40 In contrast to the study of Ilrazed et al.,41 in our study, most of proper changes from rehabilitation for patients occurred during the first six months, especially in the first two months; however, they were very low in the second half of the study. When patients were under the CR in their home and in this time return of body composition indices to baseline was observed. However, no studies have investigated the effect of home-based CR among different groups of patient such as elderly42, diabetic, obese and other subgroups of patients with coronary heart disease in a long-term follow-up. The alternative note is that in our study patient mean age was 53.8±3.8.01 (77.1% males) our population was more younger than the same studies in rehabilitation such as Milani’s study (mean= 63.1±11; 80% male) or Brochu’s study (mean=61.2±12.2; 72% male) which means that cardiovascular disease prevalence in young people is increasing in our country. Our population was the same as other studies regarding sex distribution which is due to high prevalence in males10,14 and the fact that males also come to rehabilitation centers which should be considered in in the future studies.

A few studies have demonstrated that significant weight loss can be achieved but at high cost and effort,29,43,44 however these questions remain: are patients willing to high energy expenditure exercise? is there the long term

| Table 4. The mean±SD of the reductions of body indices at the end of each phase |
|---------------------------------|----------------|----------------|----------------|----------------|
| **Body index**                  | **First month** | **Second month** | **6th month**  | **12th month** |
| Weight (kg)                     | 0.80±1.5*      | 1.37±2.80*      | 1.57±4.1       | -0.16±4.6      |
| WC (cm)                         | 1.75±3.3*      | 2.53±3.9        | 2.22±6.2       | 0.34±5.4       |
| Hip circumference (cm)          | -2.21±5.4*     | 0.63±0.4        | -1.16±6.1      | -1.27±4.1      |
| WHR                             | 0.019±0.078*   | 0.020±0.044*    | 0.030±0.063*   | 0.023±0.053*   |
| BMI (kg/m²)                     | 0.30±0.56*     | 0.51±1.03*      | 0.55±1.52*     | 0.086±1.68*    |

*Statistically significant
weight maintenance in the CR patients follow up? It should be emphasized that a less successful reduction in body indices does not undermine the beneficial effects of exercise training\textsuperscript{45}, as the Heijden’s study showed no significant changes were observed in any parameter in lean participants except a small increase in lean body mass. However, in their study, they found a controlled aerobic exercise program, without weight loss, reduced hepatic and visceral fat accumulation, and decreased insulin resistance in obese adolescents.\textsuperscript{46}

From a public health perspective, few patients seem to participate in rehabilitation programs after coronary interventions.\textsuperscript{47} so, exercise should be encouraged even if its weight loss effect is small, it can produce physiological\textsuperscript{48} and psychological benefits\textsuperscript{49} in the management of obesity, including prevention of weight gain. Another subject that should be remembered is that education is very low in our society now and media and different organization should pay attention to public education at different social levels. Physicians and scientific staff beside people with establishing charities and nongovernmental organizations should pay attention to the education as the best way for prevention.

**Study limitation**

1. Lack of control group.
2. The less number of female participants in comparison with males.
3. Lack of direct controlling on the patient diets.
4. The psychological control programs were discontinued and were not maintained in unsupervised course.

**Acknowledgments**

The authors wish to express their gratitude to all personals in rehabilitation center and especially to Dr. Farshad Farzadfar for his helpful viewpoints.

**Ethical issues:** All patients gave written informed consents and the study was approved by our local Ethics Committee.

**Conflict of interests:** The authors declare no conflicts of interest.

**References**


Altering in Circulating Adhesion Molecules in Acute Myocardial Infarction before and after Thrombolysis with Streptokinase

Hossein Saidi1, Maryam Vakilian2, Gholam Hosein Noori3, Hamed-Basir Ghafoori3*, Niloofar Abazarian3

1Department of Emergency, Rasul-Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
2Department of Emergency, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
3Department of Emergency, 7th Tir Martyrs Hospital, Iran University of Medical Sciences, Tehran, Iran

A B S T R A C T

Introduction: The role of adhesion molecules in the development and progression of coronary atherosclerosis is inevitable. It is not clear yet whether these molecules increase or decrease in level after thrombolytic therapy. This study was designed to compare concentrations of soluble forms of adhesion molecules in patients with acute myocardial infarction before and after reperfusion by thrombolysis with streptokinase (SK).

Methods: In this study, in 40 patients with acute myocardial infarction who were admitted in our Emergency Department undergoing thrombolysis with SK, plasma concentrations of six adhesion molecules [soluble E-selectin, P-selectin, L-selectin, VCAM-1 and platelet endothelial cell adhesion molecule-1 (PECAM-1)] were measured by enzyme linked immunosorbent assay (ELISA), before and 3 hours after intervention.

Results: While soluble E-selectin and PECAM-1 concentrations did not differ within the 3 hours after interventions (P>0.05), the level of P-selectin, L-selectin, ICAM-1, VCAM-1 were significantly reduced after thrombolysis with SK (P<0.05).

Conclusion: Adhesion molecules which mediate the interactions in leukocyte endothelium vary in levels after reperfusion with SK. It was shown that 4 out of 6 adhesion molecules significantly reduced after thrombolysis with SK.

Keywords: Adhesion Molecules
Myocardial Infarction
Streptokinase

Introduction
Cardiovascular disease is the most prevalent and major cause of death worldwide and burdens huge costs on the health care system.1-4 Mortality due to Ischemic Heart Diseases (IHD) decreases by early treatment and long term survival in patients increases subsequently.5 Coronary artery reperfusion is accepted as a method to achieve reduction in size of myocardial infarction.6 Thrombolysis technique with streptokinase (SK) is a confirmed method for reopening of an occluded vessel in patients with acute myocardial infarction.6 Cellular adhesion molecules (such as: P-selectin, E-selectin, L-selectin, VCAM-1, PECAM-1, ICAM-1) have an important role to play in progression of atherosclerotic plaque.7,8

Besides, those mononuclear cells which are responsible for release of matrix metalloproteinases are activated by adhesion molecules leading to plaque rupture and initiation of acute coronary syndrome. Consequently, it can be concluded that an intervention leadings to decline in adhesion molecules level could postpone the process of atherosclerotic plaque formation or rupture. On the other hand, it has been shown that patients with high levels of these adhesion molecules have poor prognosis in future.9 Some studies imply that adhesion molecules would decrease10 or increase11 in level, after reperfusion with different types of thrombolytic drugs.

Here in our hospitals in Iran, the only cost-benefit and available thrombolytic drug for reperfusion of coronary arteries in patients with acute myocardial infarction is intravenous thrombolysis with streptokinase (SK), 1.5 million IU over 60 minutes. The aim of this study was to compare concentrations of six soluble forms of adhesion molecules in patients with acute myocardial infarction before and 3 hour after attempted reperfusion by thrombolysis with streptokinase (SK).

Materials and Methods
From January to June 2011, 40 patients admitted to the emergency department of Rasul-Akram Hospital with the diagnosis of acute myocardial infarction (based on a history of typical chest pain and electrocardiographic changes) and with no contraindication of streptokinase administration were included in this study. The patients were selected using a convenient sampling method.

*Corresponding author: Hamed-Basir Ghafoori, E-mail: hbgssl@yahoo.com

Copyright © 2013 by Tabriz University of Medical Sciences
Blood samples from all 40 patients were taken prior to thrombolysis with SK, and then 3 hours after treatment. Plasma samples were extracted by centrifugation at 4°C, at 3000 rpm for 10 min. Samples were later stored at −80°C before measurement of plasma levels of the soluble forms of sE-selectin, sL-selectin, sP-selectin, sICAM-1, sVCAM-1, and sPECAM-1 using commercially available enzyme-linked immunosorbent assays (ELISAs). Results were presented as mean±standard deviation (SD) for serum levels of adhesion molecules before and after thrombolysis with SK. The statistical test used in this study was Paired-Sample t-Test. A P ≤ 0.05 was considered statistically significant. The SPSS 17 (SPSS Inc., Chicago, Illinois, USA) statistical software package was used for all calculations. Our study was approved by the ethics committee of Iran University of Medical Sciences (IUMS). Informed written consent was obtained from each patient or his or her guardian.

Results
All 40 patients who were included in the study were in the age range of 46 to 83 years old (65.90 ± 10.6 years). There were 30 male patients (75%) and 10 female patients (25%). The levels of 6 adhesion molecules were measured before and 3 hours after thrombolysis with streptokinase (1.5 million IU over 60 min). The results have been presented in Table 1.

Discussion
Adhesion molecules are considered to be indicators of activation of leukocytes, platelets, and endothelial cells. It has been shown that in patients with acute coronary syndrome, these molecules would increase in atherosclerotic plaque rupturing, ischemic, and reperfused areas. We found significantly decreased serum levels for P-Selectin after SK reperfusion. The concentration of L-Selectin was also reduced by 3 hours after SK lysis. VCAM-1 plays an important role in atherosclerosis plaque progression and even rupture of the plaque leading to thrombosis. VCAM-1 is related to the aggregation of leukocytes, on the other hand, adherence of leukocytes to vascular endothelial cells causes endothelium dysfunction. It has also been shown that plasma levels of VCAM-1 were significantly decreased. After thrombolysis in patient with acute myocardial ischemia, it has been shown that both soluble ICAM-1 and PECAM-1 increase in levels within the initial hours after reperfusion.

In the present study, we found PECAM-1 to be stable after reperfusion, but significant decline in ICAM-1 level was observed. Endothelial cells are the only source of E-selectin expression and an increase in E-selectin could reveal endothelial activity. Some studies have shown that this molecule rises in patients with myocardial ischemia and hypertension. No significant differences were observed in the concentration of E-selectin expression and an increase in E-selectin could reveal endothelial activity. Some studies have shown that this molecule rises in patients with myocardial ischemia and hypertension.

In other separated studies by Postadzhiyan, Squadrito, Parise, and Zeitler, it has been shown that adhesion molecules would decrease in levels after thrombolytic therapy. These findings have a relative conformity to our findings.

Conclusion
It seems that adhesion molecules vary in levels following reperfusion therapy with streptokinase. Overall, 4 out of 6 adhesion molecules showed significant decline in levels after reperfusion by SK thrombolytic therapy in acute myocardial infarction. The clinical importance of these results should be investigated in further studies. Besides, these results indicate that thrombolysis with streptokinase would decrease adhesion molecule levels and may lead to decline in atherosclerosis progress and recurrence of myocardial infarction.

Table 1. Serum levels of soluble adhesion molecules

<table>
<thead>
<tr>
<th></th>
<th>P-Selectin (ng/ml)</th>
<th>L-Selectin (ng/ml)</th>
<th>VCAM-1 (ng/ml)</th>
<th>ICAM-1 (ng/ml)</th>
<th>E-Selectin (ng/ml)</th>
<th>PECAM-1 (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before reperfusion</td>
<td>127.15 ± 22.84</td>
<td>479.7 ± 148.91</td>
<td>1012.75 ± 402.9</td>
<td>446.35 ± 106.02</td>
<td>87.71 ± 6.13</td>
<td>67.95 ± 15.29</td>
</tr>
<tr>
<td>Three hours after reperfusion with SK</td>
<td>108 ± 16.43</td>
<td>389.6 ± 106.24</td>
<td>858 ± 322.9</td>
<td>348.45 ± 75.6</td>
<td>101.32 ± 7.95</td>
<td>67.1 ± 17.81</td>
</tr>
<tr>
<td>P</td>
<td>0.002</td>
<td>0.006</td>
<td>0.002</td>
<td>0.0001</td>
<td>0.117</td>
<td>0.681</td>
</tr>
</tbody>
</table>
Limitations
Blood samples of the patients were taken in only two time intervals; once before thrombolysis with SK, and then 3 hours after SK administration due to funding shortage.

Ethical issues: This study was reviewed and confirmed by the ethics committee of Iran University of Medical Sciences.

Conflict of interests: The authors declare no conflicts of interest.

References
Introduction:
Lactic acid is a product of anaerobic glycolysis in favorable metabolic conditions can be changed to pyruvate. Although all tissues can consume or produce lactic acid, liver is principal tissue for consumption of lactic acid overproduced by other tissues. Lactic acidosis is a common finding in critically ill patients. High initial blood level and persistently increasing high lactate levels have been correlated with poor outcome.\(^{1}\)
Mortality in groups whose lactate levels have not been normalized in 24, 48 and 72 hr was 10%, 24% and 67% in addition there is not any difference between arterial and venous level and mixed venous blood for evaluation in these circumstances\(^{2}\) in other study serial lactate level monitoring has priority in compared to one sample for prognosis prediction.\(^ {3}\)
Normal lactate level in normal unstressed patient is \(1 \pm 0.5\) mmol/L.\(^ {4}\) this concentration ratio in arterial level depends on both production and conversion in various organ and should be maintained below 2 mmol/L.\(^ {5}\)  
In this study 31 patients under cardiac operation mainly by cardiopulmonary bypass assessed for complications and their arterial lactate changes in first day after operation to finding about the lactate level changes during and after a major heart operation and make impression on importance of these measures.

Method and Material
31 patients with congenital malformation selected for heart surgery including of 18 males and 13 females, selected for correcting operations in Madani heart center. Their physical characters like as height, weight, and types of their cardiac anomalies. Our exclusion criteria were defined as hyper metabolism conditions like diabetes, sepsis, active infection and preexisting metabolic diseases can be cleared by examination and laboratory results. They divided to simple malformation including of atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and complex type of multiple major cardiac structural defects including of cyanotic or acyanotic defects. Laboratory findings before operation and during operation were collected and their vital signs mean arterial blood pressure and central venous pressure were recorded. Arterial lactate level was measured regularly in 3 samples at first minutes of operation or before bypassing, at first hour and second hours or the ending of operation in cases with shorter operation time these samples were taken from arterial line and these sampling were repeated four times at defined intervals after operation up to 24 hours(3rd, 6, 12, 24th hour), levels lower than 1.5 mmol/lit considered normal and values between 1.5 to 4 mmol/L was high and above 4 mmol/L was considered as very high.

*Corresponding author: Majid Malaki, E-mail: madjidmalaki@gmail.com

Copyright © 2013 by Tabriz University of Medical Sciences
Anesthesia was started with 5 mg/kg of intramuscular ketamine. The intravenous anesthesia was performed with 1 mg/kg of ketamine, 1.5 mic/kg of fentanyl and 0.1 mg/kg of pancuronium. Patients lung were ventilated with oxygen, air and isoflurane and ventilation was adjusted to maintain normocarbia. The maintenance of the general anesthesia was achieved with an infusion of 5 micro/kg/h of fentanyl and isoflurane in 0% to 1% inspiratory concentration.

Noninvasive monitoring consisting of electrocardiogram, pulse oximetry and measurement of inspiratory and expiratory gas concentrations were used as well as invasive monitoring of central venous and arterial pressure was performed.

The operation was performed under low-flow hypothermic cardiopulmonary bypass (CPB), a median sternotomy was made and after systemic heparinization (activated coagulation time> 480s)

Data were collected through forms were filled out by physician the results have been drawn and expressed to percent and mean and relations between quantity material extracted by T-independent test and non quantity data processed to chi-square in SPSS software version 11.5. P value less than 0.01 was considered significantly.

Results
31 patients entered to this study mean age (Minimum, Maximum) 5.74 years (0.7-25 years), with different forms of congenital heart malformations.

Arterial lactate level was high in 2 out of 31 in first sample in operation room before bypassing the increased level of lactate in our cases occurred in 25 out of 30 patients (14 cases in very high and other 11 cases were in high level group) in first hour sampling after operation and 25 cases (6 cases very high and 19 cases had high lactate level) in second hour or near the ending of operating (Figure 1).

These arterial lactate measures increment during operation were changed in pattern after operation and number of cases with abnormal lactate level decreased slowly at 3rd, 6th, 12th and 24th hour after operation (Figure 2).

Arterial lactate level changes were compared between simple and complex repaired surgery. In simple form 6 out of 8 cases (75%) had high and very high lactate level at the end of operation while in complex cardiac repair this rate was 19 out of 23 cases (83%) (Figure 3). After operation serum lactate level by arterial line were measured at 3rd hour post operation 2 out of 8 cases (25%) with simple repaired cardiac malformation had abnormal serum lactate levels while this ratio in group with simple cardiac malformation was not changed up to 24th hour as the end point of our observation but very high serum lactate level (more than 4 mmol/l) was not seen in this group while in complex repaired group at 3rd and 6th hours after operation 10 out of 23 cases (43%) with complex repaired malformation had high and very high serum lactate level at 12th hour 6 out of 23 (26%) and at the 24th hour 3 out of 23 cases (13%) had abnormal serum lactate level (Figure 4). One patient out of 31 patients had persistent high serum lactate levels over than 4 mmol/l up to 24th hour after operation who passed away.

Bypass time is prolonged in complex cardiac defect repair significantly \((P=0.03)\) 133±47 vs 90±34 minutes, clamp time was not differed significantly \((P=0.08)\) between complex and simple repair 83±33 vs 56±33 minutes.

In patients with simple cardiac defects after operation most patient have normal lactate level in 6th hours after operation (6 out of 8) and there is not any case with very high lactate level after 6th hours after operation in simple form repaired malformation.

Discussion
Lactate elevation mechanism as cardinal finding of sepsis and septic shock is different in sepsis it backs to hyper metabolism while in septic shock it is due to tissue hypoxia. Normal lactate level in normal unstressed patient is 1±0.5 mmol / L\(^4\) Lactic acidosis is common in critically ill patients can effect on outcome. Persistently elevated is attributed with poor out come. High blood lactate levels may happen in critically patients due to shock and sepsis because of many reasons such as increased catecholamine and glucose flux from hypoperfusion or hypoxia.\(^1\)

In one study high initial level and elevated 24-hour lactate level was associated with mortality but this is not true for
Lactate after heart surgery

Figure 3. Arterial serum lactate level changes during operation in simple and complex cardiac malformations.

Figure 4. Arterial serum lactate level changes at 3rd, 6th, 12th and 24th after operation in both simple and complex cardiac malformations.

base excess level. Mortality in groups that have not been normalized in 24, 48 and 72 hr was 10%, 24% and 67% in another word, there is a good correlation between arterial and venous level and mixed venous blood as well as serially monitoring in another study peak arterial quantity has prognostic value. Lactate levels may prognostically decrease over time due to decreased production or increased clearance or both. Arterial lactate level depends on production and conversion in various organ and should be maintained below 2 mmol/L. Lactate above 7.8 carried with prediction of mortality in 80% in other study lactate in admission > 4.5 mmol was the best predictor of major adverse events.

In our study arterial lactate level between 1.5 to 4 mmol/L was moderate and values above 4mmol/L considered as high. Arterial lactate level without regarding to operating time include of clamp time and bypass time usually returns to normal at 12th hour after operation. Highly serial persistent arterial lactate level up to 24 hours was associated with mortality and prognosis during post operation period. Most patients had high arterial lactate level in mid operation but start to decrement in the end of operation and will be normalized in most up to 24 hours after operation. One patient with persistent high lactate level >4 mmol/L until 24 hours died, it means that high lactate level>4 mmol/L improve after operation in serial measurements if not increases mortality at 12th hour was associated with 50% mortality (1 out of 2), at 24th hours was associated with 100% mortality (1 out of 1).

In addition prolonged operation time that can be met in complex type repairing is associated with high incidence of prominent raised lactate level up to 12 hours post operation.

Conclusion
In spite of persistent very high arterial lactate levels (above 4 mmol/L) up to 24 hours post operation is uncommon as low as one out of 31 cases but it is associated with high mortality rate. In fact it shows serial lactate measurement can be more predictable for our management efficacy.

Ethical issues: This study was reviewed and confirmed by the ethics committee of Tabriz University of Medical Sciences.

Conflict of interests: The authors declare no conflicts of interest.

References
Warming Endotracheal Tube in Blind Nasotracheal Intubation throughout Maxillofacial Surgeries

Hamzeh Hosseinzadeh1, Koroush Taheri Talesh2, Samad EJ Golzari3, Hossein Gholizadeh4, Alireza Lotfi4, Parisa Hosseinzadeh4

1Department of Anesthesiology, Tabriz University of Medical Sciences, Tabriz, Iran
2Department of Oral and Maxillofacial, Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran
3Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
4Department of ENT, Tabriz University of Medical Sciences, Tabriz, Iran
5Tabriz University of Medical Sciences, Tabriz, Iran

ARTICLE INFO

Article Type: Original Article

Article History:
Received: 7 September 2013
Accepted: 5 November 2013

Keywords:
Blind Intubation
Warming
Endotracheal Tube
Oral and Maxillofacial Surgery
Anesthesia

ABSTRACT

Introduction: Blind nasotracheal intubation is an intubation method without observation of glottis that is used when the orotracheal intubation is difficult or impossible. One of the methods to minimize trauma to the nasal cavity is to soften the endotracheal tube through warming. Our aim in this study was to evaluate endotracheal intubation using endotracheal tubes softened by hot water at 50 °C and to compare the patients in terms of success rate and complications.

Methods: 60 patients with ASA Class I and II scheduled to undergo elective jaw and mouth surgeries under general anesthesia were recruited.

Results: Success rate for Blind nasotracheal intubation in the control group was 70% vs. 83.3% in the study group. Although the success rate in the study group was higher than the control group, this difference was not statistically significant. The most frequent position of nasotracheal intubation tube was tracheal followed by esophageal and anterior positions, respectively.

Conclusion: In conclusion, our study showed that using an endotracheal tube softened by warm water could reduce the incidence and severity of epistaxis during blind nasotracheal intubation; however it could not facilitate blind nasotracheal intubation.
and degree. Method of warming and its benefits have been little studied. Endotracheal tube in order to BNTI Is placed in warm water at a temperature of approximately 50 °C for almost 20 minutes, and so it is used for intubation. According to previous studies, the warming endotracheal tube is a good practice because it increases the flexibility of the tube when passes through the high curvature of nasopharynx, and the result will be less trauma that is important in patients with pathologies that are prone to injury and epistaxis. Elsewhere mentioned that warming is an effective method and fuss-free that reduce nasal trauma during intubation and does not create additional problems for patient. Moreover, this method requires no additional equipment and also avoids unwanted systemic effects that are endemic for topical agents.14

Materials and Methods
In a double-blind prospective clinical trial and after approval of the regional ethics committee, 60 patients with ASA class I and II who were scheduled to undergo elective maxillofacial surgeries in Tabriz Imam Reza Hospital in 1391 were recruited. After obtaining informed written consents, all patients were randomly assigned to one of the two groups are as follows: Group C (control): Blind nasotracheal intubation without warming the tracheal tube and Group W (Warmed): Blind nasotracheal intubation performed using the warmed and softened tube by warm 50 °C water for 5 minutes. Patients in both groups were premedicated using 0.02 mg/kg, fentanyl 2 mg/kg, and vasoconstrictor phenylephrine drops (4 drops in each nostril). Induction of anesthesia was performed with propofol 2 mg/kg and cisatracurium 0.15 mg/kg. Later, anesthesia was maintained isoflurane and after adequate anesthesia depth was achieved (BIS less than 50) intubation was attempted. Exclusion criteria from the study were: limited mouth opening (less than 35 mm), Mallampati III and above, thyromental distance of less than 65 mm, limitation of neck movement, sternomental distance of less than 12.5 cm, patients with a history of recurrent epistaxis, and patients with coagulation disorders or skull base fracture. Inclusion criteria were: patient willingness, ASA physical class I or II, age range of 15 to 65 years and elective maxillofacial surgeries requiring nasal intubation. Time of intubation, number of attempts and complications including epistaxis, laryngospasm, hoarseness, sore throat and hemodynamic changes in heart rate (HR), mean blood pressure (MBP) and pulse oximetry (SaO2) were recorded. All demographic information including age, sex, weight, ASA, history of surgery, type of surgery and the morbidity were noted. SPSS 16 (SPSS Inc., Chicago, IL, USA) was used for analysis of the data. Descriptive statistics (frequency, percentage, mean and standard deviation) were used to describe the data. T-test was used for comparison of the intubation time and success rate, HR, MBP and SaO2. Chi-square test was used to compare the number of attempts and complications.

Intubation procedure
A pad was placed under patient head and neuter head position was maintained. A conventional nasal tube was selected for all patients while it was warmed at 50 °C water for patients in Group W. Endotracheal tube size was selected based on the type and specific circumstances of each patient (the size which was suitable for oral intubation). The tube was inserted until one of the following situations occurred:
I= tracheal position: the target position: Endotracheal tube enters the trachea which is confirmed with breath sounds auscultation and capnography and after approval, the cuff is filled and tube is secured in place.
II= anterior position: the endotracheal tube cannot move forward and is stopped. When applying pressure to the tracheal tube, tube compression effect to the larynx can be seen from the outside. Looking at the neck, anterior movement of the larynx can be seen. In this mode the tube is pulled back and reinsert until it moves into the trachea while head and neck are in mild flexion position. III and IV = left or right positions: while inserting the trachea tube, it enters the pyriform sinus and stops. Later, the tube is pulled back and tube direction is changed towards the midline and reinserted.
V= esophagus position which is approved with the absence of breath sounds and capnography.

Results
No significant difference could be observed between both groups regarding demographic characteristics. Table 1 summarizes the comparison of pre-anesthetic evaluations in both groups. Table 2 summarizes the comparison of intubation parameters in both groups. Table 3 summarizes the complication between both groups. As can be seen, no significant difference existed between both groups in this regards. Table 4 summarizes the comparison of hemodynamic changes between both groups. As can be seen, no significant difference existed between both groups in this regards.

Discussion and conclusion
Blind nasotracheal intubation technique is particularly valuable in and used in emergency scenarios as well as elective conditions. It clinically is a method of intubation without observation of glottis9 that is used when the orotracheal intubation is difficult or impossible.10 Blind nasotracheal intubation is recommended in difficult airway algorithm.11 The success rate of this method is less and its complications increased.12 This method is the most common intubating method in difficult intubation conditions that anesthesiologists use.13 Approaches that have been adapted to minimize nasotracheal complications include the use of fiber-optics, lubricant gels, vasoconstrictors, muscle relaxants, rotational movement of the tube10, filling tube cuff in pharyngeal bed11 and
Warming nasotracheal tube

Table 1. Comparison of pre-anesthetic evaluations in both groups

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. deviation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternomental Distance (Cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>17.26</td>
<td>± 1.9134</td>
<td>0.051</td>
</tr>
<tr>
<td>Warming Group</td>
<td>18.97</td>
<td>± 1.2524</td>
<td></td>
</tr>
<tr>
<td>Thyromental Distance (Cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>8.13</td>
<td>± 1.026</td>
<td>0.903</td>
</tr>
<tr>
<td>Warming Group</td>
<td>8.1</td>
<td>± 0.875</td>
<td></td>
</tr>
<tr>
<td>Mouth opening rate (Mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>44.33</td>
<td>± 6.418</td>
<td>0.067</td>
</tr>
<tr>
<td>Warming Group</td>
<td>39.93</td>
<td>± 11.117</td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>_ _</td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Warming Group</td>
<td>_ _</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>71.7</td>
<td>±13.44</td>
<td>0.153</td>
</tr>
<tr>
<td>Warming Group</td>
<td>69.33</td>
<td>± 15.14</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>31.1</td>
<td>±10.77</td>
<td>0.684</td>
</tr>
<tr>
<td>Warming Group</td>
<td>29.93</td>
<td>±11.28</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>_ _</td>
<td></td>
<td>0.145</td>
</tr>
<tr>
<td>Warming Group</td>
<td>_ _</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Comparison of intubation parameters in both groups

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. deviation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of intubation (Sec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>72.9</td>
<td>± 53.38</td>
<td>0.099</td>
</tr>
<tr>
<td>Warming Group</td>
<td>48.53</td>
<td>± 59.02</td>
<td></td>
</tr>
<tr>
<td>Attempts intubation (Number)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>2.63</td>
<td>± 1.159</td>
<td>0.153</td>
</tr>
<tr>
<td>Warming Group</td>
<td>2.20</td>
<td>± 1.157</td>
<td></td>
</tr>
<tr>
<td>Success rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control Group</td>
<td>70%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warming Group</td>
<td>83.3%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Comparison of intubation complications

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoarseness (Number)</td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Control group</td>
<td>1 (3.3%)</td>
<td>29 (96.6%)</td>
<td></td>
</tr>
<tr>
<td>Warming Group</td>
<td>1 (3.3%)</td>
<td>29 (96.6%)</td>
<td></td>
</tr>
<tr>
<td>Sore throat (Number)</td>
<td></td>
<td></td>
<td>0.43</td>
</tr>
<tr>
<td>Control Group</td>
<td>14 (46.6%)</td>
<td>16 (53.3%)</td>
<td></td>
</tr>
<tr>
<td>Warming Group</td>
<td>10 (33.3%)</td>
<td>20 (66.6%)</td>
<td></td>
</tr>
<tr>
<td>Laryngospasm (Number)</td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Control Group</td>
<td>0 (0%)</td>
<td>30 (100%)</td>
<td></td>
</tr>
<tr>
<td>Warming Group</td>
<td>1 (3.3%)</td>
<td>29 (96.6%)</td>
<td></td>
</tr>
</tbody>
</table>
the optimal position of the head and neck.\textsuperscript{14} Depoix and colleagues showed that in 13.2\% of their cases the tube did not pass nostril via nasal intubation and in 2.3\% of cases nasal intubation was not possible and patients were intubated orally.\textsuperscript{9} In our study, we did not observe any cases in which tube did not pass through the nostril and oral intubation was not required in any case. One of the reasons was warming endotracheal tube that increases the flexibility of the tube when passing through the high curvature of nasopharynx, and then the result will be fewer traumas and less resistance to entry of endotracheal tube. Using enough lubricant with phenylephrine as a vasoconstrictor more facilitates passage of the tube from nose curvature. Blind nasotracheal intubation success rate in the control group was 70\% and in the study group was 83.3\%. Although the success rate in the study group was higher than the control group, this difference was not statistically significant. This success rate was measured in three and less than three attempts and intubation failure was considered for more than three times. Because our patients were under general anesthesia and received muscle relaxants, after three attempts, the patient was intubated with laryngoscopy under direct visualization. In a study, blind nasal intubation success rate of 100\% with using relaxants and 70\% without the use of muscle relaxants was reported\textsuperscript{12}; the results of this study are inconsistent with previous studies showing 13.2\% rate of failure.\textsuperscript{16} Failure in nasal intubation in our study despite using relaxants might have been due to the following facts: Firstly, we only did three attempts the previous studies had performed it up to 5 times. Secondly, all patients in our study were patients undergoing oral and maxillofacial surgery in a high percentage of difficult intubation and in 30\% of cases that nasal intubation had failed, intubation under direct vision was difficult as well. Cheema \textit{et al.} tried up to 5 attempts in their study and used succinylcholine; yet, they reported no cases of hypoxia that is consistent with our study.\textsuperscript{15} Most frequent tube position was esophageal followed by tracheal and anterior positions respectively. Filling tube cuff in pharynx bed has been reported to change esophageal position to the tracheal situation\textsuperscript{17} which was confirmed in our study as well. According to Thong \textit{et al.} and Ayla \textit{et al.}, warming endotracheal tube increases kinking risk for endotracheal PVC tubes.\textsuperscript{14,18,19} However, due to its advantages such as non-traumatized nose and increased ease of nasal passage, warming the tube should not be overlooked. Lu and colleagues showed that warming the tracheal tube with warm water reduced the rate and severity of epistaxis during nasotracheal intubation.\textsuperscript{20} He reported that epistaxis rate was 76.7\% in the group without softening endotracheal tube and 43.6\% in the group with softened endotracheal tube by warm water. In our study, the epistaxis in the control and study groups were 66.3\% and 33.3\% respectively. However, the severity of epistaxis in the study group was significantly lower than control group. Our study confirms the results of Lu and colleagues. Lixy \textit{et al.} compared the hemodynamic changes following nasotracheal intubation using various methods such as: glidescop, fiberoptic and Macintosh blade. In all three cases after anesthesia induction, a significant decrease in BP and RPP (Rate Product Pressure) were observed in all groups. But there was no significant change in HR. On the other hand a significant increase in MBP, RPP and DBP were observed in all groups during intubation, the increase was greater from others in fiber optics.\textsuperscript{21} In our study, the hemodynamic changes after induction of anesthesia, and after intubation, were statistically significant. Despite the lack of laryngoscopy and considering that the rate of changes was less than 20\% of baseline in our study, these changes were insignificant.

\textbf{Conclusion}

In conclusion, our study showed that using an endotracheal tube softened by warm water could reduce the incidence and severity of epistaxis during the act of blind nasotracheal intubation. However, it fails to facilitate blind nasotracheal intubation.

\textbf{Ethical issues:} This study was reviewed and confirmed by the ethics committee of Tabriz University of Medical Sciences.

\textbf{Conflict of interests:} The authors declare no conflicts of interest.

\textbf{Reference}

Warming nasotracheal tube

Procedures use by French anesthetists in cases of difficult intubation and the impact of a conference of experts. Ann Anesth Reanim 1999; 18:23-31
Molecular Diagnosis of Bacterial Infective Endocarditis in Tabriz, Azerbaijan

Reza Ghotaslou1*, Behnaz Salahi Eshlaghi2, Fatemeh Yeganeh1, Alireza Yaghoubi3

1Department of Microbiology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
2Razi Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
3Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

ABSTRACT

Introduction: The aim of this study was to analyze a PCR based approach for detection of infective endocarditis in Azerbaijan.

Methods: Ten aortic valves, 8 mitral valves and 2 tricuspid valves, were analyzed for the presence of bacterial infective endocarditis using Gram staining, culture and PCR methods.

Results: Of the 20 valves, 5 and 4 cases were positive by Gram staining and culture assay, respectively. Bacterial DNA was positive in 12 of the 20 valves (60%) by broad-spectrum PCR. Direct sequencing for species identification was possible in 10 cases.

Conclusion: PCR and direct molecular identification of the etiological agents responsible for infective endocarditis may enable specific treatment to begin at an earlier phase of the disease.

Introduction

Infective endocarditis (IE) is an important disease because of its high morbidity and mortality if untreated or not treated aggressively. Incidence of IE is between 1.7 to 6.2 cases per 100000 in the general population. Since, recurrent endocarditis is an ominous complication; the identification of causative agents could affect operative outcomes.1 The diagnosis of IE remains challenging and nowadays, diagnosis of IE is based on the Duke criteria, principally positive blood culture and abnormal echocardiography.2 The critical diagnostic finding is bacteremia, but blood cultures remain negative up to 30% of suspected IE patients despite the use of appropriate laboratory techniques.3 Sterile blood culture may be caused by slow growing or non-cultivable microbes, or previous antibiotic therapy.4 Recent advances in molecular assays, provides a significant improvement in detection of IE.5 In this research, we applied a PCR based approach and direct sequencing for detection of IE.

Materials and Methods

Blood cultures (Darvash, Iran) were incubated at 37 °C for at least 7 days. In case of growth, solutions were subcultured on Columbia agar (Merck, German), and on Brucella agar (Merck, German), both supplemented with 5% sheep blood, and incubation was done at 37 °C for 72h. Culture negative endocarditis was present when no microorganisms could be identified in serial blood cultures or valvular tissue cultures. The heart valves were processed aseptically under a laminar flow unit. Then, portions of the valve tissue were ground with a mortar and pestle and cultured on mediums, and were incubated for 2 to 3 days. In addition, a piece of valve tissue was inoculated into Brain Heart Infusion and Thioglycolate mediums and incubated for 10 days. Finally, isolated colonies stained with Gram, and were identified according to standard methods.6 DNA was extracted from the tissues valves as previously described.4 For each specimen, we used universal bacterial primers targeting conserved sequences at 16SrRNA bacterial gene, as described previously.4,7 Finally, the amplicons were sent for direct sequencing.

Results

From 2009 to 2012, 20 patients with IE (14 males and 6 females; mean age 56 years) were studied. Ten patients had the aortic valve IE, 8 and 2 patients suffered from IE of the mitral valves and tricuspid valves, respectively. The causes of operation were progressive infection despite drug treatment, infectious embolism, or increasing heart failure. The infected valves were native in 14 (70%) and prosthetic in 6 (30%) of patients. Twenty cardiac valves were analyzed for the presence of IE by Gram staining, culture and PCR methods. Before surgery, the blood culture for 2 of 20 patients was positive. For 3 patients, the single isolation of coagulase negative staphylococci was contamination. The isolated microorganisms were Staphylococcus aureus.
and *Pseudomonas aeruginosa*. Culture and molecular results were analyzed with respect to the patients’ clinical background and the Duke Criteria.

Of the 20 valves, 5 were positive by microscopy and Gram staining. The valve cultures were positive in 4 cases. Therefore, culture-positive endocarditis was present in 20%; whereas, 80% of the patients had culture-negative endocarditis. Bacterial DNA was detected in 12 of the 20 valves (60%) by broad-spectrum PCR (Figure 1). Direct sequencing for specious identification was possible in 10 cases. The remaining 2 cases were impossible to identify the microbe by sequencing. The results of microscopy, culture, and PCR are presented in Table 1.

**Discussion**

IE is a disease with high morbidity and mortality. Adequate antimicrobial management depends on the microbial diagnosis of the causative pathogen. Most cases of IE are caused by staphylococci and streptococci species. The frequency of culture negative IE varies among different previous studies, ranging from 2.5-31%. In this study, a significant percentage (80%) remained culture-negative, because of previous antibiotic treatment or the presence of microorganisms with fastidious growth. In such cases, blood culture systems require longer incubation periods (> 6 days). Also in culture negative IE, all tissue excised during cardiac surgery should be examined. The theory of culture negative IE is likely to be more difficult than those where the microorganism is known. The value of serology has been proven for some IE as Bartonella, Legionella, Chlamydia and Coxiella. In cases of surgical therapy of IE in the negative blood cultures, microbiological assessment of excised heart valves is the only way to identify the causative microorganism. Paradoxically, the improved antibiotic treatment of IE during the past decades may have increased the diagnostic failure rate because the microorganisms present on the excised valve are nonviable. This has limited our knowledge of the current spectrum of organisms causing IE. IE usually is detected by culture and serology. Recently diagnosis relies more on the PCR-based methods thanks to their accuracy, usefulness, and likely widespread availability for identification. When traditional methods are negative, PCR assay may establish the etiology of culture negative IE. We used a broad-spectrum PCR to amplify bacterial ribosomal sequence, followed by direct sequencing to detect and differentiate the causative agents of IE. In the previous studies, molecular assays such as PCR and subsequent direct sequencing were useful in diagnosing the cause of IE. Goldenberger *et al.*, first reported the use of PCR followed by sequencing, in 18 excised heart valves. Newly, it was recommended that molecular diagnosis of IE should be included in the Duke’s classification system. In this research, sensitivity of culture and Gram staining methods in comparison to PCR were 33.3% and 41.6%, respectively. In this study, molecular assay showed to be more sensitive and specific than conventional blood and tissue culturing techniques for the detection of bacteria. The main advantages of this technique are that it is effective irrespective of prior antibiotic therapy, and approximately all bacteria can be detected in a single reaction with the use of broad-spectrum primers. Also, both live and dead bacteria may result in positive PCR assays. When we considered bacterial species separately, all patients with endocarditis due to bacteria were positive by PCR. This may reflect greater amounts of DNA in infected valves or the fact that DNA of bacteria remains for longer periods in tissues. The cost of PCR-based methods are not cheap. When bearing in mind the costs of experimental therapy, numerous expensive antibiotics and multiple investigations done in the workup, these costs are modest. Moreover, availability of the medications and diagnostic modalities should be considered based on the geographical patterns. Such knowledge and understanding of the conditions would contribute to better diagnosis, treatment and management of the diseases.

![Table 1. Identified bacteria in this study](image)

<table>
<thead>
<tr>
<th>Bacteria (N)</th>
<th>Microscopy (5)</th>
<th>Culture (4)</th>
<th>Molecular assay (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus</em> spp.</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><em>Propionobacterium acnes</em></td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

![Figure 1. Gel electrophoresis of PCR products (1400 bp). Lane 1, 2 and 3: Samples that were 16s rRNA positive, Lane 4: Positive control, Lane 5: Negative control, Lane 6: DNA ladder 1000-bp](image)
Molecular diagnosis of infective endocarditis

**Conclusion**

In conclusion, the most commonly isolated microorganism was *Streptococcus* spp. and, PCR have the potential to detect the agents causing blood culture negative IE. Thus, molecular assays provide useful clinical and epidemiological information with significantly improved specificity and sensitivity.

**Acknowledgments**

This project was financially supported by Tabriz University of Medical Sciences. We also appreciate Dr. Safaie and Miss Mahmodian who kindly presented patients.

**Ethical issues:** This study was reviewed and confirmed by the ethics committee of Tabriz University of Medical Sciences.

**Conflict of interests:** The authors declare no conflicts of interest.

**References**

Evaluation of the Prevalence and Risk Factors of Delirium in Cardiac Surgery ICU

Kamran Shadvar¹, Farzaneh Baastani², Ata Mahmoodypoor³, Eissa Bilehjani³*

¹Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
²Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
³Department of Anesthesiology, Tabriz University of Medical Sciences, Tabriz, Iran

ARTICLE INFO

Article Type:
Original Article

Article History:
Received: 25 September 2013
Accepted: 28 November 2013

Keywords:
Delirium
Cardiac Surgery
ICU

ABSTRACT

Introduction: Delirium is defined as an acute cognitive disorder presenting with fluctuation in cognition, apathy and non-organized thinking. It may increase morbidity, mortality, ICU stay and cost. In patients who underwent heart surgery delirium may increase post-operative complications such as respiratory insufficiency, sternum instability and need to re-operation of the sternum. The aim of this study was to evaluate the prevalence and risk factors of delirium in patients admitted to cardiac surgery.

Materials and Methods: 18 years or older patients who had undergone cardiac surgeries and stayed for more than 24 hours in ICU following surgery were recruited. All subjects were assessed for signs & symptoms of delirium using CAM-ICU and its risk factors. All data were analyzed by SPSS 16 at the end of the study.

Results: The prevalence of delirium in these patients was 23.5% (47 patients). The mean age of patients with delirium was more than other patients ($P=0.001$). The Incidence of delirium in the patients with cardiopulmonary bypass surgery (CPB) was higher than the patients without CPB ($P=0.01$). The Incidence of delirium in the patients with Atrial fibrillation was higher than patients without it ($P=0.002$). The Incidence of delirium in the patients with CVA history was higher than the patients without CVA history ($P=0.032$). The mean time of mechanical ventilation in the delirious patients was more than other patients ($P=0.01$).

Conclusion: Older Age, CPB, history of CVA, Atrial Fibrillation, and prolonged mechanical ventilation are considered as the risk factors of delirium in cardiac surgery patients.

Introduction

Delirium is defined as an acute cognitive disorder that presents with fluctuation in cognition, apathy and non-organized thinking. Delirium also is incorrectly named as ICU psychosis or ICU syndrome.¹ It may increases morbidity, mortality, ICU stay and cost. Cognitive impairment after recovery from delirium may be long-lasting and the functional ability and quality of patient life may be affected.² In patients with cardiac surgery, delirium may increase post-operative complications such as respiratory insufficiency, sternum instability and need for re-operation the sternum.³ Some of the patients who have delirium in hospital may present signs of delirium after discharge. In these patients brain activity and cognition declines and the risk of dementia increases in comparison with the patients without a history of delirium.⁴ If the patient suffers hyperactive delirium, complications such as self-extubation, exit of life-saving catheters and asynchrony between patient and ventilator are increased which may be associated with poor prognosis.⁴ Hence, the study of prevalence and risk factors of delirium in patients undergoing cardiac surgeries in the ICU seems quite necessary. Finding the risk factors of delirium might assist early detection and reduction in risk of complications. Elimination of some known risk factors of delirium may cause reduction the length of stay, mortality and morbidity. The aim of this study was to evaluate the prevalence and risk factors of delirium in patients admitted to cardiac surgery ICU.

Materials and Methods

In a descriptive-prospective study, after obtaining approval from the Ethics Committee of the university and written informed consent from the patients, all patients admitted to the ICU following cardiac surgery were evaluated for delirium by means of CAM–ICU (Confusion assessment method of ICU).
Inclusion criteria were: Age above 18 years, cardiac surgery and stay in the ICU for more than 24 hours. Exclusion criteria were: unwillingness, history of psychological illness and antipsychotic drugs, patient death, hearing or vision disorders, RASS (Richmond Agitation sedation scale) less than or equal to – 4 and inability to respond to questions.

Change in consciousness state in the past 24 hours was assessed using ASE (Attention screening Examine). In this method, 10 letters were said to the patient and later the patient was asked to shake the examiner’s hand when special character such as (a) was heard. If the number of correct answers was less than 8, the patient was neglected. Visual Version of this test was used for patients in which squeezing the examiner’s hand could not be applied. Unorganized thinking was measured by patient answering to 4 yes or no questions. Patients who failed to respond to two questions correctly were considered to have unorganized thinking. The changes in level of consciousness of patients were evaluated with RASS. Patients with acute changes in conscious state and those with neglect, unorganized thinking or altered level of consciousness were considered to have delirium using the CAM-ICU. Risk factors of delirium in these patients were recorded and statistically analyzed. Data were analyzed by descriptive statistics (frequency, percent, mean ±SD), mean difference test for independent samples, Fisher’s exact test and analysis of variance (one-way ANOVA).

In this study, P values of less than 0.05 were considered statistically significant.

Results

Of 200 patients enrolled in this study, 47 had delirium. The prevalence of delirium in this study was 23.5%. (21 cases hyperactive, 12 cases hypoactive and 14 were mixed type delirium) (Figures 1 and 2). The mean age of the patients was 53.33±11.42 years (64.27±9.72 in delirium Patients, and 56.41±12.36 in Patients without delirium). There was a significant relationship between age and risk of delirium (P=0.001). 151 patients (75.5%) were operated with and 49 patients (24.5%) without CPB (Cardio Pulmonary Bypass). From 47 patients with delirium, 44 patients had operation with CPB but just 3 patients had operation without CPB. Prevalence of delirium in patients undergoing surgery using CPB was 29.13% and in the patients without CPB 6.12%. There was a significant relationship between surgery with CPB and the risk of delirium. (P= 0.001; Figure 3). The average ICU stay of delirium patients was 8.78±5.23 days and in Patients without delirium was 3.23±1.02 days. There was a significant relationship between delirium and ICU stay (P=0.01). Of the 47 patients who developed delirium, 8 patients had a history of CVA (17%) in comparison with 9 (8.5%) patients without delirium but had a history of CVA. There was a significant relationship between history of CVA and the risk of delirium. (P=0.032). Among the 47 patients with delirium 8 (2.17%) patients had atrial fibrillation but 4 patients (6.2%) in delirium-free group had atrial fibrillation. There was a significant relationship between atrial fibrillation and delirium (P=0.002). Duration of mechanical ventilation in delirium patients was 49.36±13.54 hours and 20.19±6.43 hours in delirium-free group. There was a significant correlation between the duration of mechanical ventilation and the incidence of delirium (Table 1).
Factors considered in the study.

<table>
<thead>
<tr>
<th>Table 1. Factors considered in the study.</th>
<th>With delirium N=47 n(%)</th>
<th>Without delirium N=153 n(%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>64.27 ± 9.72</td>
<td>56.41 ± 12.36</td>
<td>0.001</td>
</tr>
<tr>
<td>Sex</td>
<td>32 (68%)</td>
<td>104 (67.9%)</td>
<td>0.9</td>
</tr>
<tr>
<td>CPB</td>
<td>44 (93.6%)</td>
<td>107 (69.9%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration of MV (Hour)</td>
<td>49.36 ± 13.54</td>
<td>20.19 ± 6.43</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabet</td>
<td>25 (53.1%)</td>
<td>76 (49.6%)</td>
<td>0.66</td>
</tr>
<tr>
<td>CVA</td>
<td>8 (17%)</td>
<td>9 (5.8%)</td>
<td>0.032</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>13 (27.6%)</td>
<td>36 (23.5%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Thyroid disorder</td>
<td>1 (2.1%)</td>
<td>4 (2.6%)</td>
<td>0.80</td>
</tr>
<tr>
<td>Acid/base abnormality</td>
<td>11 (23.4%)</td>
<td>31 (20.9%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Renal failure</td>
<td>5 (10.6%)</td>
<td>18 (11.7%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Liver disease</td>
<td>1 (2.1%)</td>
<td>3 (1.9%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Heart failure</td>
<td>5 (10.6%)</td>
<td>21 (13.7%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Recent MI</td>
<td>12 (25.5%)</td>
<td>31 (20.2%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36 (76.59%)</td>
<td>120 (78.43%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Smoking</td>
<td>28 (59.5%)</td>
<td>95 (62%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Bun/Cr&gt;18</td>
<td>5 (10.6%)</td>
<td>21 (13.7%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>1 (2.1%)</td>
<td>3 (1.9%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>13 (27.6%)</td>
<td>36 (23.5%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>9 (19.1%)</td>
<td>24 (15.6%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>8 (17.2%)</td>
<td>4 (2.6%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>1 (2.1%)</td>
<td>3 (1.96%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Shock</td>
<td>2 (4.2%)</td>
<td>6 (3.9%)</td>
<td>0.86</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>9 (19.1%)</td>
<td>25 (16.33%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Motion limitation</td>
<td>2 (4.2%)</td>
<td>8 (5.2%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Sleep Disorder</td>
<td>20 (42.5%)</td>
<td>61 (39.8%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>1 (2.1%)</td>
<td>4 (2.6%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Cr&gt;2</td>
<td>5 (10.6%)</td>
<td>18 (11.7%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Medications associated with delirium</td>
<td>26 (55.3%)</td>
<td>82 (53.5%)</td>
<td>0.79</td>
</tr>
<tr>
<td>Tube feeding&gt;24h</td>
<td>11 (23.4%)</td>
<td>38 (24.8%)</td>
<td>0.81</td>
</tr>
</tbody>
</table>

**Discussion**

Delirium is defined as an acute cognitive impairment and neglect which fluctuate in level of consciousness or altered level of consciousness with unorganized thinking. This disorder causes increased mortality, morbidity, length of ICU stay and in patients undergoing cardiac surgery. Delirium is divided into hypoactive, hyperactive and mixed types. In Hypoactive type, patients are quiet but neglected and with decreased motion. In Hyperactive type, patients are agitated. The main characteristic of delirium is inattention. Hypoactive type is associated with a poor prognosis. In Bucerius study, it was indicated that surgery without CPB (off-pump) and the early age of the patients significantly decrease delirium in cardiac surgical patients. In our study, atrial fibrillation and history of CVA were identified as risk factors of delirium; also CPB was significantly associated with delirium. Because of the difference in the assessment method of delirium, the incidence of delirium in this study was lower than our study. In addition, thanks to a larger sample size, this study identified more significant factors for delirium, for example, in this study diabetes mellitus was identified as a risk factor of delirium but in our study there was no significant relationship between diabetes mellitus and delirium.

In Nagpul study on patients undergoing CABG with or without CPB, the mortality, postoperative myocardial infarction and renal failure were not different between the two groups; however, there was significant relationship between delirium and other neurological dysfunctions in two groups. In this study, 2.3% of patients undergoing off-pump CABG and 12.5% of on-pump CABG suffered from delirium (P= 0.01). In our study, there was a significant association between delirium and CPB. In the
Hernandez study, no significant relationship was reported between delirium and other neurological dysfunctions in two groups.7 Possible reasons for the higher prevalence of delirium in patients who have undergone surgery using CPB are periods of hypotension during CPB and non-pulsatile blood flow during surgery, but a lower risk of delirium in off-pump patients can be due to the fact that ascending aorta is not canalized thus reducing the risk of atherosclerotic embolization.8 In Kazmierski Study, the prevalence and risk factors of delirium were assessed in patients undergoing cardiac surgery with CPB using the DSM-IV (Diagnostic and statistical Manual of Mental disorders IV). The incidence of delirium in this study was 16.3%, and the factors that significantly associated with delirium were: age, preoperative cognitive impairment, episodes of major depressive disorder, anemia, atrial fibrillation, duration of mechanical ventilation. These results are in line with our study. Atrial fibrillation, advanced age, and prolonged mechanical ventilation in our study also had a significant association with delirium.9 AF may cause delirium by the risk of cerebral embolism, hypoperfusion and periods of arterial hypotension. On the other hand due to hypoperfusion, cerebral hypoxia probability may increases and this can reduce synthetise of acetyl coenzyme A, glutamate and acetylcholine in the citric acid cycle. The activity of brain cholinergic and glutaminergic fall could be responsible for delirium.10 In Rudolph study, delirium risk factors were examined using CAM-ICU in 122 patients aged over 60 years who underwent cardiac surgery. The incidence of delirium in this study was 52% and factors that were significantly associated with delirium were abnormal levels of serum albumin, depression, cognitive disorders, and a history of CVA.11 The incidence of delirium in this study was greater than our study due to the age of the participants in this study. Also history of CVA was considered as an underlying cause of delirium in our study but abnormal levels of serum albumin and depression were not monitored.

In Reissmuller study, 107 patients undergoing cardiac surgery were evaluated for delirium using CAM-ICU. The incidence of delirium in this study was 23% and risk factors were age over 60 years, longer duration of mechanical ventilation and longer CPB time, which is in line with our study.12 In Norkieue study, the assessment of risk factors for delirium in patients undergoing cardiac surgery using DSM-IV was performed. The incidence of delirium in this study was 31% and risk factors were: atrial fibrillation, use of IABP (Intra-Aortic Balloon Pump), Intraoperative hemofiltration, age over 65 years, emergency cardiac surgery, peripheral vascular disease, diabetes and hypertension.13 Being line with our study, atrial fibrillation, age, diabetes and hypertension were mentioned as risk factors for delirium; however, IABP and hemofiltration were not examined in our study. In Chang study, delirium and its risk factors after cardiac surgery were evaluated in 288 patients using DSM-IV. The incidence of delirium was 41.7% and the factors that were significantly associated with delirium were age over 65 years, mechanical ventilation more than 24 hours, infection after surgery, hematocrit less than 30% and a history of CVA.14 In comparison with our study, the incidence of delirium was higher in this study that may be due to differences in the assessment method of delirium. Age, prolonged mechanical ventilation and previous CVA in our study were significantly associated with delirium; however, hematocrit effect was not investigated in our study.

In Banach study, delirium and its risk factors were assessed in 260 patients after heart surgery using the DSM-IV. The incidence of delirium in this study was 11.2% and factors significantly associated with delirium were dysrhythmias (atrial fibrillation), hypertension, history of CVA, operation time more than 3h and alcohol abuse.15 The incidence of delirium in this study was lower than our study because of their exclusion criteria. The history of CVA and atrial fibrillation in our study significantly associated with delirium but not with hypertension which might have been due to smaller sample size of our study.

In summary, the incidence of delirium varies from 8.4% in Bucerius study to 41.7% in Chang study. These differences could be due to differences in assessment method of delirium, method of study and sample size. In our, Bucerius, Rudolph and Chang studies, the history of CVA was identified as one of the risk factors for delirium. In our, Kazmierski, chang and Veliz studies, prolonged mechanical ventilation was known as a risk factor for delirium, properly due to poor general health condition in patients with prolonged mechanical ventilation and respiratory failure. On the other hand, receiving anesthetics and muscle relaxants could have affected their mental function.16 Atrial fibrillation in our and Banach, Norkieue and Bucerius studies was significantly associated with the delirium that may due to increased risk of cerebral emboli and hypoperfusion and arterial hypotension. Cerebral hypoperfusion and hypoxia can decrease the cholinergic and glutaminergic function of the brain that could be the underlying cause of delirium. Diabetes and hypertension were considered as risk factors of delirium in Bucerius, Bazach and Norkieue studies; however, we could not find any significant relationship between them; as previously discussed, this could be due to differences in the sample size.

In our and in Bucerius and Nceppel studies, there was a significant association between delirium and surgery with CPB, but in Hernandez study there was not any significant differences between off-pump surgery and delirium which may be due to the lack of sclerotic embolization after canalization of ascending aorta in off-Pump method.
Delirium in ICU

Conclusion
Our study revealed that cardiac surgery using CPB, older age, history of CVA, atrial fibrillation and prolonged mechanical ventilation are considered as risk factors of delirium. By identifying the factors of delirium in ICU patients and early detection and treatment of delirium complications can be prevented. Therefore, it is recommended that, according to the prevalence of delirium, daily scoring patients with CAM-ICU by caregiver is a simple and non-time consuming method that can be helpful in early detection and prevention of complications. Identifying patients with high Risk of developing delirium based on known risk factors can help early detection of delirium. Treatment of atrial fibrillation after heart surgery could possibly be helpful in reducing delirium; however further studies are required to confirm this hypothesis.

Ethical issues: This study was reviewed and confirmed by the ethics committee of Tabriz University of Medical Sciences.

Conflict of interests: The authors declare no conflicts of interest.

References
Factors Influencing Mortality after Bioprosthetic Valve Replacement; A Midterm Outcome

Hassan Javadzadegan¹, Amir Javadzadegan², Jafar Mehdizadeh Baghbani²

¹Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
²Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

ABSTRACT

Introduction: Although valve repair is applied routinely nowadays, particularly for mitral regurgitation (MR) or tricuspid regurgitation (TR), valve replacement using prosthetic valves is also common especially in adults. Unfortunately, the valve with ideal hemodynamic performance and long-term durability without increasing the risk of bleeding due to long-term anticoagulant therapy has not been introduced. Therefore, patients and physicians must choose either bioprosthetic or mechanical valves. Currently, there is an increasing clinical trend of using bioprosthetic valves instead of mechanical valves even in young patients apparently because of their advantages.

Methods: Seventy patients undergone valvular replacement using bioprosthetic valves were evaluated by ECG and Echocardiography to assess the rhythm and ejection fracture. Mean follow-up time was 33 months (min 9, max 92).

Results: Mortality rate was 25.9% (n=18) within 8 years of follow-up. Statistical analysis showed a significant relation between atrial fibrillation rhythm and mortality (P=0.02). Morbidities occurred in 30 patients (42.8%). Significant statistical relation was found between the morbidities and age over 65 years old (P=0.005). In follow-up period, 4 cases (5.7%) underwent re-operation due to global valve dysfunction.

Conclusion: Our study shows that using bioprosthetic valve could reduce the risk of morbidity occurrence in patient who needs valve replacement. However, if medical treatments fail, patients should be referred for surgery. This would reduce the risk of mortality because of lower incident of complications such as atrial fibrillation and morbidities due to younger patients' population.

Introduction
Valvular heart disease is one of the common conditions cardiologists and surgeons encounter during assessment process of patients. In the situation of serious regurgitation or stenosis an intervention on the valve such as repair, valvuloplasty or valve replacement should be performed. Although valve repair applied usually nowadays, particularly for mitral regurgitation (MR) or tricuspid regurgitation (TR), valve replacement using prosthetic valves is common especially in adults.¹ Unfortunately, the valve with ideal hemodynamic performance and long-term durability without increasing risk of bleeding due to long-term anticoagulant therapy has not been introduced yet. Therefore, patients and physicians must choose either bioprosthetic or mechanical valve each of which has cons and pros making decision difficult. Mechanical valves are more durable but need lifelong anticoagulation and increase the risk of thromboembolism. In contrast, tissue valves do not need long-term anticoagulation but carry the risk of structural failure and reoperation.²³ Currently, the use of bioprosthetic valves instead of mechanical valves is increasing even in young patients apparently because of its advantages.⁴ In this study, we report a case series of patients undergone valve replacement using bioprosthetic valve and followed for a few years.

Materials and Methods
From July 2000 to Sep. 2008, seventy patients (with the mean age of 54.8 years, 24 males and 46 females) undergone valvular replacement using bioprosthetic valves were studied. Isolated aortic valve replacement (AVR), isolated mitral valve replacement (MVR), isolated tricuspid valve replacement, AVR with MVR and MVR with TVR were performed in 21, 23, one, 10 and 5 patients, respectively. Mean follow-up time was 33 months (min 9, max 92 months). All survived patients were assessed echocardiographically.

Results
Atrial fibrillation was found in 34 patients (48.6%).
Table 1. Patients' characteristics before operation

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>mean: 54.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>F/M</td>
<td>46/24</td>
</tr>
<tr>
<td>Rhythm</td>
<td></td>
</tr>
<tr>
<td>AF</td>
<td>34 (48.6)</td>
</tr>
<tr>
<td>CHB</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>NSR</td>
<td>34 (48.6)</td>
</tr>
<tr>
<td>EF</td>
<td></td>
</tr>
<tr>
<td>≥ 60</td>
<td>7 (10)</td>
</tr>
<tr>
<td>40-59</td>
<td>48 (68.6)</td>
</tr>
<tr>
<td>20-39</td>
<td>15 (21.4)</td>
</tr>
<tr>
<td>&lt; 20</td>
<td>N/A</td>
</tr>
<tr>
<td>Functional class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>N/A</td>
</tr>
<tr>
<td>II</td>
<td>23 (32.9)</td>
</tr>
<tr>
<td>III</td>
<td>42 (60)</td>
</tr>
<tr>
<td>IV</td>
<td>5 (7.1)</td>
</tr>
<tr>
<td>History of endocarditis</td>
<td></td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td></td>
</tr>
<tr>
<td>History of CABG</td>
<td></td>
</tr>
<tr>
<td>History of valve surgery</td>
<td></td>
</tr>
</tbody>
</table>

AF: Atrial Fibrillation, CHB: Complete Heart Block, NSR: Normal Sinus Rhythm, EF: Ejection Fraction

EKG findings are shown in Table 1. A mortality rate of 25.7% (n=18) was observed within 8 years of follow-up. Statistical analysis revealed a significant relation between atrial fibrillation rhythm and mortality (P=0.02). There were no statistical relation between mortality and other factors such as age more that 65 years old (P=0.931), sex (P=0.633), EF<30% (P=0.063), functional class (P=0.103), history of endocarditis (0.512), history of coronary heart disease (P=0.292), history of CABG (P=0.609), and combined CABG and valvular operation (0.262). Furthermore, there was no significant relation between operation type and mortality (P=0.325).

Cause of mortality due to valve function found in one patient (1.4%), other cardiac related causes were found in 6 patients (8.6%), non cardiac cause in 3 patients (4.3%). Mortality in 8 patients (11.4%) occurred due to cardiopulmonary arrest rather than distinguishable factors (cardiac or non-cardiac). Mortality occurred during first month after operation in 9 patients (12.8%), between the second month and first year in 4 patients (5.7%), in no one during second year and in 5 cases in the 3rd and 4th year. Mean time for morbidities which occurred in 30 patients (42.8%) was 8 months (min 1 max 60). Significant statistical relation was found between the morbidities and age over 65 years old (P=0.005) but not between morbidities and other above-mentioned factors listed above. Rate of morbidities is listed in Table 2. Symptom-free period was 20.3 months for all patients, 12 months for over 65 years old and 23.5 months for the rest. In the period of follow-up, 4 cases (5.7%) underwent re-operation. Mean free of operation time was 22 months (min 1, max 60) in these patients. These cases were evaluated echocardiographically and valve global dysfunction was distinguished. There was no significant relation between valve dysfunction and the above-mentioned factors.

Discussion

In 1961, Starr and Edwards described successful prosthetic valve replacement. Some patients who underwent valve replacement with the original Starr-Edwards prostheses in the 1960s are alive to this day. In the last 40 years, more than 80 models of prostheses have been developed for patients requiring valve replacement; however, no ideal valve has been discovered yet.5-6 Although there is wide consensus on the type of valve to be placed in younger and older patients, valve choice in the ages between 55 and 70 years is very difficult, because in this age span patients are no longer truly young and not yet truly old. This is the threshold age where it is difficult to balance the risk of the anticoagulation therapy with the need for a reoperation.7 Furthermore, patients in this age span comprise a large group of patients in need of valve replacement.4,5 In recent decades two randomized trials have been compared survival and valve related morbidities associated to use of mechanical and bioprosthetic valves helping physicians in the choice of type of valve suitable for their patients. However, these studies have many limitations that potentially biasing the choice of one valve versus the other. High perioperative mortality rate, old style valves that are not available now and large number of redo sternotomy occurred in these studies which could be considered as some of the limitations of these studies.5,8-11 Although some studies proved that no difference exists in mortality rate after mechanical or tissue valve replacement1-13, these studies provoked that reoperation was higher after tissue valve replacement than mechanical and valve related morbidities were more common after mechanical valve implantation. It would be postulate that life style alterations after a mechanical valve replacement in a patient needing valve surgery are more likely. Oakley et al. mathematically proved that risk of mortality for 1st operation has no correlation with type of the valve and
overall risk of morbidities and mortality is approximately 2 fold when using mechanical valve. These data might be an explanation to trend toward using bioprosthetic valve by surgeons; however, the need of long term result of randomized studies is obvious.

In our study, survival rate was not in an acceptable range after a mid-term follow-up possibly as a result of patients’ co-morbidities; however, causes of death in almost half of patients who expired were not clarified limiting the conclusion. Also, the fact of postponing the surgery derived from cardiologists’ or patients’ late decision should be considered. The poor quality of life index and cardiac status of patients’ are endorsing this theory. Valve related cause of death was reported just for one case that seems favorable. More than half of patients had no episode of any kind of morbidities during follow-up and morbidities significantly related to age more than 65 years old.

Conclusion

It could be concluded that tissue valves could be used for young patients (under 65 y/o) with no concern about the rate of consequences. Of course, a low rate of valve dysfunction happening in our cases would assist this thesis. However, large scale long-term studies should be performed to prove this idea.

Our data discuss that no hesitation about performing other procedures is acceptable because neither CABG nor other valve procedures which performed during the valve replacement had influence on patients’ outcome. Since atrial fibrillation had a significant effect on mortality rate, we discuss that therapeutic rout such as surgical, interventional and medical, would be preferable before or during valve replacement to control the atrial fibrillation.

Ethical issues: All patients gave written informed consents and the study was approved by our local Ethics Committee.

Conflict of interests: The authors declare no conflicts of interest.

References

Effects of Emotional Stimuli on Cardiovascular Responses in Patients with Essential Hypertension Based on Brain/Behavioral Systems

Mohammadreza Taban Sadeghi¹, Hossein Namdar¹, Shahram Vahedi, Naser Aslanabadi¹, Davoud Ezzati², Babak Sadeghi²

¹Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
²Department of Psychology, Faculty of Education and Psychology, University of Tabriz, Tabriz, Iran

ABSTRACT

Introduction: Effects of emotional stimuli on hemodynamics in patients with essential hypertension based on brain/behavioral systems have not been studied broadly.

Methods: Eighty five essential hypertensive male patients who had completed Carver-White BIS/BAS scale were enrolled to the study. Later, 25 BIS and 25 BAS patients were selected and their blood pressure and heart rate were recorded prior to stimuli induction. Participants were then exposed to stressor pictures. After that, 15 minutes of relaxation and cognitive tasks were performed. Finally, the participants were exposed to pleasant pictures. The blood pressure and heart rate were recorded after presenting of 2 stimuli.

Results: Our study showed that BIS patients achieved higher scores in diastolic blood pressure and heart rate in comparison with BAS patients after presenting stressful stimuli. Also, BAS patients achieved lower scores in systolic blood pressure and heart rate in comparison with BIS patients after presenting pleasant stimuli.

Conclusion: In summary, BIS patients experience negative emotions more than BAS patients. Therefore, the role of induced mood states is important in relation to physical health.

Introduction

Cardiovascular diseases are the leading cause of morbidity and mortality in various countries worldwide. Being important at all stages of human life, cardiovascular diseases are still very common.¹ Heart diseases, due to a combination of physical and psychological stressors such as pain, loss of health, loss of job, extreme sensory deprivation, imminent death, and varying degrees of psychological reactions like hopelessness, fatigue, and fear cause a feeling of worthlessness, and low self-esteem in patients.² Hypertension is a phenomenon that has an important role in cardiovascular diseases.³⁴ This phenomenon is a public health problem and its prevalence throughout the globe, particularly in developed countries is rising.⁶ Worldwide, out of every 8 deaths, one is due to hypertension, making it the third leading cause of mortality in the world.⁷

One of the factors suggested as a predictor of heart diseases, and the subject of many studies is stress.⁸ Stress is one of the factors that affect the autonomic nervous system (especially, the sympathetic nervous system). Stress can be regarded as a non-specific response of a living creature to any demand or need, while the stressor is any stimulus that can lead to stress (person’s response). Our relationship with the environment is affected by many material and psychological elements. But they depend on our response to the social and environmental stressors as well.⁹ Causes of death have changed dramatically since the early 20th century. Studies reveal that 70% to 80% of diseases are associated with stress. Diseases associated with lifestyle including cardiovascular diseases and cancers that cause people’s death are related to stress response.¹⁰ Hu et al. argue that reacting to stress ends in physiological changes, reduced health, and increased illness.¹¹ The role of positive emotions in coping is currently a subject of interest to researchers. It is possible that positive and negative emotions could coincide in stressful situations, and in fact this is what happens in reality. For instance, positive emotions can neutralize some of the unpleasant complications of negative emotions, especially the physiological ones. In a study, when people were talking about their relationship with their spouses who had died six months earlier, they had a sincere smile on their lips, however, two years after the incidence, signs of grief had diminished and their relationship with others was better (normal). In another study, it was revealed that those who are able to find positive meanings after a traumatic event, for instance spiritual growth or valuing life, can respond more rationally to experimental stress.
Stimuli (in vitro).\textsuperscript{12}

In recent years, there has been a deluge of psychological studies on the relationship between negative emotions and brain-behavioral systems and heart diseases, particularly essential hypertension.\textsuperscript{13}

Gray, in accordance with different reward and punishment systems in the brain and personal differences in sensitivity to various stimuli, identified three brain-behavioral systems that underlie differences in personality. Furthermore, the dominance and activity of each of these systems in a person leads to different emotional states and provokes different modes of confrontation. These systems are behavioral activation system that is related to positive emotions, behavioral inhibition system that establishes anxiety and fight or flight system that generates rage, fear and panic.\textsuperscript{14}

The physiological-psychological evidence states that both motivational systems of activation/inhibition are affected by the sympathetic and parasympathetic branches of the automatic nerves that actively work opposite each other.\textsuperscript{15} Gray and Mc Naughton believe that sensitivity of behavioral inhibition system is the predictor of person’s negative emotional stresses in stressful situations, regardless of the nature of stressors, and it seems, behavioral inhibition predicts a person’s poor and passive coping.\textsuperscript{16} The results of studies by Gray, Mc Naughton, Guth, and Sharon consider the activity of the behavioral inhibition system to be associated with heart diseases, and believe this to be due to creation of negative emotions and increased activity of sympathetic system.\textsuperscript{16-18}

Despite the importance of psychological factors in the incidence of heart diseases, unfortunately, only a few studies have been conducted in Iran in respect of the relationship between pleasant and stressful stimuli and brain-behavioral systems with this disease. While these parameters may not singularly affect the incidence of heart diseases, in combination, they amplify each other’s effects. To address this shortfall, and considering the diverse and sometimes conflicting findings about the relationship between attributes of personality and essential hypertension, the present study examined the relationship between the parameters mentioned and essential hypertension. Since by identifying the relationship between these parameters and hypertension, and comparing the results with healthy people, we can effectively reduce the rate of essential hypertension by increasing awareness, providing correct information to those at risk, implementing clinical interventions like psychological counseling with the aim to provide skills necessary to deal with stress, reducing risky behaviors and encouraging people to change their lifestyle.

Materials and Methods

The participants in this study initially included 85 male patients with essential hypertension that received relevant information and explanation with respect to the objectives of the study and the questionnaire. After presentation of all the necessary explanations, first, the short form of Carver & White brain-behavioral systems questionnaire was performed on the participants, and ultimately 50 male patients with essential hypertension (25 BIS patients and 25 BAS patients), who had scored higher marks in the questionnaire than the rest were selected (matching participants in terms of demographic parameters). Before presentation of stimulus, participants’ heart rate and blood pressure were measured and recorded. Then, in order to assess the effect of stress on blood pressure and heart rate, they were exposed to stressful stimuli. These stimuli included 13 slide images of war crimes shown over 3 minutes, (14 seconds each) presented on laptops. After presentation of these slides, participants’ blood pressures and heart rate were measured by a digital brachial sphygmomanometer. They were then rested for 15 to 20 minutes. While resting, participants performed a cognitive exercise (successive subtraction of 7 from 100) to neutralize the effect of previous stimulus. Subjects were then exposed to pleasant stimuli that included 13 slide images of children under a year old over 3 minutes (14 seconds each). After presentation of these slides, blood pressure and heart rate of the subjects were measured again by a digital brachial sphygmomanometer. Once the procedure had ended, the results obtained from blood pressure and heart rate readings were examined and the data were prepared for final analysis. This questionnaire, with 24 self-reporting items was designed by Carver & White in 1994.\textsuperscript{19} The BIS sub-scale includes 7 items that measure behavioral inhibition sensitivity or response to threat and feeling of anxiety when faced with signs of threat. The BAS sub-scale includes 13 items and measures behavioral activation system sensitivity. The items are in the 5-option Likert style; with score 1 indicating ‘very true for me’ to score 5 indicating ‘very false for me’. In a study by Atrifard, BIS internal consistency was 47%, BAS internal consistency was 47% and its other subscale like response to reward, drive, and fun-seeking were 73%, 60%, and 18% respectively.\textsuperscript{20} For data analysis, descriptive statistics with measures of central tendency (mean and standard deviation) and inferential statistics with multivariate covariance analysis (MANCOVA) were used.

Results

Table 1 shows the descriptive statistics of both participating groups. At two stages (pre-test and post-test), the increase in blood pressure and heart rate was higher in BIS patients compared to BAS patients. The results of covariance analysis of cardiovascular response in two groups are presented in Table 2. In this analysis, pre-test scores were statistically controlled. It can be seen that there was a significant difference between the two groups in diastolic blood pressure ($P<0.001$) and heart rate ($P<0.018$) after presentation of stressful stimulus. But the difference between the groups in systolic blood pressure
after stressful stimulus was insignificant. Table 3 presents the difference in means between two groups, in which diastolic blood pressure ($P<0.001$) and heart rate ($P<0.018$) increased significantly in BIS patients compared to BAS after stressful stimulus. Also, systolic blood pressure ($P<0.033$) and heart rate ($P<0.013$) significantly reduced in BAS patients after pleasant stimulus compared to BIS patients. In other areas, the difference was insignificant.

To ensure normal distribution of data and compliance with conditions of use of parametric statistics, the Kolmogrov-Smirnov test was utilized, and results obtained indicated normal distribution of data ($P>0.05$). The BOX test was used to examine the assumption of equality of covariance parameters, and the assumption was verified by the results with no significant difference between them ($P>0.05$). To verify the assumption of equality of population groups’ variances, Lawn test was employed, and results indicated equality of variance parameters and no significant difference between them ($P>0.05$). Additionally, the regression slope test was used to determine presence or otherwise of a linear relationship between pre-test and post-test scores, and results showed that there was no significant interaction between the groups and pre-test scores in systolic and diastolic blood pressures and heart rate. In other words, the regression slopes were homogeneous and the assumption was proven.

### Discussion

In line with Gray & Mc Naughton\(^{16}\) findings, the present study showed that sensitivity of behavioral inhibition system is predictor of negative emotion stresses in stressful situations, regardless of the natural stressors. Also, it seems behavioral inhibition is predictor of person’s poor and passive coping. The results of studies by Gray & Mc Naughton\(^{16}\), Guth\(^{17}\), and Sharon\(^{18}\) regard activity of behavioral inhibition system to be associated with heart diseases, and believe this to be due to negative emotions and sympathetic system activity. Eyesneek\(^{21}\) claims that neurotic people have higher levels of activity in sympathetic area of the autonomic nervous system. This is the body’s warning system that responds to stressful events by increasing respiratory rate, heart rate, blood flow to muscles, and release of adrenaline. In fact, neurotics react with excitement to event unimportant to others, which can simultaneously activate behavioral inhibition system, and according to Gray & Mc Naughton’s findings, highly active behavioral inhibition system leads to anxiety attributes in personality. Experimental studies have also shown that activity of behavioral inhibition system is associated with high cortical arousal, particularly in right hemisphere of the brain, and electroencephalography (EEG) and neuronal imaging data reveal that the presence of threatening stimuli is related to higher arousal of

### Table 1. Mean and Standard deviation of systolic and diastolic blood pressure and heart rate divided into groups, and time

<table>
<thead>
<tr>
<th>Component</th>
<th>After pleasant stimuli Mean ± SD</th>
<th>After stressful stimuli Mean ± SD</th>
<th>Before stimulus Mean ± SD</th>
<th>After pleasant stimuli Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure in BIS patients</td>
<td>139.06 ± 5.1</td>
<td>145.93 ± 8.69</td>
<td>135.6 ± 8.69</td>
<td>139.06 ± 5.1</td>
</tr>
<tr>
<td>Diastolic blood pressure in BIS patients</td>
<td>89.6 ± 7.09</td>
<td>106.23 ± 7.32</td>
<td>91 ± 10.25</td>
<td>89.6 ± 7.09</td>
</tr>
<tr>
<td>Heart rate in BIS patients</td>
<td>89.13 ± 4.65</td>
<td>90.8 ± 8.09</td>
<td>83.4 ± 8.45</td>
<td>89.13 ± 4.65</td>
</tr>
<tr>
<td>Systolic blood pressure in BAS patients</td>
<td>125 ± 5.38</td>
<td>136.26 ± 8.88</td>
<td>133.4 ± 10.91</td>
<td>125 ± 5.38</td>
</tr>
<tr>
<td>Diastolic blood pressure in BAS patients</td>
<td>84.2 ± 5.75</td>
<td>76.81 ± 6.68</td>
<td>79.46 ± 7.36</td>
<td>84.2 ± 5.75</td>
</tr>
<tr>
<td>Heart rate in BAS patient</td>
<td>66/26 ± 5.76</td>
<td>77.2 ± 10.68</td>
<td>77.8 ± 8.72</td>
<td>66/26 ± 5.76</td>
</tr>
</tbody>
</table>

BIS patients= Behavioral Inhibition System patients, n=25
BAS patients= Behavioral Approach System patients, n=25

### Table 2. Results of covariance analysis (Systolic and Diastolic blood pressure and Heart rate) in BIS & BAS patients

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>F</th>
<th>sig</th>
<th>Partial Eta Squared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure after stressful stimuli</td>
<td>0.194</td>
<td>0.663</td>
<td>0.008</td>
</tr>
<tr>
<td>Diastolic blood pressure after stressful stimuli</td>
<td>17.125</td>
<td>0.001</td>
<td>0.407</td>
</tr>
<tr>
<td>Heart rate after stressful stimuli</td>
<td>6.441</td>
<td>0.018</td>
<td>0.205</td>
</tr>
<tr>
<td>Systolic blood pressure after pleasant stimuli</td>
<td>2.225</td>
<td>0.148</td>
<td>0.082</td>
</tr>
<tr>
<td>Diastolic blood pressure after pleasant stimuli</td>
<td>1.23</td>
<td>0.283</td>
<td>0.046</td>
</tr>
<tr>
<td>Heart rate after pleasant stimuli</td>
<td>0.395</td>
<td>0.535</td>
<td>0.016</td>
</tr>
</tbody>
</table>

DF=1, P≤0.05
Table 3. Paired comparison groups in systolic and diastolic blood pressure and heart rate

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Group</th>
<th>Group</th>
<th>Mean difference</th>
<th>Std. Error</th>
<th>Sig*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in systolic blood pressure (stressful stimuli)</td>
<td>BIS patient</td>
<td>BAS patient</td>
<td>2.074</td>
<td>4.706</td>
<td>0.663</td>
</tr>
<tr>
<td>Changes in diastolic blood pressure (stressful stimuli)</td>
<td>BIS patient</td>
<td>BAS patient</td>
<td>11.947</td>
<td>2.887</td>
<td>0.001</td>
</tr>
<tr>
<td>Changes in heart rate (stressful stimuli)</td>
<td>BIS patient</td>
<td>BAS patient</td>
<td>10.596</td>
<td>4.175</td>
<td>0.018</td>
</tr>
<tr>
<td>Changes in systolic blood pressure (pleasant stimuli)</td>
<td>BIS patient</td>
<td>BAS patient</td>
<td>9.879</td>
<td>6.554</td>
<td>0.033</td>
</tr>
<tr>
<td>Changes in diastolic blood pressure (pleasant stimuli)</td>
<td>BIS patient</td>
<td>BAS patient</td>
<td>-6.009</td>
<td>9.364</td>
<td>0.524</td>
</tr>
<tr>
<td>Changes in heart rate (pleasant stimuli)</td>
<td>BIS patient</td>
<td>BAS patient</td>
<td>10.966</td>
<td>9.658</td>
<td>0.013</td>
</tr>
</tbody>
</table>

*P≤0.05

the right prefrontal cortex, whilst neuroticism is also associated with relatively high activity of the right frontal. Stress can also cause heart diseases through physiological changes. It seems stress has direct effects on the coronary arteries and heart muscles. In response to stress or exposure to a threatening or dangerous situation, heart rate increases, blood pressure rises, and many other changes in other body systems occur. For instance, skin blood vessels tighten, muscles contract and blood flow to the brain and muscles increases. As a result of these changes, heart rate rises and the heart’s oxygen requirement increases, which can cause heart attack or angina (chest pain) in people with heart diseases. Moreover, stress can cause increased blood clotting capability. This clot can partially or completely block a coronary artery, leading to a heart attack. Also, with increased hormones (adrenaline) in response to stress, together with increased blood flow, they can damage the lining of arteries and thicken or toughen vessel walls (once healed), thus preparing the grounds for creation of plaque. All these cases can explain why people with heart diseases in stressful situations are affected by angina, and also why these attacks more often occur in such circumstances.

Several studies have shown the importance of sympathetic activity and its subsequent effect on cardiovascular diseases. There is considerable evidence in support of the association of sympathetic reaction with cardiovascular diseases. For example, rise in heart rate is caused by sympathetic heart activity, and is inhibited by parasympathetic heart activity. Heart rate can also be caused by the effect of activities independent of the autonomic system. In normal heart condition, parasympathetic effects promote health, self-regulation, and a state of calm behavior that protects the heart and diminishes sympathetic reaction in stress. Conversely, reduced parasympathetic control of heart rate is associated with cardiovascular diseases, causing elevated blood pressure, and death.

The results of this study also reveal a significant reduction in systolic blood pressure and heart rate in BAS patients compared to BIS after presentation of pleasant stimulus. In line with these findings, Rafienia et al. found that in positive moods, systolic blood pressure reduces compared to negative mood conditions. This could concur with Gray’s forecast in relation to sensitivity to reward in BAS patients. But, in opposition to results of the present study, Lewis et al. showed that there was no significant difference between the subjects’ mean heart rate in positive and negative mood conditions. According to Eyesneck hypothesis, extrovert people are more sensitive to positive stimuli than introvert people. If this hypothesis is correct, then extroverts are more responsive to induced positive emotions (affects) than introverts. In his hypothesis, Gray expresses high sensitivity of BAS people to indications of reward, which somehow reflects early arousal component of extroversion.

Based on Gray’s hypothesis, it can be concluded that people with hypertension respond more strongly or quickly to new stimuli, innate fear stimuli, and conditional aversive stimuli than normal people with behavioral inhibition outputs (impaired current behavior) with increased arousal (that can be continuation of the impaired action). Also, in these conditions, increased attention to the environment when more information is received, especially about new elements in environment, is more observed in hypertensive people than in normal people.

Study limitations and recommendations

Like other studies, the present study was also faced with limitations that affect generalization of its results. Firstly, this study was conducted on people over 40 years of age only; secondly, the participants were all male; and finally, the sample size was small. It is recommended that in future studies, all age groups be included, of both sexes, and with larger sample size.
**Conclusion**

In relation to Gray’s hypothesis, it can be asserted that, since BIS patients experience more negative emotions than BAS patients, BIS patients have higher diastolic blood pressure and heart rates compared to BAS patients. Thus, in addition to medical treatment to better control blood pressure and prevent pressure fluctuations throughout the day, BIS patients should also receive psychological counseling and training.

**Ethical issues:** This study was reviewed and confirmed by the ethics committee of Tabriz University of Medical Sciences.

**Conflict of interests:** The authors declare no conflicts of interest.

**References**

Critical illness is a life-threatening course of the disease affecting almost all human organs; unfortunately, it can lead to significant morbidity or mortality. Critical illness is mostly heralded by physiological deterioration. It is globally accepted that all clinical staff are extremely influential through their vigilance and intensive care provided for the critically-ill.1 Early-weaning systems and modes have contributed immensely to the prevention of deterioration and serious adverse events in these patients.2 Outcome depends vastly on prompt identification, diagnosis and treatment; hence, all doctors should have the knowledge to identify the critically-ill patient and initiate the situation management as soon as possible. The use of gloves and gowns for all contacts versus routine care among patients in medical and surgical ICUs has recently been shown not to be associated with a significant difference in the MRSA or VRE acquisition1. In their study, Harris et al. reported that all health care workers (nurses, physicians, respiratory therapist, etc.) wore gloves and gowns for all contacts with patients and when entering each patient’s room.3 Admission to an intensive care unit is per se a highly-stressful event for both patients and their relatives. Traditionally, infection control concerns and a belief that liberal visiting by patients’ relatives interferes with the provision of patient care has led many units to impose restricted visiting policies. However, recent studies suggest that partially-unrestricted vs. restricted visiting policy not only improves visitors’ satisfaction and reduces anxiety but also does not result in an increase in ICU-acquired infections.4,5 Hence, considering the increase in the popularity of open and partially-restricted visitor policies, provision of infection control (gowns and gloves) for visitors’ contacts with the patients seems to be of great important in decreasing infection in the critically-ill patients.

Ethical issues: Not applicable
Conflict of interests: The authors declare no conflicts of interest.

References
Unusual Clinical Presentation of a Giant Left Ventricle Hydatid Cyst

Alireza Alizadeh-Ghavidel1, Majid Kyavar2, Anita Sadeghpour3, Zia Totonchi4, Yalda Mirmesdagh1, Nooshin Almassi5, Shabnam Madadi2

1Heart Valve Disease Research Center, Rajaei Cardiovascular Medical & Research Center, Tehran, Iran
2Cardiology and Cardiac Imaging Department, Rajaei Cardiovascular Medical & Research Center, Tehran, Iran
3Echocardiography Research Center, Rajaei Cardiovascular Medical & Research Center, Tehran, Iran
4Cardiac Anesthesia Department, Rajaei Cardiovascular Medical & Research Center, Tehran, Iran
5Infectious Disease Consultant, Rajaei Cardiovascular Medical & Research Center, Tehran, Iran

ABSTRACT

A 39-year-old woman was hospitalized in our center due to chest and left shoulder pain. Having a history of tamponade and tuberculosis, she was under treatment for the previous two months. Echocardiography, chest CT and MRI documented intramyocardial and pericardial hydatid cyst which was later confirmed by further pathological studies. Later, the cyst was removed surgically.

Learning objective
Perforated hydatid cyst can be presented as granulomatous pericarditis. Hydatid cyst should be taken into consideration in the differential diagnosis of all cystic masses in all anatomic locations, especially with rare localizations and when they occur in endemic areas.

Introduction
Hydatid disease (HD) may affect almost any part of the body. However, the involved organs mostly include the liver (75%) and the lungs (15%). Hydatid cysts rarely present in the pericardial cavity. Among radiographic techniques, CT imaging and MRI can acceptably detect hydatid cysts. Yet, hydatid cysts with unusual localizations may cause serious difficulties in differentiating the diagnosis. Therefore, in this study we report a case with misdiagnosed pericardial hydatid cyst.

Case report
The patient, a 39-year-old woman, was admitted to our center with intermittent retrosternal chest discomfort, dyspnea of exertion (DOE) and pain in the left shoulder from 3 days ago. With a history of tamponade during her pregnancy period, she had previously undergone subxiphoid drainage followed by a pericardiectomy procedure due to her persistent DOE in which there was no evidence of pericardial cyst; however the histopathologic findings of the pericardial sample reported granulomatous changes. Therefore, an empirical therapy of anti-tuberculosis had been initiated for 2 months. Despite the mentioned interventions, her DOE lingered on and she was referred to our center. Physical examination did not reveal any further abnormal findings. Her blood pressure was 110/70 mmHg and heart rate was 85 beats/min. Complete blood count revealed mild anemia with hemoglobin: 10.3 g/dl and erythrocyte sedimentation rate (ESR): 43 mm/h. Liver and kidney function test results were within normal limits. The posteroanterior chest x-ray film demonstrated a spherical mass located at the left contour of mediastinum. Echocardiography and CT investigations were performed. Echocardiography demonstrated a multiple echo-free space cystic formation in posterolateral wall of left ventricle (LV) with no particle on it suggestive for intramyocardial and pericardial hydatid cyst (Figure 1. A,B). Multiple pericardial cysts at posterior aspect of left chamber without obvious calcification measured about 28×27 mm and 36 × 36 mm were seen on CT. Cardiac MR imaging (dynamic MR imaging with gadolinium) was also performed for better evaluation. On T1 weighted and true-FISP MR images, there was a large multilobulated and septated cystic mass in the posterolateral wall of LV with size about 32.8× cm, 42.98× cm and 21.4× cm that was similar to intramyocardial and pericardial hydatid cyst (Figure 2. A,B). Multiple pericardial cysts at posterior aspect of left chamber without obvious calcification measured about 28×27 mm and 36 × 36 mm were seen on CT. Cardiac MR imaging (dynamic MR imaging with gadolinium) was also performed for better evaluation. On T1 weighted and true-FISP MR images, there was a large multilobulated and septated cystic mass in the posterolateral wall of LV with size about 32.8× cm, 42.98× cm and 21.4× cm that was similar to intramyocardial and pericardial hydatid cyst (Figure 2. A,B). Based on previous data (granulomatous pericarditis) and epidemiologic evidence and typical radiologic findings for hydatid cyst, empiric treatment for TB in addition to hydatid cyst was initiated pre-operatively. Simultaneously, we started to investigate previous data for culture results.
for TB which turned out to be negative after 2 months. Finally she underwent cardiac surgery under general anesthesia and standard median sternotomy. After decortication and releasing the strong adhering bands and standard single cava cannulation the cardiopulmonary bypass (CPB) was started and cardiac arrest was induced. The apex was completely attached to the lateral wall of left hemithorax and lungs, which was hardly detached. A large cystic lesion was observed on posterolateral wall of left ventricle. After covering the surrounding tissue with silver nitrate solution soaked sponge, an incision was made and 3 large hydatid cysts and some daughter cysts were evacuated. The wall of the cyst was unroofed and the region was washed with silver nitrate solution. The patient was weaned from CPB off without inotropic support. There was no evidence of residual cyst in intraoperative trans-esophageal echocardiography. Early postoperative period was uneventful. Surgical view and gross pathology of hydatid cysts have been demonstrated in Figures 3A and 3B, respectively. Histopathological examination findings confirmed the diagnosis. The rational for starting Albendazol before surgery was lowering the intracystic pressure, preventing cyst rupture during surgery and preventing the seeding of daughter cysts. Throughout the follow-up period, we planned to treat the patient for a longer course and followed her up with IgG ELISA levels which were negative until 3 months from the treatment onset.

Discussion

HD is caused by echinococcus granulosus which is a tape worm and is still among common health problems due to its endemic status in some parts of the world. HD may locate in any parts of the body mostly in liver, lungs and brain. Some unusual sites for HD involvement include heart, pericardium, kidney, intraperitoneum, retroperitoneum, bone, soft tissue, and breast. Pericardial hydatid cysts are typically developed at the right costophrenic angle. Cardiac hydatid cysts mostly occur in the ventricular septum. However in this case the cysts were located in the posterolateral wall of left ventricle.
the posterolateral aspect of the left ventricle. Symptoms vary depending on size, location and involvement of neighboring structures. Some studies similar to our study reported symptoms of chest pain, shoulder pain, dyspnea and persistent cough in patients with pericardial hydatid cyst.2,6 There are different methods in order to investigate cardiopericardial hydatosis and echocardiography is the procedure of choice in this matter.2 However, Sakarya et al. and Thameur et al. have suggested that CT scan is better than echocardiography considering its ability to distinguish solid from liquid tumors and also CT scan is an effective and reliable tool for the surgeons which can provide the exact site of the abnormality.2,7 In our case, CT scan was performed and multiple pericardial cysts at posterior aspect of left chamber without obvious calcification were revealed. Similar to the studied of Desnos et al. and sakarya et al., cardiac MR imaging (dynamic MR imaging with gadolinium) was also performed.2,8 A large multilobulated and septated cystic mass in the posterolateral wall of LV, similar to intramyocardial and pericardial hydatid cyst was detected in MR findings. However, similar to the statement of Engin et al., hydatid cysts with unusual localization may cause serious difficulties in order to differentiate the diagnosis.1 Diagnosis of hydatid cyst mainly depends on radiologic stage it is presented at. In our case, the fist presentation was with cyst rupture leaving no radiologic specification. Rupture of the cyst may explain pericardial effusion, and tamponade while secondary reactive changes in histopathology of the pericardium can explain the granulomatous changes in first episodes of the disease. Hence, after her first surgery, granulomatous changes were misleading and misdiagnosis of TB was made because of its high prevalence. However, after observing hydatid cyst and as TB occurrence in association with hydatid cyst is very rare, we also searched for granulomatous pericarditis and we found out that rupture of hydatid cyst can interestingly cause granulomatous pericarditis. Nevertheless, due to modern imaging techniques and laboratory tests, misdiagnosed HD seems unacceptable and in order to prevent the misjudgment of HD with rare localization the combination of clinical history, imaging findings and serologic test results should be collected and evaluated. Although the myocardial cystectomy may be performed without cardiac arrest or even CPB, we believed our approach would be safer due to the history of a previous pericardiectomy and cyst location.

Conclusion
In endemic areas, HD should be taken into consideration as a differential diagnosis of all cysts in all anatomic locations and even rare conditions such as pericardial tamponade. Consequently, a combination of clinical history, imaging findings, and serologic test results should be utilized in order to prevent any misdiagnosis and its related complications.

Ethical issues: This study was reviewed and confirmed by the ethics committee of Rajaei Cardiovascular Medical & Research Center.
Conflict of interests: The authors declare no conflicts of interest.

References
Pediatric Guillain-Barré Syndrome and Autonomic Dysfunction

Ertugrul Kurtoglu1*, Sevket Balta2, Yasin Karakus1, Erdogan Yasar1

1Department of Cardiology, Malatya State Hospital, Malatya, Turkey
2Department of Cardiology, Gulhane Medical School, Ankara, Turkey

Received: 20 November 2013, Accepted: 1 December 2013

Guillain-Barré syndrome (GBS), the most common cause of acute childhood paralysis worldwide, is an acute inflammatory demyelinating polyradiculoneuropathy with the ability to affect all myelinated peripheral nerves.1 Heart rate variability (HRV), which is recognized as a quantitative marker of the autonomic nervous system, may be used for the early detection of autonomic dysfunction (AD) in childhood GBS.2 However, other factors such as diabetes mellitus, thyroid disorders, higher body mass index and blood pressure may have a confounding effect on HRV.3,4 In addition, patients who are planned to undergo HRV analysis should also undergo echocardiographic evaluation to exclude valvular (mitral valve prolapsus), myocardial (dilated cardiomyopathy) and congenital (atrial septal defects) abnormalities, all of which may also potentially effect HRV.5,6 Lastly, although frequency domain indices of HRV is usually presented in absolute value of power, the representation of low frequency and high frequency in normalized unit may represent the controlled and balanced behaviour of the sympathetic and parasympathetic branches of the autonomic nervous system.7 These mentioned factors seem to have been overlooked by Samadi et al. in the “Assessment of Autonomic Dysfunction in Childhood Guillain-Barré syndrome reporting AD in half of children with mild GBS with no significant association with disease activity.”8

Commentary

Ethical issues: Not applicable
Conflict of interests: The authors declare no conflicts of interest.

References
We would like to thank Kurtoglu et al. for their kind interest and useful comments about our article.\textsuperscript{1,2} We completely agree that those factors that could affect the autonomic nervous system should be excluded in any research that involves evaluating heart rate variability. Of course we have implemented and mentioned all these exclusion criteria (age $>$ 18, history of or receiving treatment for hypertension, affected by other CNS disease, intubated patients needing any sedative drugs or intravenous inotropic support, patients with significant structural heart disease with or without cardiac arrhythmias, history of diabetes mellitus and abnormalities in thyroid function) in the original research proposal and final thesis. Unfortunately we have neglected to mention these criteria in our published article. We apologize for this oversight.

**Ethical issues:** Not applicable.

**Conflict of interests:** The authors declare no conflicts of interest.

**References**
