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Fast track recovery of high risk coronary bypass surgery patients☆

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Abstract

Objective: Fast track recovery protocols on younger, low risk patients result in shorter hospital stays and decreased costs. However, data is lacking on the impact of these protocols on high risk patients based on an objective scoring system. **Methods**: In this study, a high risk cohort of patients (EuroSCORE ≥ 6, $n = 158$) was compared with a low risk cohort of patients (EuroSCORE < 6, $n = 1004$) to define the safety and efficacy of fast track recovery among high risk patients. A standard perioperative data is collected prospectively for every patient. **Results**: Time to extubation was longer in the high risk group (299 ± 253 vs. 232 ± 256 min; $P = 0.003$), but intensive care unit (ICU) stay (25.6 ± 28.7 vs. 21.5 ± 9.4 h; $P =$ ns), and postoperative length of stay (5.8 ± 2.4 vs. 5.6 ± 2.7 days; $P =$ ns) was similar when compared with the low risk group. Of the high risk patients 81% were extubated within 6 h, 87% were discharged from the intensive care unit within 24 h, and 67% were discharged from the hospital within 5 days. Multiple regression analysis showed that any red blood cell transfusion ($P = 0.02$), and cross clamp time >60 min ($P = 0.03$) were the predictors of delayed extubation (≥ 6 h) in the high risk group. The predictors of extended ICU stay were any red blood cell transfusion ($P = 0.0001$), and peripheral vascular disease ($P = 0.05$). Any red blood cell transfusion was the only predictor for mortality ($P = 0.02$) and readmission to the hospital within the first 30 days ($P = 0.02$) in this cohort of patients. **Conclusions**: This study confirms the safety and efficacy of fast track recovery protocol among high risk patients undergoing coronary artery bypass surgery. All patients are basically suitable for fast track recovery and the preoperative risk factors are poor predictors of prolonged ventilation, increased ICU and hospital stay. Red blood cell transfusion is associated with delayed extubation and discharge from the ICU, and increased mortality and hospital readmission rate.
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Keywords: Coronary artery bypass grafting; High risk; Fast track recovery

1. Introduction

Over the last decade, increased financial restrictions imposed on the medical profession have prompted the search for new methods of anesthesia and postoperative care allowing faster recovery of the cardiac surgical patients. These selected patients are targeted for extubation within 6–8 h of the completion of cardiac procedure, an intensive care unit (ICU) length of stay less than 24 h, and total hospital length of stay of 4–6 days [1–6]. Fast track recovery protocols (FTRP) on younger, low risk patients result in shorter hospital stay and decreased costs [4,6]. There are few studies, which focused on the safety and efficacy of these protocols among different isolated high risk patient populations (e.g. advanced age, and poor left ventricular function) and cardiac procedures other than coronary artery bypass grafting (CABG) [7–10]. However, data is lacking on the impact of FTRP on high risk patients based on an objective scoring system. In this study, a high risk cohort of patients was compared with a low risk cohort of patients to define the safety and efficacy of fast track recovery among high risk patients.

2. Materials and methods

2.1. Patient selection and data collection

In February 1999, we instituted a FTRP for all patients

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undergoing cardiac surgery. Our objectives were to extubate cardiac surgical patients within 6 h of ICU arrival and discharge them from the ICU within 24 h and from the hospital in 5 days without compromising the quality of care. A standard perioperative data is collected prospectively for every patient undergoing cardiac surgery at our institution. The dataset includes five different sections to be filled in consecutively by the anesthetist, the surgeon, the perfusionist, the ICU, and the ward nurses. This report analyses data for patients having on-pump isolated CABG between February 1999 and December 2001. During that time period, 1162 consecutive patients underwent isolated CABG. All patients were preoperatively scored using EuroSCORE. The definitions for the risk factors were described elsewhere [11]. EuroSCORE was less than six in 1004 patients which constituted the low risk group, and more than or equal to six in 158 which constituted the high risk group. No patient was excluded from the study for any reason.

2.2. Anesthesia and operative technique

Midazolam 125 μg/kg IM was used for premedication. Anesthetic induction consisted of midazolam 50 μg/kg, pancronium 0.15 mg/kg, and fentanyl 25–35 μg/kg. After endotracheal intubation, 50% O_2, 50% N_2O, and 3–4% desflurane was used for all hemodynamically stable patients. Desflurane and N_2O were discontinued at times of hemodynamic instability. Maintenance anesthesia and muscle relaxation was accomplished with midazolam and vecuronium 80 μg/kg/h. Furosemid 0.5 mg/kg was routinely administered. During cardiopulmonary bypass (CPB) hematocrit, mean arterial pressure, and pump flow was kept between 20 and 30%, 50–80 mmHg, and 2.2–2.5 l/m^2, respectively. Adequacy of tissue perfusion was monitored with arterio-venous partial carbondioxide difference ($P_{v-a}CO_2$), lactate level, urine output, and base deficit. Moderate hypothermia was used during CPB and midazolam and vecuronium dose was decreased to 60 μg/kg/h when the body temperature reached to 32°C. Myocardial viability was preserved with topical hypothermia and antegrade cold hyperkalemic crystalloid cardioplegia (Plegisol®, Abbott Laboratories, IL, USA) except in patients with an left ventricular ejection fraction less than 0.25 in whom antegrade + retrograde blood cardioplegia associated with terminal warm blood cardioplegia was used. During rewarming midazolam and vecuronium dose was increased back to 80 μg/kg/h. After the termination of CPB midazolam and vecuronium dose was decreased to 50 μg/kg/h and discontinued at skin closure.

2.3. Postoperative clinical management

On arrival in the ICU, patients were placed on mechanical ventilation. The ventilator mode was switched to SIMV + pressure support and ventilator settings were adjusted as: respiratory rate 12/min, tidal volume 8–10 ml/kg, FIO_2:0.6, PEEP 0–5 mmHg, pressure support 10 mmHg, and trigger sensitivity −2 cm H_20. All patients were warmed with forced air warming until the rectal temperature reached 37°C. Meperidine 0.4 mg/kg IV to a total dose of 50 mg over 6 h, was used to treat shivering. All patients were evaluated for extubation every half an hour. As soon as the spontaneous breathing resumed respiratory rate was gradually decreased to 4/min and pressure support to 4 mmHg. If there were no contraindications for the use of beta-blockade, metoprolol was used intravenously to control hypertension. All hemodynamically stable patients without excessive chest tube drainage and $PaCO_2$ <48 mmHg, pH >7.30, and PaO_2/FIO_2 >250 were extubated. After the patient was extubated, 40–50% oxygen was administered by face mask. Oxygen hemoglobin saturation and the respiratory rate were continuously monitored. Arterial blood gases were obtained at 30, 60, and 120 min postextubation. Repeated doses of diclofenac sodium 1.25 mg/kg IM was used for postoperative analgesia. Patients over 70 years with a hemoglobin value less than 8 g/dl, and patients aged 70 years or less with a hemoglobin value less than 7 gr/dl received packed red blood cells. We aimed to discharge all patients on the fifth postoperative day. The decision to discharge is based on a satisfactory routine checkup on day 4 consisting of clinical examination, full blood cell count, urea and electrolyte levels, electrocardiogram, and chest roentgenogram. If the patient is medically unfit on day 5, hospitalization is prolonged, and further investigations may be performed depending on the clinical status. As the objective of our FTRP was to extubate the patients within 6 h of the completion of cardiac procedure, to discharge from the ICU within 24 h, and to discharge from the hospital on fifth postoperative day, these time points were taken as reference in this study.

2.4. Definitions

Data characterizing perioperative clinical outcome were entered prospectively. Hospital mortality included all deaths within 30 days of operation irrespective of where the death occurred and all deaths in the hospital after 30 days among patients who had not been discharged after the operation. Postoperative blood loss was defined as total chest tube drainage. Neurological complication included permanent and transient strokes. Renal complication included acute renal failure, defined as the requirement of hemodialysis or an elevated creatinine level (>200 μmol/l). Pulmonary complication included chest infection, ventilation exceeding 24 h, reintubation, and tracheostomy. Infective complication included septicemia and sternal and leg wound infections, defined by positive culture and requirement of antibiotic therapy.

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2.5. Statistical analysis

Data are reported as a percentage or as a mean ± standard deviation. Univariate comparisons were computed using the χ^2 test or Fisher's exact test for categorical variables and *t* tests for continuous variables. Any factor that showed evidence to increase the time to extubation (>6 h), ICU length of stay (>24 h), and hospital length of stay (>5 days) with a *P* value of less than 0.1 were entered into multiple logistic regression. Statistical analysis was performed using SPSS statistical software (SPSS Inc., Chicago, IL). Variables were considered significant at *P* values less than 0.05.

3. Results

Single team carried out all of the operations. Of the 158 patients in the high risk group eight patients (5.1%) had two, 68 patients (43%) had three, 45 patients (28.5%) had four, 23 patients (14.6%) had five, and 14 patients (8.8%) had six to ten risk factors. In the low risk group, 149 patients (14.8%) had no, 377 patients (37.5%) had one, 320 patients (31.9%) had two, 148 patients (14.7%) had three, and ten patients (1.0%) had four risk factors.

The distributions of a number of prognostic variables are shown in Table 1. All of the prognostic characteristics except hypertension and hypercholesterolemia were distributed unevenly between groups ($P < 0.05$). Interestingly, only current smokers were significantly much more in the low risk group.

The distributions of outcomes between groups are presented in Table 2. The high risk patients were extubated approximately 1 h later on average, had more pulmonary complications, and had more red blood cell transfusions compared to the low risk group. New onset renal failure, ICU readmission, and mortality rates were also significantly higher in the high risk group. Factors leading to increased ventilation (>6 h), ICU stay (>24 h), postoperative length of stay (>5 days), and mortality on univariate analysis are shown in Tables 3–6, respectively. Multiple regression analysis showed that age >70 years ($P = 0.02$; OR = 1.1, 95% CI 0.6–1.5), any red blood cell transfusion ($P = 0.0001$; OR = 1.7, 95% CI 1.2–2.2), total chest tube output >1000 ml ($P = 0.0001$; OR = 2.1, 95% CI 1.6–2.6), and chronic renal failure ($P = 0.003$; OR = 2.1, 95% CI 1.1–3.0 were the predictors of delayed extubation (≥6 h) in the low risk group; and any red blood cell transfusion ($P = 0.02$; OR = 1.2, 95% CI 0.4–2.0), and cross clamp time >60 min ($P = 0.03$; OR = 1.2, 95% CI 0.2–2.3) in the high risk group. Any red blood cell transfusion ($P = 0.01$; OR = 1.6, 95% CI 1.0–2.2), and

Table 1
Distributions of prognostic variables[a]

Prognostic variable	Low risk group ($n = 1004$)	High risk group ($n = 158$)	*P* value
Age at operation (years)	59 ± 9	68 ± 8	0.001
≥70 years (%)	12.2	48.7	0.001
Female sex (%)	19	36.7	0.001
EuroSCORE	2.4 ± 1.6	7.9 ± 2.6	0.001
Unstable angina (%)	23.6	51.9	0.001
NYHA Class 3 or 4 (%)	7.4	23.4	0.001
Congestive heart failure (%)	3	13.3	0.001
Previous myocardial infarction (%)	39.8	57.6	0.001
Myocardial infarction <90 days (%)	12.8	18.4	0.001
Diabetes (%)	17.7	26	0.02
Hypercholesterolemia (%)	34.4	29.1	ns
Hypertension (%)	38.3	46.2	ns
Current smoker (%)	69.7	52.5	0.001
Chronic renal failure (%)	1.9	7	0.001
COPD (%)	8.6	17.1	0.001
Peripheral vascular disease (%)	5.9	13.9	0.001
Preoperative IV nitroglycerin (%)	4.5	33.5	0.001
Preoperative IV inotrope (%)	0	1.3	0.01
Preoperative heparin infusion (%)	3.6	25.9	0.001
Ejection fraction 0.30–0.50 (%)	26.7	37.3	0.001
Ejection fraction <0.30 (%)	2.7	32.3	0.001
Cardiogenic shock (%)	0	1.3	0.001
Preoperative ventilatory support (%)	0	1.3	0.02
Operative priority			
Urgent (%)	1.9	25.3	0.001
Emergent (%)	4.7	5.7	0.001
Salvage (%)	–	5.7	0.001
Reoperation (%)	1.5	3.8	0.04

[a] NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease; IABP, intraaortic balloon pump; ns, not significant.

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Table 2
Distributions of outcomes

Outcome	Low risk group	High risk group	*P* value
Bypass time >90 min (%)	8.7	11.5	ns[a]
Cross clamp time >60 min (%)	14.1	18.7	ns
Number of distal anastomoses	2.8 ± 1	2.9 ± 1	ns
Time to extubation (min)	232 ± 256	299 ± 253	0.003
Post operative blood loss >1000 ml (%)	9.9	13.4	ns
Intensive care unit stay (hour)	21.5 ± 9.4	25.6 ± 28.7	ns
Pulmonary complication (%)	1.2	3.8	0.04
Renal complication (%)	0.2	2.5	0.01
Neurological complication (%)	0.5	1.3	ns
Infective complication (%)	0.5	1.9	ns
Any red blood cell transfusion (%)	19.9	37.3	0.001
Intensive care unit readmission (%)	2	5.1	0.04
Postoperative length of stay (day)	5.6 ± 2.7	5.8 ± 2.4	ns
Ventilated >6 h (%)	7.4	19.1	0.001
Intensive care unit stay >24 h (%)	4.3	13.3	0.001
Postoperative length of stay >5 days (%)	25.6	33.3	0.05
Hospital readmission (%)	2.3	2.5	ns
Mortality (%)	0.6	3.2	0.01

[a] ns, not significant.

total chest tube output >1000 ml ($P = 0.001$; OR = 1.9, 95% CI 1.2–2.5) were the predictors of extended ICU stay in the low risk, and any red blood cell transfusion ($P = 0.0001$; OR = 1.9, 95% CI 0.9–3.0) in the high risk patients. Preoperative IV nitroglycerin ($P = 0.04$; OR = 0.9, 95% CI 0.3–1.5) and heparin infusion ($P = 0.004$; OR = 1.1, 95% CI 0.4–1.8) were the predictors of increased length of hospital stay (≥5 days) in the low risk group. For mortality, total chest tube output >1000 ml ($P = 0.04$; OR = 2.2, 95% CI 0.3–4.2) was the only risk factor in the low risk patients and any red blood cell transfusion ($P = 0.02$; OR = 2.0, 95% CI −0.3–4.2) in the high risk patients. In the high risk group any red blood cell transfusion ($P = 0.02$) was the only risk factor for readmission to the hospital within the first 30 days.

Table 3
Factors leading to delayed extubation (>6 h) on univariable analysis[a]

	Low risk group	High risk group
Age >70	0.0001	
Hypertension	0.06	
COPD	0.09	
Peripheral vascular disease	0.07	
Chronic renal failure	0.0001	
Myocardial infarction <90 days	0.04	
Bypass time >90 min	0.001	
Cross clamp time >60 min	0.003	0.01
Any red blood cell transfusion	0.0001	0.004
Postoperative blood loss >1000 ml	0.0001	0.02
Preoperative use of IV inotropes		0.004
Operative priority (non-elective)		0.08

[a] COPD, chronic obstructive pulmonary disease.

4. Comment

Potential benefits of an early extubation program are decreased cardiac and respiratory morbidity [12], increased cardiac performance [13–15], lower rate of nosocomial pneumonia [16], reduced cancellation of surgery owing to the increased availability of ICU beds, and decreased cost of patient care [17]. However, it is not clear whether these benefits may be extrapolated to the high risk patients since most studies on this issue exclude patients with preoperative risk factors described as predictors for prolonged mechanical ventilation. Our study failed to show any preoperative risk factor to be a predictor of delayed extubation. In a controlled clinical trial comparing low and high risk patients, Plumer et al. [18] were not able to find a difference in the mean time to extubation, and in the incidence of complications after extubation. They compared 65 patients; who had at least one of the following risk factors: emergency surgery, severe left-ventricular dysfunction, previous heart surgery, recent myocardial infarction, age

Table 4
Factors leading to increased intensive care unit stay (>24 h) on univariable analysis[a]

	Low risk group	High risk group
COPD	0.09	
Post operative blood loss >1000 ml	0.001	
Cross clamp time >60 min	0.007	
Bypass time >90 min	0.001	0.05
Any red blood cell transfusion	0.0001	0.0001
Preoperative use of IV inotropes		0.09
NYHA Class 3 or 4		0.01

[a] NYHA = New York Heart Association; COPD = chronic obstructive pulmonary disease.

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Table 5
Factors leading to increased postoperative length of stay (>5 days) on univariable analysis[a]

	Low risk group	High risk group
Age >70	0.05	
Previous myocardial infarction	0.02	
Myocardial infarction <90 days	0.04	
Hypercholesterolemia	0.05	
COPD	0.1	
Preoperative use of IV nitrate	0.007	
Preoperative use of IV heparin	0.002	
Ejection fraction	0.04	
Operative priority (non-elective)	0.002	
Any red blood cell transfusion	0.04	
Bypass time >90 min	0.03	
Cross clamp time >60 min	0.003	
Current smoker		0.04

[a] COPD, chronic obstructive pulmonary disease.

75 years or older, and history of several myocardial infarctions; with 201 patients who had no risk factors. The mean time to extubation in the high risk vs. low risk patients was 364 vs. 361 min, P = ns, the incidence of complications after extubation was 5.5 vs. 5.2%, P = ns, and ICU length of stay was 2 vs. 1.67 day, $P = 0.047$, respectively. The percent of the patients extubated within 6 h was approximately 60% in both groups. Thirty-eight patients (14%) were excluded from the study due to intra or perioperative complications. In their study, the only risk factor for delayed extubation was recent (less than 3 months) myocardial infarction. They concluded as do we, that all patients are basically suitable for early extubation, the preoperative risk factors are poor predictors of prolonged ventilation, and the necessity of prolonged ventilation is primarily determined by intra or perioperative complications and management. In a randomized controlled trial, Reyes et al. showed that early extubation led to a reduction in the ICU length of stay without increasing the postoperative complications [19]. A potential drawback for early extubation is the requirement for reintubation and mechanical ventilation after prior successful weaning from ventilator support and extubation, which is called as extubation failure. In a recent study Rady and Ryan; after finding out that extubation failure increases the utilization of ICU and hospital resources; suggested a modification in the protocols for early extubation and ICU discharge in the presence of certain preoperative and operative predictors of extubation failure to avoid unnecessary increase in the cost of care after cardiac surgery [20]. However, in our study, extubation failure was statistically not different in high risk patients compared to low risk patients, 1.3 vs. 0.4% $P = 0.2$, respectively. The finding that delayed extubation is an independent risk factor for prolonged ICU stay [21] was not confirmed in this study. This is probably due to the high extubation rate within 12 h in both high and low risk groups, 96.8 vs. 98%; $P = 0.37$, respectively.

Table 6
Predictors of mortality on univariable analysis[a]

	Low risk group	High risk group
Preoperative use of IV nitrate	0.03	
Preoperative use of IV heparin	0.02	
Operative priority (non-elective)	0.005	
NYHA Class 3 or 4	0.06	
Post operative blood loss >1000 ml	0.05	
Any red blood cell transfusion		0.04
Cross clamp time >60 min		0.10

[a] NYHA, New York Heart Association.

Although the number of patients with an ICU stay more than 24 h was significantly higher in the high risk group, the mean duration of ICU stay did not reach a statistically significant difference. The same high success rate could not be obtained for postoperative length of stay of less than or equal to 5 days in both groups, however, 93.9 vs. 90.2% of the patients were discharged on day 7 in low and high risk groups, respectively ($P = 0.11$).

The most striking finding obtained from this study was the effect of blood use on outcome, especially in the high risk patients. Red blood cell transfusion after CABG has already shown to be associated with increased length of ICU and hospital stay [22], incidence of infection [23], and mortality [24].

Vamvakas et al. [22] demonstrated that allogeneic blood transfusion was independently associated with longer postoperative stays in the hospital or the ICU. After adjustment for the effects of confounding factors, they showed that the postoperative length of hospitalization increased by 0.837%, and the postoperative length of stay in the ICU increased by 0.873% per red blood cells (RBC) unit transfused [22].

In a recent study, RBC transfusions were also found to be independently associated with a higher incidence of post-CABG bacterial infections [23]. The risk of infection increased in proportion to the number of units of RBC transfused. After controlling for patient and disease characteristics, invasive treatments, surgical time, and the transfusion of other substances, the adjusted rates of bacterial infection were 4.8% for no RBC transfusion, 15.2% with one to two units, 22.1% with three to five units, and 29.0% with greater than or equal to six units [23].

Moreover, in a recent study it has been shown that blood transfusions during or after coronary artery bypass operations were associated with a 70% increase in 5-year mortality after correction for comorbidities and other factors [25].

In this study, any RBC transfusion was found to be an independent risk factor for delayed extubation, discharge from the ICU, mortality, and hospital readmission in the high risk cohort.

In conclusion, this study confirms the safety and efficacy of FTRP among high risk patients undergoing CABG. RBC transfusion is associated with delayed extubation and

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discharge from the ICU, and increased mortality and hospital readmission rate.

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Appendix A. Conference discussion

Dr R. Engelman (*Springfield, Massachusetts*): I really appreciate the fact of bringing back fast track and showing in this manner the fact that it is acceptable and actually works very effectively, even in the high risk patient.

What I would indicate is that in the U.S. the biggest problem for fast track recovery is not the physician, surgeons and associated staff within the hospital but the inability to maintain an outpatient support system for these patients, who, I am sure in your experience as well, require some assistance on the outside. And I would ask you, in your environment what is the support mechanism you have for the ability to discharge these patients within five days? Do you have some assist outside the hospital, some manner in which the patients can receive some associated care after they have been discharged?

Dr Alhan: Unfortunately in our country such an assistant is not available, only the family, and we teach the family this important issue, however, in the hospital our staff is always on the patient and early mobilization, early exercise programs, including climbing stairs, are taken.

Dr Engelman: That is basically the same problem we have in the U.S.A.

Dr J. Gummert (*Leipzig, Germany*): I would like to ask you one question. You pointed out that red blood cell transfusion is the only risk factor, but wouldn't you rather think that this is just a surrogate marker for different other reasons?

Dr Alhan: Sorry?

Dr Gummert: That the red blood cell transfusion mimics other reasons that lead to the transfusion of red blood cells, so the red blood cell transfusion alone is not the reason for not extubating the patient but rather that there are other reasons behind it?

Dr Alhan: Well, in our logistic regression red blood cell transfusion is highly significant for all readmission rates, mortality, and also ICU stay.

Dr Gummert: Right, but, for instance, if you have a patient in cardiogenic shock, of course you need more red blood cells because you have to perhaps put him on hemodialysis and so on, so there are a lot of reasons in high risk patients to give them red blood cells. So this is just summarizing it.

Dr Alhan: Well, actually it is not necessary to use blood in every patient, in very ill patients. It is just a matter of strategy, it is just a matter of protocol. And in our group low hematocrit levels as low as 18 are well tolerated on the pump, and also after surgery we don't replace patients' blood with hematocrit levels such as 20, 21, and within one month they rise.

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