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Early Outcome of Fast-Track Extubation in Opium Addicted Patients after Off-Pump Coronary Artery Bypass Graft

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ABSTRACT

Background: Researchers have tried to determine a clinical Fast-Track Extubation (FTE) for an efficient and safe approach to post-operative management in high-risk patients undergoing cardiac surgery. Opium consumption is one of the risk factors for coronary artery disease and is more prevalent among the patients with heart problems.

Objective: The present study aimed to determine the early outcomes of FTE in opium addicted patients after Off-Pump Coronary Artery Bypass Graft (OPCABG) surgery.

Methods: This single-centered retrospective cohort study was conducted on the patients who had undergone OPCABG between February 2008 and February 2011. The patients were divided into opium-negative and opium-positive groups. The patients were prepared for rapid recovery, emphasizing pre-operative physiotherapy, respiratory training, low dose fentanyl anesthesia, diuretic use, and autologous blood salvage to avoid the untoward effects of allogenic blood transfusion. Significant factors in successful FTE were analyzed by multivariate regression analysis. P-values less than 0.05 were considered to be statistically significant.

Results: Mortality was higher among the opium addicted patients ($P = 0.007$). Most of the patients with extubation time > 12 hours were opium addicted ($P < 0.001$). The results of multivariate regression analysis showed that age, gender, post-operative Myocardial Infarction (MI), smoking, extubation time, transfusion, and post-operative renal complications were the significant predictors of extubation time in the opium addicted patients.

Conclusion: FTE could be successfully performed in most of the patients undergoing OPCABG. Managing addicted patients and making effort to control post-operative MI, renal complications, smoking, and extubation time are important issues for a successful FTE.

1. Background

'Opium' is a Latin word meaning "Juice". It is obtained as a white resin from the incised unripe fruit of the poppy plant Papaver somniferous (1). The prevalence of opium addiction is high in Coronary Artery Disease (CAD) (2) and respiratory diseases like tuberculosis, Chronic Obstructive Pulmonary Disease (COPD), asthma, and bronchiectasis where it is used to suppress cough (3). Opium use has been known as a risk factor for CAD and respiratory track disease in several studies (4, 5). Opium consumption as a medical remedy is particularly more prevalent among the patients with heart problems. These patients generally use opium to manage their cardiac disease, while this widespread careless use has increased the risk of CAD (6).

With the improvements in anesthesia and surgical techniques, Fast-Track Extubation (FTE) has become of great interest because of its safety and low cost (7). This approach was first applied in 1990s when the insurance system was focused on the methods for reducing costs and improving hospital efficiency (8, 9). The advantages of FTE after cardiac surgery have been well established (10). Several studies (11-14) have also tried to find fast-track pathways as a safe and effective method to reduce post-operative complications after Coronary Artery Bypass Graft (CABG) surgery. The ability to identify high-risk patients and operative risk factors may help develop surgical and medical modifications, which allow FTE.

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2. Objectives

In general, most of the patients with CAD are opium users. Considering the relationship between opioid consumption and cardiovascular complications, the present study aims to determine the early outcomes of FTE in opium addicted patients after Off-Pump Coronary Artery Bypass Graft (OPCABG) surgery.

3. Patients and Methods

3.1. Patient Population

This single-centered retrospective cohort study was conducted on the patients who had undergone OPCABG surgery between February 2008 and February 2011. This study was approved by the Ethics Committee of Kermanshah University of Medical Sciences. The study data were collected through census. All the patients had been operated by a single surgeon. The patients who had undergone other procedures such as valve repair or replacement and left ventricular aneurysm resection as well as those with Ejection Fraction (EF) less than 25%, congestive heart failure or pulmonary edema during attendance in the Intensive Care Unit (ICU), sever COPD, hemodynamic instability, severe arrhythmia, inotropic drug usage (> 5 micro/min), Intra-Aortic Balloon Pump (IABP) insertion, core temperature below 35 ^{o}C, and inadequate spontaneous ventilation were excluded from the study. The patients were divided into opium-negative and opium-positive groups. The study followed the protocol of a short post-operative intubation time and rapid physical rehabilitation. The day before the operation, the patients were trained by an experienced nurse to manage post-operative positive pressure respiration, coughing, respiratory toilet, and respiratory physiotherapy. They were also provided with detailed instructions for chest physiotherapy. If post-operative bleeding fulfilled the criteria for re-exploration, the patients were explored during the first 3 - 4 hours post-operatively and were then planned for extubation. If bleeding occurred late (first 10 hours) after attendance in the ICU, the patients were sedated and excluded from the study. Radial arterial pressure and central venous pressure from the subclavian vein were monitored in all patients. In the next morning, the mediastinal drains and venous and arterial lines were removed. The patients who had clear fluids were transferred to the ward sitting on their beds. From the second post-operative day, the patients were allowed to move freely in the surgical ward. The definition of a fully mobile patient was made when s/he was able to climb stairs or work outdoors without assistance.

3.2. Surgical Technique

The day before the operation, the patients were trained by an experienced nurse to manage post-operative positive pressure respiration, coughing, pulmonary toilet, and respiratory physiotherapy. They were also provided with detailed instructions regarding chest physiotherapy. All patients were operated with median sternotomy and using the standard technique of Cardiopulmonary Bypass (CPB) with off-pump technique, as previously described (15, 16). FTE was planned for all the patients who stayed in the ICU. The anesthetic operation technique was selected in order to facilitate FTE regardless of pre-operative morbidity conditions. The induction was started by the continuous infusion of fentanyl and was followed by a single shot of atracurium for muscle paralysis. Anesthesia was then maintained by further continuous fentanyl infusion and by inhaled isoflurane with an oxygen and air mixture at 1:1 ratio. Atracurium was also administrated continuously for muscle relaxation. Serial electrocardiograms and estimation of serum Creatinine Phosphokinase Myocardial Band (CPK MB) were assessed to detect perioperative ischemia.

3.3. Anesthesia

The anesthesia protocol was designed based on a discussion among cardiac surgeons, ICU attending physicians, nursing staff, and respiratory therapists to permit FTE and included a combination of midazolam (0.1 mg kg-1), fentanyl (5 mg kg-1), and pancuronium supplemented with isoflurane. Hypertension was controlled by trinitroglycerin and tachycardia was controlled by application of esmolol. Intra-operative monitoring included an electrocardiograph with ST segment analysis, continuous arterial blood pressure measurement, intermittent blood gas analysis, and measurement of body temperature. The following criteria were used for extubation: being awake and responsive, satisfactory blood gases (PO2 > 60 mmHg, PCO2 < 45 mmHg), adequate spontaneous ventilation based on clinical ventilation, stable hemodynamic conditions with no or minimum inotropic drugs, and chest tube drainage less than 100 ml per hour.

Anesthesia was gradually reduced and terminated after transfer to ICU. For pain management, diclofenac was administrated as a suppository. Normothermia of the patients was also secured by increasing the room temperature and using heating mattresses. Contraindications for immediate post-operative extubation were congestive heart failure, core temperature below 35^{o}C, and inadequate spontaneous ventilation.

3.4. Statistical Analysis

The data have been presented as mean ± SD. Discrete variables were summarized by percentages. Multiple linear regression analysis was used to predict the variables associated with early or prolonged extubation. The patients were also divided into two groups with respect to their extubation times (≤ 12 and > 12 hours). Significant variables with P-values less than 0.1 in the univariate analysis were entered into the logistic regression analysis. All data analyses were carried out by the SPSS software, version 20 and P-values less than 0.05 were considered to be statistically significant.

4. Results

Comparison of the opium addicted and non-addicted patients regarding the study variables has been presented in Table 1. Accordingly, opium addicted patients were younger (P < 0.001) and had lower EF (P < 0.001). In addition, the incidence of Atrial Fibrillation (AF), stroke, reintubation, IABP insertion, hypertension, smoking, post-operative MI, post-operative inotrope drug use, post-operative renal

Table 1. Perioperative Characteristics in Addicted and Non-Addicted Patients

Variables	Opium-Negative Patients (N = 1164)	Opium-Positive Patients (N = 325)	P-value
Age (y)	60.7 ± 9.8	56.2 ± 10.1	0.001
Male/female (%)	69.6%/95.5%	30.4%/4.1%	< 0.001
Weight	71.3 ± 12.8	74.8 ± 11.3	< 0.001
EF	43 ± 11%	39 ± 11%	< 0.001
Diabetes	(351.5) 30.2%	(92.6) 28.5%	0.581
Hypertension	(180) 19.7%	(70) 25.7%	< 0.001
AF	(38.4) 3.3%	(48.42) 14.9%	< 0.001
Pre-operative MI	(24.4) 2.1%	(32.8) 10.1%	0.001
Smoking	(204.8) 17.6%	(260.3) 80.1%	< 0.001
Stroke	(13) 1.4%	(9) 3.3%	0.044
IABP	(12) 1.3%	(21) 7.6%	< 0.001
Reintubation	(17) 1.8%	(18) 6.8%	0.005
In-hospital respiratory apnea	(3) 0.3%	(21) 7.7%	< 0.001
Post-operative respiratory infection	(17) 1.8%	10.8 ± 5.6	< 0.001
Post-operative MI	(40.74) 3.5%	(17.8) 5.5%	0.120
Post-operative transfusion	0.9 ± 1.3	1.02 ± 1.5	0.589
Post-operative bleeding	536 ± 657	567 ± 310	0.505
Post-operative inotropic drug use	(17) 1.8%	(18) 6.5%	< 0.001
Post-operative renal complications	(14) 1.5%	(17) 6.29%	< 0.001
COPD	(34) 3.7%	(33) 12%	< 0.001
Intubation time	11.5 ± 5.5	15.9 ± 9.8	< 0.001
Number of grafts	2.7 ± 0.6	2.6 ± 0.5	0.022
Length of hospital stay	9.5 ± 2.6	10.8 ± 5.6	0.007
ICU stay	25.9 ± 7	27.5 ± 5.7	< 0.001
Mortality	(13) 1.4%	(11) 4%	0.007

Data have been given as mean ± SD or number (%).
Abbreviations: COPD, chronic obstructive pulmonary disease; EF, ejection fraction; AF, atrial fibrillation; IABP, intra-aortic balloon pump; MI, myocardial infraction; ICU, intensive care unit

Table 2. The Predictors of Extubation Time in the Addicted Patients by Multivariate Linear Regression Analysis

Variables	OR	95% CI	P-value
Age (y)	0.059	0.011 - 0.986	0.044
Gender (Female/Male)	0.122	0.045 - 1.998	< 0.001
Weight	0.099	0.084 - 2.551	< 0.001
EF	0.786	0.111 - 1.009	< 0.001
Post-Operative MI	1.004	0.176 - 3.006	0.004
Diabetes	0.145	0.045 - 0.789	0.050
Opium Usage	2.045	0.651 - 3.441	0.004
Number of Grafts	0.076	0.056 - 1.098	< 0.001
Transfusion	0.034	0.011 - 0.859	0.044
AF	0.127	0.063 - 1.002	0.009
IABP	5.576	1.067 - 10.084	0.016
Stroke	1.432	0.453 - 4.080	< 0.001
Hospital Stay	-0.061	-0.115 - 0.007	0.026
Inotropic Drugs Use	0.061	0.032 - 0.091	< 0.001

Abbreviations: EF, ejection fraction; AF, atrial fibrillation; IABP, intra-aortic balloon pump; MI, myocardial infraction

complications, post-operative respiratory infection, COPD, length of ICU stay, and intubation time were higher in the opium addicted patients.

The results of multivariate linear regression analysis (Table 2) indicated that age, gender, weight, EF, post-operative MI, opium use, number of grafts, transfusion, AF, IABP, stroke, reintubation, post-operative renal complications, and inotrope use were associated with longer extubation time. The results of multivariate logistic regression (Table 3) also revealed that age, gender, post-operative MI, smoking, extubation time, transfusion, and post-operative renal complications were the significant predictors of extubation time in opium addicted patients.

Based on the results presented in Table 4, the patients with higher age, opium usage, post-operative bleeding, transfusion volume, IABP insertion, Cardiovascular Accident (CVA), reintubation, AF, inotropic usage, longer hospital stay, greater number of grafts, smoking, post-operative MI, renal complications, respiratory apnea, and post-operative respiratory infection had an extubation time > 12 hours. Moreover, mortality was higher, while EF was lower among the patients with extubation time > 12 hours.

Table 3. The Results of Multivariate Logistic Regression Analysis for the Addicted Patients

Variables	OR	95% CI	P-value
Age (year)	0.963	0.945 - 0.981	< 0.001
Gender (%)	0.305	0.159 - 0.584	< 0.001
Post-operative MI (%)	3.499	1.337 - 9.160	0.011
Smoking (%)	13.439	9.1000 - 19.856	< 0.001
Extubation time (%)	1.078	1.076 - 1.111	< 0.001
Transfusion (%)	0.865	0.745 - 0.999	0.049
AF	5.045	1.874 - 13.631	0.001

Abbreviations: AF, atrial fibrillation; MI, myocardial infarction

Table 4. The Comparison of the Two Groups with Respect to Extubation Time

	Extubated (≤ 12 hr) (N = 1164)	Extubated (> 12 hr) (N = 325)	P-value
Variables			
Age (y)	59.180 ± 9.5	60.751 ± 10.8	0.001
Opium use	17% (132)	34.3%(144)	< 0.001
Post-operative bleeding	488.108 ± 638	643.976 ± 783	< 0.001
Transfusion volume	0.717 ± 0.98	1.478 ± 1.7	< 0.001
IABP	0%	7.9%(33)	0.001
CVA	0.8% (6)	3.8%(16)	< 0.001
Male/female	67.7/32.3	78.1/21.9	< 0.001
Diabetes	29.7% (230)	29.3% (123)	0.765
ICU stay (hours)	26.178 ± 6.9	26.497 ± 6.4	0.153
EF	44.490 ± 10.8	38.938 ± 12.7	< 0.001
Reintubation	0. 9% (7)	6.7% (28)	< 0.001
AF	1.7% (13)	13.3% (56)	< 0.001
Inotropic drug using	0.9% (7)	6.7% (28)	< 0.001
Mortality	1.2% (9)	3.6% (15)	0.05
Hospital stay	9.452 ± 2.7	10.231 ± 4.7	< 0.001
Number of grafts	2.807 ± 0.5	2.695 ± 0.670	< 0.001
Hypertension	19.6% (152)	23.8% (100)	0.091
COPD	4.6% (36)	7.4% (31)	0.055
Smoking	28.5% (225)	38.8% (163)	< 0.001
Post-operative MI	2.2% (17)	7.1% (30)	< 0.001
Renal complications	1% (8)	5.5% (23)	0.007
Respiratory apnea	0.5% (4)	4.8% (20)	< 0.001
Post-operative respiratory infection	0.9% (7)	7.9% (33)	< 0.001

Abbreviations: COPD, chronic obstructive pulmonary disease; EF, ejection fraction; AF, atrial fibrillation; IABP, intra-aortic balloon pump; MI, myocardial infraction; ICU, intensive care unit; CVA, cardiovascular accident

5. Discussion

The results of the current study showed that FTE after cardiac surgery reduced the length of ICU stay and the subsequent hospital costs. Diagnosis of high-risk patients and risk factors make it possible to accelerate the extubation time. The study results revealed a significant association between opium addiction and delay in extubation time. The results also showed that age and EF were lower in the opium addicted patients compared to the non–addicted ones. As illustrated in Table 4, lower EF and higher opium usage increased the duration of extubation. A previous study also indicated that opium addiction reduced the average age in heart disease (17). Similarly, Wong et al. reported that advanced age, gender, IABP, inotropes, excessive bleeding, and atrial arrhythmia were the risk factors associated with delayed extubation time in CABG patients (18).

According to Table 2, the results of univariate analysis showed that among the pre-operative variables, age, gender, EF, diabetes, pre-operative MI, hypertension, COPD, number of grafts, transfusion, IABP, stroke, length of hospital stay, inotrope use, and post-operative apnea had a significant effect on prediction of extubation time. Cheng et al. also reported that age, inotrope drugs, IABP, and arrhythmia were the predictors of unsuccessful extubation (11). Ott R.A. et al. (19) described their results of FTE among elderly patients. They found that age was not a risk factor for early extubation (19). In contrast, the present study results indicated that elderly patients (> 70 years) had a longer extubation time (44.1% > 12 hours) compared to the younger ones (33.7% > 12 hours). The presence of significant differences in morbidities in the elderly patients in the current study compared to a similar study using the on-pump method clearly support the benefits of off-pump surgery in older patients.

Stroke is an important complication after CABG. The incidence of stroke in OPCABG has been reported to be 0.3 - 2% (20). Despite preventive efforts, such as Doppler examination of the carotid artery, ascending aorta for calcification, and intra-operative palpation for calcified plaque, this complication is an unavoidable post-surgical

event (21). In the current study, stroke occurred in 3.3% of the opium-addicted patients in comparison to 1.4% of the non-addicted ones. The results demonstrated that pre-operative and intraoperative patient profiles were of limited utility in predicting the likelihood of post-operative stroke. A previous study (22) showed that increased age was an important risk factor for stroke, but this was not confirmed in the current study. Thus, unknown factors, such as thrombophilia, predisposition of OPCABG patients to thrombosis, or low dose of consumed heparin, might explain the difference in the incidence of CVA in younger patients with OPCABG compared to elderly patients with on-pump CABG.

Early extubation after surgery is a main step for rapid post-operative recovery and may reduce the need for longer ICU care due to the lower need for high doses of opioids for anesthesia and overnight sedation. In the present study, the addicted patients were weaned off the ventilator post-operatively at a mean of 15.9 ± 9.8 hours in comparison to 11.5 ± 5.5 hours in the non-addicted patients ($P < 0.001$). The threshold for re-exploration was chest tubes drainage > 300 mL/h for two hours or 1000 ml in total in order to avoid the transfusion of large allogeneic blood products. Therefore, most of the patients were re-explored shortly after the operation and 50% of them could be weaned off the ventilator within six hours after the initial operation. The impetus for FTE in our center is primarily the limited number of ICU beds in contrast to others cardiac centers, which is an economic issue. Leslie K et al. also reported that FTE reduced the CABG surgery costs by 25% (23).

Opium usage was one of the important causes of unsuccessful FTE in the present study patients. Nonetheless, opium use has not been reported as a risk factor for prolonged intubation in the previous studies. Opium has many components likes codeine, morphine, oxycodone, methadone, and papaverin and its deficit cannot be compensated merely by drugs, such as morphine and methadone. Oral use of opium increases its serum level and may be associated with post-operative apnea. FTE is an important step for fast post-operative rehabilitation and may reduce the need for long intensive care to a large number of patients. Cheng et al. (11), Arom et al. (24), and Hickey et al. (25) disclosed that FTE reduced pulmonary complications, encouraged early mobilization, and shortened the length of hospital stay. Furthermore, FTE improved post-extubation intra pulmonary shunt fraction and might avoid over-sedation and the resultant depression of the respiratory center that prolongs the ICU stay (11).

It has been reported that operation on the beating heart was accompanied with lower post-operative complications, thereby reducing the length of ICU stay (26). The profiles of the present study patients indicated that conventional CABG via the off-pump method did not necessarily require complicated and costly resources. Indeed, short ICU and hospital stay has been often considered as a criterion for successful treatment. Lee et al. found that FTE was more cost-effective after CABG surgery (27). However, no studies in the medical literature have evaluated the costs of FTE complications after CABG surgery. In these conditions, patients are normally kept in the hospital in order to fulfil the demands for medical, social, and emotional well-being. With the application of a common philosophy for all steps during and after operation, extubation within 12 hours was attainable and safe in the majority of the patients undergoing OPCABG. In the present study, all surgeries had been performed using the off-pump technique. This method is performed within a shorter time period in comparison to CPB. A previous study demonstrated that prolonged duration of surgery and CPB increased the risk of delayed extubation (26).

The limitations of the current study included its retrospective design and small number of patients. Although these limitations did not permit to conclude a decisive response, the study results indicated that age, gender, EF, diabetes, pre-operative MI, hypertension, COPD, number of grafts, transfusion, IABP, stroke, length of hospital stay, inotrope use, and post-operative apnea had a significant effect on the prediction of extubation time. The results also revealed that pre-operative or intraoperative patient profiles and findings were of limited utility in predicting the likelihood of post-operative stroke. Overall, FTE after cardiac surgery enhanced the cardiac function, reduced the length of ICU stay and the subsequent costs, and improved outcomes.

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Authors' Contribution

A.H., F.S. and A.A. contributed to the development of the original idea and the protocol, abstracted and analyzed the data, and prepared the manuscript.

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References

1. Rastogi V. *Modern Biology*. Pitambar Publishing; 1997.
2. Masoumi M, Shahesmaeili A, Mirzazadeh A, Tavakoli M, Ali AZ. Opium addiction and severity of coronary artery disease: a case-control study. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences*. 2010;**15**(1):27-32.
3. Morice AH, Menon MS, Mulrennan SA, Everett CF, Wright C, Jackson J, *et al*. Opiate therapy in chronic cough. *American journal of respiratory and critical care medicine*. 2007;**175**(4):312-5.
4. Najafipour H, Masoomi M, Shahesmaeili A, Haghdoost AA, Afshari M, Nasri HR, *et al*. Effects of opium consumption on coronary artery disease risk factors and oral health: Results of Kerman Coronary Artery Disease Risk factors Study a population-based survey on 5900 subjects aged 15-75 years. *International journal of preventive medicine*. 2015;**6**:42.
5. Rahmati A, Shakeri R, Khademi H, Poutschi H, Pourshams A, Etemadi A, *et al*. Mortality from respiratory diseases associated with opium use: a population-based cohort study. *Thorax*. 2017;**72**(11):1028-34.
6. Farahani MA, Ghaffari F, Seyed Fatemi N. Opium addiction in patients with coronary artery disease: a grounded theory study. *Medical journal of the Islamic Republic of Iran*. 2015;**29**:267.
7. Reis J, Mota J, Ponce P, Costa-Pereira A, Guerreiro M. Early

extubation does not increase complication rates after coronary artery bypass graft surgery with cardiopulmonary bypass. *European journal of cardio-thoracic surgery*. 2002;**21**(6):1026-30.
8. Hawkes C, Foxcroft DR, Yerrell P. Clinical guideline for nurse-led early extubation after coronary artery bypass: an evaluation. *Journal of advanced nursing*. 2010;**66**(9):2038-49.
9. Pande RU, Nader ND, Donias HW, D'Ancona G, Karamanoukian HL. REVIEW: Fast-Tracking Cardiac Surgery. *The heart surgery forum*. 2003;**6**(4):244-8.
10. Cheng DC, Karski J, Peniston C, Raveendran G, Asokumar B, Carroll J*, et al*. Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. A prospective, randomized, controlled trial. *Anesthesiology*. 1996;**85**(6):1300-10.
11. Cheng DC, Karski J, Peniston C, Asokumar B, Raveendran G, Carroll J*, et al*. Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: a prospective randomized controlled trial. *The Journal of thoracic and cardiovascular surgery*. 1996;**112**(3):755-64.
12. Engelman RM, Rousou JA, Flack JE, 3rd, Deaton DW, Humphrey CB, Ellison LH*, et al*. Fast-track recovery of the coronary bypass patient. *The Annals of thoracic surgery*. 1994;**58**(6):1742-6.
13. Myles PS, Daly DJ, Djaiani G, Lee A, Cheng DC. A systematic review of the safety and effectiveness of fast-track cardiac anesthesia. *Anesthesiology*. 2003;**99**(4):982-7.
14. Paone G, Higgins RS, Havstad SL, Silverman NA. Does age limit the effectiveness of clinical pathways after coronary artery bypass graft surgery? *Circulation*. 1998;**98**(19 Suppl):II41-5.
15. Sabzi F, Asadmobini A, Ghasemi F. In-hospital outcome of patients undergoing off-pump coronary artery bypass graft with and without coronary endarterectomy. *Res Cardiovasc Med*. 2017;**6**:e38872.
16. Sabzi F, Hemati N, Zokaei AH, Moradi G, Dabiri S. Off-pump coronary bypass grafting causing stunned myocardium. *The Journal of Tehran University Heart Center*. 2012;**7**(3):143.
17. Reece AS, Hulse GK. Impact of lifetime opioid exposure on arterial stiffness and vascular age: cross-sectional and longitudinal studies in men and women. *BMJ open*. 2014;**4**(6):e004521.
18. Wong DT, Cheng DC, Kustra R, Tibshirani R, Karski J, Carroll-Munro J*, et al*. Risk factors of delayed extubation, prolonged length of stay in the intensive care unit, and mortality in patients undergoing coronary artery bypass graft with fast-track cardiac anesthesia: a new cardiac risk score. *Anesthesiology*. 1999;**91**(4):936-44.
19. Ott RA, Gutfinger DE, Miller MP, Selvan A, Codini MA, Alimadadian H*, et al*. Coronary artery bypass grafting "on pump": role of three-day discharge. *The Annals of thoracic surgery*. 1997;**64**(2):478-81.
20. Chen JW, Lin CH, Hsu RB. Mechanisms of early and delayed stroke after systematic off-pump coronary artery bypass. *Journal of the Formosan Medical Association = Taiwan yi zhi*. 2015;**114**(10):988-94.
21. Fukuda I, Gomi S, Watanabe K, Seita J. Carotid and aortic screening for coronary artery bypass grafting. *The Annals of thoracic surgery*. 2000;**70**(6):2034-9.
22. Kiessling AH, Huneke P, Reyher C, Bingold T, Zierer A, Moritz A. Risk factor analysis for fast track protocol failure. *Journal of cardiothoracic surgery*. 2013;**8**:47.
23. Leslie K, Sessler DI. The implications of hypothermia for early tracheal extubation following cardiac surgery. *Journal of cardiothoracic and vascular anesthesia*. 1998;**12**(6 Suppl 2):30-4; discussion 41-4.
24. Arom KV, Emery RW, Petersen RJ, Schwartz M. Cost-effectiveness and predictors of early extubation. *The Annals of thoracic surgery*. 1995;**60**(1):127-32.
25. Hickey RF, Cason BA. Timing of tracheal extubation in adult cardiac surgery patients. *Journal of cardiac surgery*. 1995;**10**(4 Pt 1):340-8.
26. Totonchi Z, Baazm F, Chitsazan M, Seifi S, Chitsazan M. Predictors of prolonged mechanical ventilation after open heart surgery. *Journal of cardiovascular and thoracic research*. 2014;**6**(4):211-6.
27. Lee JH, Kim KH, vanHeeckeren DW, Murrell HK, Cmolik BL, Graber R*, et al*. Cost analysis of early extubation after coronary bypass surgery. *Surgery*. 1996;**120**(4):611-7; discussion 7-9.