European Journal of Cardio-Thoracic Surgery 0 (2017) 1–8
doi:10.1093/ejcts/ezx015

ORIGINAL ARTICLE

Cite this article as: Tauriainen T, Kinnunen E-M, Koski-Vähälä J, Mosorin M-A, Airaksinen J, Biancari F. Outcome after procedures for retained blood syndrome in coronary surgery. Eur J Cardiothorac Surg 2017; doi:10.1093/ejcts/ezx015.

Outcome after procedures for retained blood syndrome in coronary surgery

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Received 2 August 2016; received in revised form 22 November 2016; accepted 20 December 2016

Abstract

OBJECTIVES: Incomplete drainage of blood from around the heart and lungs can lead to retained blood syndrome (RBS) after cardiac surgery. The aim of this study was to assess the incidence of and the outcome after procedures for RBS in patients undergoing isolated coronary artery bypass grafting (CABG).

METHODS: A total of 2764 consecutive patients who underwent isolated CABG from 2006 to 2013 were investigated retrospectively. Patients undergoing any procedure for RBS were compared with patients who did not undergo any procedure for RBS. Multivariate analyses were performed to assess the impact of procedures for RBS on the early outcome.

RESULTS: A total of 254 patients (9.2%) required at least one procedure for RBS. Multivariate analysis showed that RBS requiring a procedure for blood removal was associated with significantly increased 30-day mortality [8.3% vs 2.7%, odds ratio (OR) 2.11, 95% confidence interval (95% CI) 1.15–3.86] rates. Procedures for RBS were independent predictors of the need for postoperative antibiotics (51.6% vs 32.1%, OR 2.08, 95% CI 1.58–2.74), deep sternal wound infection/mediastinitis (6.7% vs 2.2%, OR 3.12, 95% CI 1.72–5.66), Kidney Disease: Improving Global Outcomes acute kidney injury (32.7% vs 15.3%, OR 2.50, 95% CI 1.81–3.46), length of stay in the intensive care unit (mean 8.3 vs 2.0 days, beta 1.74, 95% CI 1.45–2.04) and composite major adverse events (21.3% vs 6.9%, OR 3.24, 95% CI 2.24–4.64). These findings were also confirmed in a subgroup of patients with no pre- or postoperative unstable haemodynamic conditions.

CONCLUSION: RBS requiring any procedure for blood removal from pericardial and pleural spaces is associated with an increased risk of severe complications after isolated CABG.

Keywords: Coronary artery bypass grafting • Coronary artery bypass surgery • Bleeding • Retained blood • Reoperation • Thoracentesis • Pleural drainage

IINTRODUCTION

Excessive blood loss is known to be associated with a number of complications after cardiac surgery [1–3]. Evacuation of shed blood from the pericardium during the early postoperative period by chest tubes is of particular importance. Recently, an interest in retained blood as a possible predictor of adverse effects after cardiac surgery has arisen. The collection of bloody fluid in the pericardium and pleura caused by excessive bleeding, clogging of drains [4–7] or other mechanisms is hypothesized to generate a continuum of complications, which Boyle *et al.* [4] named retained blood syndrome (RBS). RBS is defined as the acute, subacute or chronic collection of blood or a haematoma requiring removal from the pericardial or pleural spaces. In the acute phase, RBS can manifest as cardiac tamponade or a haemothorax usually requiring urgent resternotomy. Bloody pericardial and pleural effusions characterize the syndrome in the subacute phase, which is treated by pleural drainage, thoracentesis and pericardial fenestration. The chronic phase includes fibrothorax and constrictive pericarditis induced by effusion and inflammation resulting from stagnant leftover blood [4]. Recent studies have shown that retained blood can be observed in as many as one fifth of patients undergoing cardiac surgery [4, 5, 8] and in up to 64% of patients undergoing an urgent cardiac operation [8]. RBS seems to be associated with poor postoperative outcomes [8]. However, studies addressing this issue are scarce. The purpose of the present study was to evaluate the incidence of procedures performed for retained blood and to assess the impact of procedures for RBS on the outcome after coronary artery bypass grafting (CABG).

METHODS

Patient population

This retrospective observational, single-centre study included 2764 consecutive patients who underwent isolated CABG from June 2006 to December 2013 at the Oulu University Hospital, Finland. Complete data on pre-, intra- and postoperative variables were available for all of these patients from an institutional electronic cardiac surgery registry containing data on baseline and operative variables as well as on immediate postoperative adverse events. Data on the preoperative use of antithrombotic agents were collected retrospectively. Data on the types and amount of transfused blood products such as red blood cells (RBCs), platelets and solvent/detergent-treated plasma (Octaplas; Octapharma AG, Lachen, Switzerland) were retrieved from a prospective electronic hospital registry. Data on the amount of chest drainage at 12 h after surgery were retrieved from a prospective electronic registry of the intensive care unit. Clinical variables were defined according to the EuroSCORE II definition criteria [9]. The glomerular filtration rate was estimated using the Modification of Diet in Renal Disease formula [10]. Bleeding risk was estimated according to the Papworth bleeding risk score [11]. The European Multicenter Study on Coronary Artery Bypass Grafting (E-CABG) bleeding classification system [12] was used to stratify the severity of perioperative bleeding according to the following criteria: grade 0, no RBC transfusion or transfusion of one unit of RBCs; grade 1, transfusion of platelets, fresh frozen plasma or Octaplas and/or of 2–4 units of RBCs; grade 2, transfusion of 5–10 units of RBCs and/or reoperation for bleeding; grade 3, transfusion of >10 units of RBCs. Data on patients' deaths were provided through 31 January 2016 from the Finnish Population Registry Center (Väestörekisteri), which collects the death certificates of all inhabitants of Finland. We assume that there are no missing data on any immediate or late deaths of individuals in this study population.

Perioperative antithrombotic treatment

In this series, until 2012, acetylsalicylic acid was interrupted for at least 7 days, whereas after 2012, it was continued until the procedure. Vitamin K antagonist was interrupted at least 2 days before the procedure and heparin bridging was not adopted. Patients with acute coronary syndrome or a mechanical heart valve received enoxaparin preoperatively. P2Y12 inhibitors were discontinued for at least 5 days when feasible. Heparin (3.0 mg/kg) was administered intravenously during the operation to maintain an activated coagulation time of more than 450 s. Protamine sulphate (3.0 mg/kg) was given at the end of the procedure to neutralize the heparin. These patients did not receive aprotinin. Tranexamic acid was administered intraoperatively at the discretion of the anaesthesiologist. RBCs were transfused on the day of the operation if the haemoglobin level was <90 g/l and later if the haemoglobin level was <80 g/l. Octaplas and platelets were transfused according to the severity of the perioperative bleeding, INR levels and platelet count. rFVIIa was used only in cases of unrelenting massive bleeding.

Patients received enoxaparin 40–80 mg once a day from the evening of the day of the operation if the chest drainage output was less than 1000 ml. Aspirin 100 mg was restarted on the first postoperative day. Warfarin was restarted on the first postoperative day in those patients under long-term anticoagulation. P2Y12 inhibitors were administered after the operation only in case of allergy to aspirin or a recent percutaneous coronary intervention.

Operative techniques and management of chest drainages

Intermittent antegrade and retrograde cold blood cardioplegia was used for myocardial protection in patients undergoing on-pump coronary surgery. The Octopus stabilizer (Medtronic, Minneapolis, MN) as well as intracoronary shunts were routinely used in patients who had off-pump surgery.

Blood lost intraoperatively was collected in a cell-saver reservoir and was reinfused during or at the completion of the procedure.

One 24 Fr pericardial drain and one 30 Fr mediastinal drain were inserted in all patients. Pleural drains of 28 Fr in size were inserted when the mediastinal pleura was accidentally opened, when prophylactic pericardial fenestration was made or in case of preoperative lung oedema or pleural effusion. Blood from the mediastinum and the pleura was collected after the operation in a sterile collection chamber connected to a 15-cm H_2O wall suction system via an underwater seal and then discarded. Nurses regularly milked the mediastinal drains to clear them during the postoperative period; the drains were removed within 24 h after the operation. No active clearance device was used in these patients. Pleural drains were removed along with mediastinal drains or, in the case of postoperative blood loss >1000 ml, as soon as the drainage output was <200 ml/day.

Diagnosis and treatment of retained blood syndrome

Retained blood syndrome or RBS was defined as any condition requiring reopening of the surgical incision and washout of the pericardial and pleural spaces, pericardial window, insertion of a chest tube and/or thoracentesis to remove blood from the pericardial or pleural space within 30 days from the index procedure. Only patients with frank blood effusion were considered to have retained blood. Resternotomy was performed on the same day as the operation in cases of excessive bleeding for haemostasis and removal of retained blood. Bleeding into the pericardium or pleural spaces was suspected in cases of a drop >10 g/l of the haemoglobin level compared to a previous postoperative measurement (haemoglobin levels were routinely monitored at least once a day) or unstable cardiorespiratory conditions. In such cases, a chest radiograph and echocardiographic scans were performed to diagnose excessive pericardial and pleural fluid. The diagnosis of RBS was confirmed when frank blood was removed. Resternotomy or pericardial fenestration was performed to remove retained blood when a patient's oxyhaemodynamic conditions were suboptimal or in the presence of a pericardial effusion/haematoma with signs of tamponade on an echocardiogram. Thoracoscopic fenestration was usually performed when excessive retained blood was detected more than 2 weeks after the operation and cardiorespiratory conditions allowed selective right bronchial intubation and lateral positioning of the patient on the operating table. Otherwise, pericardial blood was removed through a subxiphoid access. A pleural drain was

inserted or thoracentesis was performed when excessive pleural effusion was detected on a chest radiograph or when the patient's oxygen saturation level was suboptimal.

Outcomes

The primary outcomes of this study were all-cause in-hospital and 30-day deaths. Secondary outcomes were the length of stay in the intensive care unit, stroke, atrial fibrillation, ventricular fibrillation or asystole, postoperative use of antibiotics, deep sternal wound infection, mediastinitis, low cardiac output syndrome, repeat revascularization, surgery for gastrointestinal complications, acute kidney injury according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria [13], nadir haemoglobin level during the postoperative period, chest drain output 12 h after the operation, severity of bleeding according to the E-CABG bleeding classification and the E-CABG complication score and E-CABG complication grade 3 (renal failure requiring renal replacement therapy, mediastinitis, stroke, early repeat myocardial revascularization, ventricular fibrillation/asystole, surgery for a gastrointestinal complication and/or extracorporeal membrane oxygenation) as composite outcome measures [12]. For this study, bleeding-related parameters, i.e. use of blood products and reoperation for bleeding, were excluded from these composite outcomes. Low cardiac output syndrome was defined as postoperative cardiac index <2.0 l/min/m^2 measured at least twice. The other outcomes were defined according to the E-CABG definition criteria as previously described [12].

Ethical considerations

This study was approved by the Institutional Review Board of the Oulu University Hospital. This study was not financially supported.

Statistical analysis

Statistical analysis was performed using SPSS statistical software (version 23.0, IBM Corporation, New York, USA). Continuous variables are reported as mean ± standard deviation. Nominal variables are reported as counts and percentages. Risk estimates are reported as a beta coefficient or odds ratio (OR) with a 95% confidence interval (95% CI). No attempt to replace missing values was made. The Fisher's exact test and the χ^2 test were used to evaluate the differences in nominal variables between study groups. The Mann–Whitney test was used to evaluate differences of continuous variables between study groups. Logistic, linear and ordinal regression analyses were performed to adjust the effect of baseline variables on outcomes. The impact of procedures for retained blood on the outcomes was adjusted in logistic, linear and ordinal regression analyses for those variables with $P < 0.05$ in univariate analysis: patient's age, body mass index, recent myocardial infarction, critical preoperative status, dialysis and urgency status. Predictors of RBS were identified in logistic regression including covariates with $P < 0.05$ in univariate analysis as listed in Table 1. All tests were two-sided with the alpha level set at 0.05 for statistical significance.

RESULTS

Procedures for retained blood syndrome

Overall, 254 patients (9.2%) required at least one procedure for removal of retained blood in the pericardial or pleural cavity. Characteristics of these patients compared with those not requiring removal of retained blood are summarized in Tables 1 and 2. One procedure for removal of retained blood was performed in 211 patients (7.6%); 2 procedures were performed in 39 patients (1.4%); 3 procedures in 3 patients (0.1%); and 5 procedures in 1 patient (0.03%). Resternotomy for removal of retained blood was performed in 181 patients (6.5%) after a mean of 1.8 ± 4.1 days. Forty-five of these patients (24.9%) had a resternotomy ≥ 2 days after the index procedure. Pericardial fenestration was performed in 40 patients (1.4%); pleural drainage in 50 patients (1.8%; in 3 patients, it was done twice); and thoracentesis, in 25 patients (0.9%; in 3 patients it was done twice). Pericardial fenestration was performed in 1 patient thoracoscopically and in 39 patients through the subxiphoid access. In these patients, haemodynamic signs and symptoms of pericardial tamponade were observed in 32 patients and echocardiographic findings of tamponade without oxyhaemodynamic instability, in 25 patients. Excluding patients who underwent resternotomy, procedures for RBS were performed in 73 patients (2.6%). During follow-up, surgery for pericarditis was performed in 2 patients and 1 of them has had resternotomy for RBS. No patients in this series required an operation for fibrothorax.

Predictors of procedures for RBS in univariate analysis are listed in Tables 1 and 2. Logistic regression (Hosmer–Lemeshow test: $P = 0.286$) identified age ($P = 0.03$, OR 1.02, 95% CI 1.00–1.03), preoperative dialysis ($P = 0.001$, OR 4.93, 95% CI 2.00–12.33) and critical preoperative status ($P = 0.006$, OR 1.77, 95% CI 1.18–2.66) as independent predictors of RBS.

Impact of retained blood syndrome on the immediate outcome

Patients with RBS had a significantly lower nadir haemoglobin level (mean, 76 ± 10 g/l vs 84 ± 13 g/l, $P < 0.0001$) compared to those who did not require any procedure for RBS. Such a difference was also observed when patients who underwent resternotomy for bleeding were excluded from the analysis (mean, 78 ± 11 g/l vs 84 ± 13 g/l, $P < 0.0001$). However, chest drain output was significantly higher in the overall group of patients who underwent procedures for RBS (mean, 965 ± 732 ml vs 456 ± 305 ml, $P < 0.0001$), but not in those with RBS who did not require resternotomy (mean, 480 ± 368 ml vs 456 ± 305 ml, $P = 0.95$). Procedures for RBS were performed more frequently in patients with severe bleeding as stratified by the E-CABG bleeding severity classification (Table 3).

Multivariate analysis of the overall series showed that RBS requiring blood removal was an independent predictor of increased in-hospital stay and 30-day mortality rate (Table 3). A subanalysis excluding patients who required resternotomy for RBS showed that procedures for RBS other than resternotomy were associated with an increased risk of early death, but such a difference did not reach statistical significance in multivariate analysis (Table 3).

Procedures for RBS were independent predictors for most of the secondary outcomes (Table 3). These patients had a

Table 1: Baseline characteristics

Baseline variables	Overall series, *n* = 2764	No procedure for RBS, *n* = 2510	Procedure for RBS, *n* = 254	*P*-value	Procedure for RBS excluding resternotomy, *n* = 73	*P*-value
Age, years	67.0 ± 9.1	66.9 ± 9.1	68.2 ± 9.2	0.02	69.2 ± 10.0	0.02
Females, *n* (%)	582 (21.1)	539 (21.5)	43 (16.9)	0.09	10 (13.7)	0.11
Body mass index	28.1 ± 4.5	28.1 ± 4.5	27.4 ± 4.5	0.01	27.6 ± 4.9	0.13
Haemoglobin, g/l	137 ± 16	137 ± 16	137 ± 16	0.71	135 ± 17	0.45
Platelets, (10^9/l)	242 ± 75	241 ± 74	254 ± 106	0.73	254 ± 106	0.74
eGFR, (ml/min/1.73 m^2)	86 ± 25	86 ± 25	83 ± 28	0.06	80 ± 29	0.03
Dialysis, *n* (%)	22 (0.8)	15 (0.6)	7 (2.8)	<0.01	3 (4.1)	0.01
Pulmonary disease, *n* (%)	274 (9.9)	249 (9.9)	25 (9.8)	0.97	10 (13.7)	0.29
Diabetes, *n* (%)	788 (28.5)	714 (28.4)	74 (29.1)	0.82	22 (30.1)	0.75
Stroke, *n* (%)	95 (3.4)	84 (3.3)	11 (4.3)	0.41	3 (4.1)	0.72
Extracardiac arteriopathy, *n* (%)	265 (9.6)	238 (9.5)	27 (10.6)	0.55	10 (13.7)	0.23
Atrial fibrillation, *n* (%)	282 (10.2)	252 (10.0)	30 (11.8)	0.37	12 (16.4)	0.08
Previous PCI, *n* (%)	201 (7.3)	188 (7.5)	13 (5.1)	0.17	4 (5.5)	0.52
Previous cardiac surgery, *n* (%)	46 (1.7)	42 (1.7)	4 (1.6)	1.00	1 (1.4)	1.00
Left ventricular ejection, *n* (%) fraction ≤50%	699 (25.3)	625 (25.9)	74 (30.5)	0.12	26 (37.1)	0.03
Recent myocardial infarction, *n* (%)	1319 (47.7)	1181 (47.1)	138 (54.3)	0.03	41 (56.2)	0.15
Critical preoperative status, *n* (%)	217 (7.9)	186 (7.4)	31 (12.2)	0.01	13 (17.8)	<0.01
Preoperative IABP, *n* (%)	11 (0.4)	9 (0.4)	2 (0.8)	0.30	0	1.00
Recent ventricular tachycardia, *n* (%)	83 (3)	73 (2.9)	10 (3.9)	0.36	6 (8.2)	0.01
Cardiac massage, *n* (%)	43 (1.6)	38 (1.5)	5 (2.0)	0.58	3 (4.1)	0.11
Potent antiplatelet drugs within 5 days from surgery*, *n* (%)	512 (18.5)	456 (18.2)	56 (22.0)	0.13	18 (24.7)	0.16
Warfarin within 2 days from surgery, *n* (%)	77 (2.8)	67 (2.7)	10 (3.9)	0.24	3 (4.1)	0.46
Papworth bleeding score	1.0 ± 0.8	1.0 ± 0.8	1.2 ± 0.8	<0.01	1.3 ± 0.8	<0.01

Continuous variables are reported as mean ± standard deviation. Categorical variables are reported as counts and percentages. *P*-values refer to comparison with patients who did not undergo procedures for retained blood.

RBS: retained blood syndrome; PCI: percutaneous coronary intervention; IABP: intra-aortic balloon pump; eGFR: estimated glomerular filtration rate.

[a]Clopidogrel, ticagrelor and prasugrel.

Table 2: Operative data

Operative variables	Overall series, *n* = 2764	No procedure for RBS *n* = 2510	Procedure for RBS *n* = 254	*P*-value	Procedure for RBS excluding resternotomy *n* = 73	*P*-value
Urgency status						
Elective, *n* (%)	1260 (45.6)	1161 (46.3)	99 (39.0)	<0.01	27 (37.0)	0.29
Urgent, *n* (%)	1306 (47.3)	1180 (47.0)	126 (49.6)		40 (54.8)	
Emergency, *n* (%)	198 (7.2)	169 (6.7)	29 (11.4)		6 (8.2)	
Off-pump surgery, *n* (%)	1449 (52.4)	1319 (52.5)	130 (51.2)	0.68	44 (60.3)	0.36
Bilateral mammary artery graft, *n* (%)	221 (8.0)	204 (8.1)	17 (6.8)	0.42	6 (8.2)	1.00
Distal anastomoses, *n*	4.0 ± 1.1	3.9 ± 1.1	4.0 ± 1.1	0.25	4.0 ± 1.2	0.45
Cross-clamping time, min	85 ± 29	85 ± 29	88 ± 29	0.07	77 ± 37	0.80
CPB time, min	111 ± 38	110 ± 38	116 ± 37	0.02	101 ± 46	0.75
Length of the operation, min	249 ± 69	248 ± 70	258 ± 60	0.04	256 ± 50	0.25
Any pleural drainage, *n* (%)	1449 (52.4)	1310 (52.3)	139 (53.5)	0.71	28 (38.4)	0.02
Bilateral pleural drainage, *n* (%)	452 (16.4)	402 (16.0)	50 (19.7)	0.13	12 (16.4)	0.92
Prophylactic pericardial window, *n* (%)	157 (5.7)	143 (5.7)	14 (5.5)	0.90	5 (6.8)	0.68

Continuous variables are reported as mean ± standard deviation. Categorical variables are reported as counts and percentages. *P*-values refer to a comparison with patients who did not undergo procedures for retained blood.

RBS: retained blood syndrome; CPB: cardiopulmonary bypass.

significantly lower nadir haemoglobin level than patients who did not require procedures for RBS. Analysis excluding patients who underwent resternotomy for RBS showed that retained blood requiring pericardial fenestration, thoracentesis or pleural drainage was associated with an increased risk of new atrial fibrillation, the need for postoperative antibiotics, deep sternal wound infections and mediastinitis, acute kidney injury and gastrointestinal complications (Table 3). The increased rate of adverse events in patients with RBS translated to a prolonged stay in the intensive care unit.

Procedures for RBS, with or without resternotomy, were associated with a significantly increased risk of a composite outcome

Table 3: Outcomes

	Overall series *n* = 2764	No procedure for RBS *n* = 2510	Procedure for RBS *n* = 254	Univariate analysis *P*-value	Adjusted risk estimate (95% CI)	Resternotomy for bleeding *n* = 175	Univariate analysis *P*-value	Adjusted risk estimate (95% CI)	Procedure for RBS excluding resternotomy *n* = 73	Univariate analysis *P*-value	Adjusted risk estimate (95% CI)
In-hospital death, *n* (%)	66 (2.4)	50 (2.0)	16 (6.3)	<0.01	**2.26, 1.14–4.48**	13 (7.2)	<0.01	**2.55, 1.18–5.51**	3 (4.1)	0.20	1.77, 0.48–6.66
30-day mortality, *n* (%)	89 (3.2)	68 (2.7)	21 (8.3)	<0.01	**2.11, 1.15–3.86**	19 (10.5)	<0.01	**3.00, 1.56–5.74**	2 (2.7)	1.00	0.52, 0.10–2.58
ICU stay, days	2.2 ± 2.5	2.0 ± 2.1	3.4 ± 4.4	<0.01	**1.74, 1.45–2.04**	3.7 ± 4.1	<0.01	**1.53, 1.20–1.85**	4.6 ± 5.1	<0.01	**2.32, 1.82–2.81**
Stroke, *n* (%)	58 (2.1)	48 (1.9)	10 (3.9)	0.03	1.57, 0.75–3.32	8 (4.4)	0.02	1.83, 0.80–4.21	2 (2.7)	0.65	0.95, 0.22–4.18
New atrial fibrillation, *n* (%)	946 (38.1)	843 (37.3)	103 (46.0)	0.01	**1.33, 1.01–1.75**	87 (44.1)	0.11	1.19, 0.86–1.64	33 (54.1)	0.01	**1.80, 1.04–3.09**
Ventricular fibrillation/ asystole, *n* (%)	49 (1.8)	39 (1.6)	10 (3.9)	0.01	1.97, 0.93–4.19	7 (3.9)	0.02	2.01, 0.88–4.97	3 (4.1)	0.11	1.88, 0.50–7.00
Low cardiac output syndrome, *n* (%)	383 (13.9)	328 (13.1)	55 (21.7)	<0.01	**1.74, 1.24–2.45**	37 (20.4)	<0.01	**1.73, 1.16–2.59**	18 (24.7)	<0.01	1.71, 0.94–3.08
Repeat CABG or PCI	14 (0.5)	9 (0.4)	5 (2.0)	<0.01	**5.72, 1.87–17.43**	4 (2.2)	<0.01	6.78, 2.04–22.49	1 (1.4)	0.25	3.49, 0.41–29.60
Postoperative use of antibiotics, *n* (%)	937 (33.9)	806 (32.1)	131 (51.6)	<0.01	**2.08, 1.58–2.74**	80 (44.2)	<0.01	**1.51, 1.09–2.09**	51 (69.9)	<0.01	**4.78, 2.80–8.14**
Deep SWI/mediastinitis, *n* (%)	72 (2.6)	55 (2.2)	17 (6.7)	<0.01	**3.12, 1.72–5.66**	8 (4.4)	0.06	2.01, 0.89–4.54	9 (12.3)	<0.01	**6.01, 2.68–13.47**
Surgery for gastrointestinal complications	32 (1.2)	22 (0.9)	10 (3.9)	<0.01	**3.80, 1.67–8.64**	6 (3.3)	<0.01	**3.17, 1.16–8.71**	4 (5.5)	<0.01	**5.94, 1.86–18.97**
Acute kidney injury, *n* (%)	457 (16.9)	377 (15.3)	80 (32.7)	<0.01	**2.50, 1.81–3.46**	54 (30.9)	<0.01	**2.42, 1.64–3.52**	26 (37.1)	<0.01	**2.81, 3.103–8.82**
Nadir haemoglobin, g/l	83 ± 13	84 ± 13	76 ± 10	<0.01	**-6.31, -7.80 to -4.83**	75 ± 8	<0.01	**-7.49, -9.17 to -5.71**	78 ± 11	<0.01	**-3.41, -6.11 to -0.71**
Blood loss at 12 h, ml	503 ± 394	456 ± 305	965 ± 732	<0.01	**503.3, 455.5–551.0**	1167 ± 752	<0.01	**707, 653–761**	480 ± 368	0.95	20.52, -50.21 to 91.26
E-CABG bleeding grades, *n* (%)				<0.01	**-3.24, -3.54 to -2.93**		<0.01	**-4.34, -4.78 to -3.90**		<0.01	**-1.13, -1.58 to -0.68**
Grade 1	1117 (40.4)	1091 (43.5)	26 (10.2)			0			26 (35.6)		
Grade 2	506 (18.3)	332 (13.2)	174 (68.5)			153 (84.5)			21 (28.8)		
Grade 3	68 (2.5)	31 (1.2)	37 (14.6)			28 (15.5)			9 (12.3)		
E-CABG complication grade 3, *n* (%)	186 (7.2)	172 (6.9)	54 (21.3)	<0.01	**3.24, 2.24–4.64**	40 (22.1)	<0.01	**3.40, 2.24–5.17**	14 (19.2)	<0.01	**2.80, 1.48–5.32**
E-CABG complication score[a], *n* (%)	3.3 ± 4.7	3.0 ± 4.2	6.1 ± 7.0	<0.01	**2.51, 1.96–3.06**	5.7 ± 6.8	<0.01	**2.16, 1.53–2.78**	7.1 ± 7.4	<0.01	**3.44, 2.49–4.40**

Continuous variables are reported as mean ± standard deviation. Categorical variables are reported as counts and percentages. Risk estimates are beta coefficients or odds ratios with 95% confidence intervals. Risk estimates in bold indicate statistical significance in multivariate analysis. *P*-values and adjusted estimates refer to comparison with patients who did not undergo procedures for retained blood.

RBS: retained blood syndrome; ICU: intensive care unit; E-CABG: European Multicenter Study on Coronary Artery Bypass Grafting; PCI: percutaneous coronary intervention; SWI: sternal wound infection.

[a]Excluding bleeding-related outcomes.

Table 4: Impact of retained blood syndrome on the outcome of patients without preoperative or postoperative unstable haemodynamic conditions

	No procedure for RBS, *n* = 1657	Procedure for RBS, *n* = 112	Univariate analysis, *P*-value	Adjusted risk estimate (95% CI)
In-hospital death, *n* (%)	12 (0.7)	4 (3.6)	0.02	3.46, 0.66–18.09
30-day mortality, *n* (%)	20 (1.2)	4 (3.6)	0.06	0.64, 0.08–5.46
ICU stay, days	1.4 ± 1.5	2.2 ± 1.7	<0.01	**0.55, 0.32–0.77**
Stroke, *n* (%)	20 (1.2)	2 (1.8)	0.65	0.69, 0.09–5.36
New atrial fibrillation, *n* (%)	589 (35.5)	39 (34.8)	0.88	0.92, 0.60–1.42
Ventricular fibrillation/asystole, *n* (%)	10 (0.6)	2 (1.8)	0.17	3.02, 0.62–14.74
Low cardiac output syndrome, *n* (%)	0	0		
Repeat CABG or PCI, *n* (%)	0	0		
Postoperative use of antibiotics, *n* (%)	435 (26.3)	49 (43.8)	<0.01	**2.05, 1.37–3.08**
Deep SWI/mediastinitis, *n* (%)	34 (2.1)	7 (6.3)	<0.01	**3.04, 1.21–7.64**
Operation for gastrointestinal complications	5 (0.3)	1 (0.9)	0.33	0, 0–0
Acute kidney injury, *n* (%)	140 (8.6)	22 (20.2)	<0.01	**2.66, 1.53–4.63**
Nadir haemoglobin, g/l	86 ± 12	77 ± 10	<0.01	**-6.84, -9.06 to -4.61**
Blood loss at 12 h, ml	460 ± 258	1025 ± 780	<0.01	**551, 490–612**
E-CABG bleeding grades, *n* (%)			<0.01	**-3.78, -4.26 to -3.30**
Grade 1	670 (40.4)	9 (8.0)		
Grade 2	122 (7.4)	85 (75.9)		
Grade 3	6 (0.4)	7 (6.3)		
E-CABG complication grade 3, *n* (%)	56 (3.4)	12 (10.7)	<0.01	**2.74, 1.30–5.82**
E-CABG complication score*	2.0 ± 2.9	3.7 ± 5.2	<0.01	**1.19, 0.64–1.74**

Continuous variables are reported as mean ± standard deviation. Categorical variables are reported as counts and percentages. Risk estimates are beta coefficients or odds ratios with 95% confidence intervals. Risk estimates in bold indicate statistical significance in multivariate analysis.

*Excluding bleeding-related outcomes.

RBS: retained blood syndrome; ICU: intensive care unit; CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention; SWI: sternal wound infection; E-CABG: European Multicenter Study on Coronary Artery Bypass Grafting.

defined with E-CABG complication grades and scores (Table 3). The excessive risk of E-CABG grade 3 complications in patients who underwent a procedure for RBS (21.3% vs 6.9%, $P < 0.0001$, adjusted OR 3.22, 95% CI 2.24–4.64) compared to those patients who did not have RBS is worth noting. The increased risk of E-CABG grade 3 complications associated with procedures for RBS was also observed when those patients who underwent resternotomy (19.2% vs 6.4%, $P < 0.0001$, adjusted OR 2.80, 95% CI 1.48–5.32) were excluded from the analysis.

Impact of resternotomy for bleeding on the immediate outcome

A comparative analysis of the outcomes of patients who underwent resternotomy for bleeding and those who did not experience RBS showed that resternotomy for bleeding was associated with increased risk of in-hospital death (7.2% vs 2.0%, adjusted OR 2.55, 95% CI 1.18–5.51) and 30-day death (10.5% vs 2.7%, adjusted OR 3.00, 95% CI 1.56–5.74). Furthermore, resternotomy for bleeding was an independent predictor of a number of other adverse events (Table 3), most notably KDIGO acute kidney injury (30.9% vs 15.3%, adjusted OR 2.42, 95% CI 1.64–3.52), low cardiac output (20.4% vs 13.1%, adjusted OR 1.73, 95% CI 1.16–2.59), E-CABG complication grade 3 (22.1% vs 6.9%, adjusted OR 3.40, 95% CI 2.24–5.17) and increased E-CABG complication score (mean 5.7 vs 3.0, adjusted beta 2.16, 95% CI 1.53–2.78) (Table 3).

Impact of retained blood syndrome on the immediate outcome of patients with preoperative and postoperative stable haemodynamic conditions

Because it is difficult to disentangle the impact of RBS from that of critical haemodynamic conditions on adverse events occurring after CABG, we performed a separate analysis in a subgroup of patients without critical preoperative status such as those receiving inotropes, experiencing out-of-hospital cardiac arrest or ventricular arrhythmias, with intra-aortic balloon pump as well as without postoperative low cardiac output, prolonged need of inotropes, need of intra-aortic balloon pump or who required further myocardial revascularization immediately after CABG. In this haemodynamically stable patient population, procedures for RBS were performed in 112 (6.3%) patients and 83 (4.7%) patients underwent resternotomy for bleeding. RBS was associated with an increased risk of KDIGO acute kidney injury (20.2% vs 8.6%, adjusted OR 2.66, 95% CI 1.53–4.63), deep sternal wound infection/mediastinitis (6.3% vs 2.1%, adjusted OR 3.04, 1.21–7.64), E-CABG complication grade 3 (10.7% vs 3.4%, adjusted OR 2.74, 95% CI 1.30–5.82) and increased E-CABG complication score (mean 3.7 vs 2.0, adjusted beta 1.19, 95% CI 0.64–1.74) (Table 4).

DISCUSSION

In the present study, the incidence of RBS was 9.2%, which was lower than that in previous studies reporting a rate of RBS of about 19% [5, 8]. Herein, we observed that procedures for

removal of retained blood were performed more often in patients who had severe bleeding as assessed by the E-CABG bleeding severity classification and were associated with several postoperative complications. Most importantly, in-hospital and 30-day mortality rates were significantly increased in patients who had undergone any procedure for RBS. However, when patients who required resternotomy were excluded, procedures other than resternotomy were associated with an increased risk of in-hospital death (4.1% vs 2.0%), which did not reach statistical significance in multivariate analysis. Balzer *et al.* [8] investigated patients undergoing CABG or a valve operation and observed that procedures for evacuation of retained blood (including resternotomy) were associated with increased in-hospital deaths (OR 4.04, 95% CI 2.59–6.35) [8]. They reported a rate of in-hospital mortality of 19.7% in patients with RBS [8], which is much higher than that observed in the present study (6.3%).

This study showed that procedures for RBS, including resternotomy or not, were independent predictors of the need for postoperative antibiotics, deep sternal wound infection/mediastinitis, acute kidney injury, length of stay in the intensive care unit and composite adverse events defined as E-CABG complication score and grading. Of particular interest was the excessive risk of E-CABG grade 3 complications in patients who underwent any procedure for RBS, even in patients who did not require resternotomy and among those with stable haemodynamic conditions. Similar results on the detrimental effect of procedures for RBS on the outcome after cardiac surgery have been reported by other investigators as well [4, 5, 8].

We observed that chest drain output was significantly greater in patients who needed resternotomy than in control patients. In contrast, chest drain output in RBS patients was similar to that in control patients when resternotomies were excluded from the analysis. This observation suggests that, in some cases, blood is retained in the pericardium after the chest tubes clog up. However, we suspect that bleeding into the pericardium or pleural spaces may still occur after the removal of chest tubes. Although this study was not planned to assess this issue, the role of the individual surgeon must be emphasized. Indeed, the individual surgeon has been shown to have a significant impact on chest tube output as well as on resternotomy for excessive bleeding [14, 15]. Importantly, most of the sources of bleeding requiring resternotomy can be classified as surgical [3, 14, 16]. Excessive blood loss requiring resternotomy can be considered a remarkable adverse event because resternotomy for bleeding is associated with a number of severe complications [3, 14, 17].

Another possible cause for retained blood is the clogging of drainage tubes. The lumen of the drain may become occluded because of thrombosis within the drains when clearance is not optimal or even because of kinking or malposition of the drain. The clot usually develops inside the chest, which can make it difficult to recognize [4]. In a survey conducted by Shalli *et al.* [7], 100% of surgeons had encountered clogged chest tubes and 88% were aware that it could lead to adverse effects. Chest tube occlusion is a surprisingly common problem. It can be present in as many as 36% of patients. Clogging of chest tubes is more frequently associated with nonelective operations, renal failure, increased number of transfused RBCs during the operation and administration of platelets postoperatively [6]. Occlusion of the drains can be prevented by active suction devices. Sirch *et al.* [5] found that when active clearance of the chest tubes was used after cardiac surgery, the prevalence of RBS decreased from 19.5 to 11.3%. The suction apparatus also reduced chest tube output and mechanical ventilation hours [5]. When clogging is detected, manipulating the drain could clear the occlusion [7]. Ege *et al.* [18] reported cases of cardiac tamponade as a result of a clogged pericardial drain.

Drainage tube clogging seems to be associated with an increased risk of atrial fibrillation [5, 6], which is one of the most frequent adverse effects after cardiac surgery. Its incidence is at least around 20% according to different authors [19, 20]. The prevalence of atrial fibrillation can be reduced by proper clearance of the collection of pericardial fluid [5, 18, 21]. Atrial fibrillation and other supraventricular arrhythmias are also reduced in patients who undergo posterior pericardiotomy [20]. Our results demonstrated that retained blood in the pericardium is associated with an increased risk of postoperative atrial arrhythmias.

As suggested by Boyle *et al.* [4], pericardial and pleural effusions characterize subacute RBS. The prevalence of pericardial effusion has been reported to be between 1.5 and 22% in patients having cardiac surgery [22, 23]. Early effusions are more common after CABG [23], but late pericardial effusions and cardiac tamponade were more common after valvular operations [22–24]. A large proportion of patients with significant pericardial effusion have been reported to develop cardiac tamponade later on [22, 24]. In the study conducted by Light *et al.* [25], the prevalence of pleural effusion in CABG patients at 4 weeks was as high as 62.4% with no difference in comparison to patients who underwent combined CABG and valve procedures. Pleural fluid aspirates within 30 days of the index operation contained large amounts of red blood cells, indicating retained blood [25], but later effusions were usually classified as chronic inflammation [26].

Retained blood could be the stimulus for postpericardiotomy syndrome, which is characterized by friction rub, fever without any evidence of infection, pleuritic chest pain, pleural effusion and new or worsening pericardial effusion [4]. The incidence of postpericardiotomy syndrome varies according to the diagnostic criteria, but most cases present within the first month [27]. In some patients, this condition can progress to fibrosis and constrictive pericarditis [27], as hypothesized also by Boyle *et al.* [4]. However, in our series, an operation for pericarditis was performed in only 2 patients and 1 of them has had resternotomy for RBS.

Some limitations related to this study should be acknowledged. First, most of data were collected retrospectively, and the procedure for fluid collection was defined by the operating surgeon and not confirmed by any specific laboratory test. Second, a problem lies in the analysis of outcomes and their relation to the needed reintervention without referring to the timing of the adverse events. An analysis of the timing of the occurrence of these adverse events is complex and not feasible in a retrospective study. However, some adverse events such as sternal wound infection develop a few days after the operation, whereas other complications such as acute kidney injury may develop before RBS is recognized. The strength of the present analysis lies in the fact that the amount of blood loss and that of blood products used were recorded in prospective clinical registries, which makes the estimation of the severity of perioperative bleeding reliable.

In conclusion, RBS requiring any procedure for blood removal from the pericardial and pleural spaces is a relatively common complication after CABG and is associated with an increased risk of severe adverse events.

Conflict of interest: none declared.

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