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Mid-term clinical outcomes in cardiac surgery of Jehovah's witnesses

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Introduction **Surgical treatment of Jehovah's witnesses is a special challenge for cardiac surgery. The purpose of this study was to evaluate perioperative management and mid-term clinical outcome of Jehovah's witnesses who underwent cardiac surgery.**

Methods **Between January 1990 and June 2009, 34 Jehovah's witnesses (22 men, mean age 66 ± 8 years) underwent cardiac surgery. Surgical procedures included 17 coronary artery bypass grafts (CABG): 3 CABG and aortic valve replacements (AVR); 1 CABG and mitral valve plasty (MVP); 6 AVR; 1 subaortic membrane resection; 2 mitral valve replacements (MVR) and 2 MVP; 1 mitro-aortic valve replacement; and 1 cardiac foreign body removal. There were four urgent operations; 14 patients had NYHA class II–III. Sixteen patients received erythropoietin preoperatively. Preoperative haemoglobin (Hb) value was 14.2 ± 1.4 g/dl.**

Results **Extracorporeal circulation time was 127 ± 66 min, aortic cross-clamping 84 ± 45 min. Haemoglobin value 24 h after surgery was 11.2 ± 1.7 g/dl, haematocrit 34.1 ± 5.2%. None required surgical reoperation for bleeding.**

Intensive care unit stay was 2.3 ± 4.3 days, hospital stay 12.3 ± 10.4 days; there was no hospital mortality. Postoperatively, erythropoietin was administered to 19 patients. Follow-up was completed in 100%. Reoperation was necessary 8 years later in one patient for mitral bioprosthesis degeneration; the patient died 8 months later. All other patients are alive 59 ± 60 months after surgery; actuarial survival is 100% and 80 ± 2% at 5 and 10 years, respectively.

Conclusion **In our limited experience, early and late surgical results of Jehovah's witnesses patients are satisfactory. Appropriate preoperative management, optimization of Hb values, intraoperative measures to reduce the risk of bleeding and total blood loss recovery are the goals to achieve these results.** ***J Cardiovasc Med*** **11:170–174 © 2010 Italian Federation of Cardiology.**

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Introduction

Surgical management of congenital and acquired heart diseases in Jehovah's witnesses still constitutes a challenge for many cardiac surgeons, although the medical literature – starting from the first studies of Cooley – has confirmed feasibility, low morbidity and mortality, and very satisfactory results in this high-risk population [1,2].

Jehovah's witnesses accept the majority of surgical procedures and the administration of fluids such as colloids and crystalloids [3], whereas they refuse transfusion of whole blood and its derivatives (concentrated red blood cells, platelets and plasma) [4]. Other blood derivatives, such as albumin, immunoglobulins, vaccines and coagulation factors, are accepted or not on an individual basis [5], as well as the use of erythropoietin. Moreover, preoperative blood storage for subsequent transfusion is not considered acceptable [6], whereas acute normovolaemic haemodilution (ANH), cell-saver using [7,8] and cardiopulmonary bypass (CPB) procedures need individual approval, as long as the blood remains in contact with the whole circulation [9].

This retrospective study reports our experience, approach and results at the Cardio-thoracic Surgery Department of Udine University Hospital.

Materials and methods

Between January 1990 and June 2009, 34 Jehovah's witnesses underwent cardiac surgery at our hospital; all patients signed a written informed consent that included their refusal to receive transfusion of blood and derivatives, and their acceptance of any potential repercussion, including the risk of death, agreeing – in the meanwhile – to have cell-saver use during surgery.

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Different positions were expressed by patients relating to consent for specific pharmacological agents; the use of coagulation factors, albumin and immunoglobulins were allowed according to personal choice, whereas all patients accepted the use of erythropoietin, given when haemoglobin (Hb) levels were below 13 g/dl preoperatively, and below 10 g/dl postoperatively.

Our population was composed of 12 women and 22 men with a mean age of 66 ± 8 years (range 48–83 years). The erythropoietin was administered before surgery in 16 patients (9 women); the mean preoperative Hb value was 14.2 ± 1.4 g/dl.

The preoperative characteristics are summarized in Table 1. Mean preoperative ejection fraction of the left ventricle (LVEF) was $64 \pm 9\%$.

Four urgent operations were performed for unstable angina in three patients and progressive displacement of intramyocardial foreign bodies in one case. Reoperation was performed for aortic valve restenosis 30 years after commisurotomy.

Surgical procedures were very different: 17 patients underwent myocardial revascularization (coronary artery bypass grafting; CABG) – four with an off-pump approach – and most of them had three-vessel disease; three CABG and aortic valve replacement (AVR), one CABG and mitral valve plasty (MVP), six AVR – in three cases with replacement of the ascending aorta, in one case due to iatrogenic aorta dissection – and one resection of the subaortic membrane combined with decalcification of the aortic leaflets. Two patients underwent mitral valve replacement (MVR), two MVP and one mitro-aortic valve replacement. The prostheses used for replacement were biological in eight patients (seven pericardial and one porcine prosthesis) while mechanical in four; MVP was performed by Carpentier–Edwards Physio Ring.

A 48-year-old patient underwent urgent surgery to remove foreign bodies from the chest wall and the heart (five large sewing needles): two foreign bodies were identified and removed from the right ventricular free wall and by right ventriculotomy from the infundibular septum.

Table 1 Preoperative patient characteristics

	Patients (*n*)	%
Hypertension	23	67.6
Diabetes	7	20.5
Hypercholesterolaemia	17	50.0
Paroxysmal and permanent atrial fibrillation	4	11.7
Previous MI	7	20.5
Renal insufficiency	2	5.8
Peripheral vascular disease	2	5.8
COPD	1	2.9
Urgent status	4	11.7
NYHA II–III	14	41.1
CCS II–III	21	61.7
Obstructive coronary disease	21	61.7
Valve disease	16	47.0

CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NYHA, New York Heart Association.

In the operating room, a standard patient preparation with ECG, SpO_2, invasive arterial pressure, and temperature monitoring was placed.

The right internal jugular vein was cannulated and a pulmonary artery catheter (Edwards Lifesciences SvO_2 – CCO; Edwards Lifesciences, Irvine, California, USA) was placed.

Anaesthesia induction and its maintenance were performed using propofol, remifentanil and cisatrucurium. Endotracheal intubation and multiplane trans-oesophageal echocardiography were achieved.

Patients underwent anticoagulation using 3 mg/kg of heparin sulphate to maintain an activated clotting time (ACT) of at least 480 s. Blood products were not administered and the only fluids received by the patients were colloids and crystalloids; priming of the extracorporeal circulation (ECC) consisted of isotonic solution (Ringer lactate 1000–1200 ml); cardioplegic arrest was obtained by anterograde and retrograde intermittent cold crystalloid cardioplegia. An ultrafiltration system and administration of diuretic drugs were applied to avoid excessive haemodilution as a result of the addition of priming and cardioplegia solution. CABG was performed in normothermia, whereas moderate hypothermia (32°C) was used for valve replacement or combined operations.

Blood salvage was performed by decreasing blood losses – meticulous haemostasis, limiting use of swabs – and recovering as much lost blood as possible by cell-salvage circuit.

After protamine reversal of heparin, blood shed from the surgical field and collected in a cardiotomy and blood remaining in the CPB circuit were washed and concentrated in a cell-salvage circuit (Haemonetics Corporation, Braintree, Massachusetts, USA), and re-infused through a circuit that guarantees the continuity of the system.

In the postoperative period, 19 patients received treatment with erythropoietin (4000 IU/three times a week), whereas all of them were given folic acid orally daily (7.5 mg) and iron (125 mg).

In all patients with prosthetic valves, anticoagulation therapy was continued for 3 months maintaining an International Normalized Ratio (INR) between 2.0 and 3.0 in cases of biological implants and prosthetic rings, and for life in cases of mechanical prosthesis with INR between 2.5 and 3.5. Patients undergoing CABG were treated with aspirin (100 mg/day).

Table 2 Haemoglobin and haematocrit evolution

	Preoperative	Intraoperative	I postop day	Discharge
Ht (mean ± DS) (%)	42.7 ± 3.6	27.6 ± 5.3	34.1 ± 5.2	31.5 ± 4.1
Range	34.4–49.6	20.0–42.0	24.5–45.0	25.3–45.1
Hb (mean ± DS) (g/dl)	14.2 ± 1.4	9.0 ± 1.7	11.2 ± 1.7	10.3 ± 1.5
Range	11.4–16.8	6.8–13.7	7.2–14.7	7.7–15.3

Hb, haemoglobin; Ht, Haematocrit.

Results

Mean ECC time was 127 ± 66 min and mean aortic cross-clamping time was 84 ± 45 min.

Mean lowest intraoperative values were 9.0 ± 1.7 g/dl for Hb and 27.6 ± 5.3% for haematocrit.

Conduits used for myocardial revascularization were left internal mammary artery and saphenous vein magna; the number of anastomoses per patient was 2.3 ± 1, revascularization was complete in all cases but one.

Intensive care unit (ICU) stay was 2.3 ± 4.3 days, Hb value 1 h after arrival in ICU was 11.2 ± 1.7 g/dl and the same 24 h later, whereas haematocrit was, respectively, 33.9 ± 4.9% at 1 h and 34.1 ± 5.2% at 24 h (Table 2).

Mean intubation time was 20 ± 29 h (range 5–168 h); one patient required prolonged mechanical ventilation and tracheotomy as a result of iatrogenic aortic dissection.

In the first postoperative 24 h, blood loss through thoracic drains was 506 ± 211 ml (range 280–1180 ml) and surgical revision for bleeding was not required in any patients.

Major postoperative complications (Table 3) were: stroke with facial hemiparesis and right upper extremity hyposthenia in one patient (later fully recovered and probably secondary to significant anaemia, with a minimum Hb of 5.4 g/dl despite treatment with erythropoietin) and need for a pericardial window because of subtamponate pericardial collection within 30 days from the operation in the absence of lower values of Hb and haematocrit compared with the discharge (one patient).

Postoperative atrial fibrillation was paroxysmal in 11 patients, persistent in two patients and permanent in one, being already present in the preoperative period.

Hospital stay was 12.3 ± 10.4 days (range 6–69 days) (Table 4), with no hospital mortality.

Table 3 Postoperative complications

	Patients (*n*)	%
Postoperative stroke	1	2.9
Pericardial collection	1	2.9
Severe respiratory insufficiency	1	2.9
Postoperative AF	14	41.1

AF, atrial fibrillation.

Table 4 Postoperative parameters

	Mean ± DS	Range
MV time (h)	20 ± 29	5–168
Bleeding in 24 h (ml)	506 ± 211	280–1180
ICU stay (days)	2.3 ± 4.3	1–26
Hospital stay (days)	12.3 ± 10.4	6–69

ICU, intensive care unit; MV, mechanical ventilation.

During follow-up (100% completed – average 59 ± 60 months; range 2 months–18 years), one patient required reoperation for degeneration of a mitral prosthesis 8 years after the first procedure, and died 8 months afterwards from an unknown cause. The reoperation was performed for congestive heart failure, and the failed prosthetic mitral valve was replaced with another bioprosthesis associated with tricuspid valve repair according to De Vega; the postoperative period was complicated by low cardiac output and severe respiratory failure requiring tracheotomy.

All the other patients are alive and in good condition with actuarial survival at 5 years of 100% and 80 ± 2% at 10 years.

Discussion

Jehovah's witnesses, for religious beliefs, refuse blood transfusions; therefore, it is necessary to implement – preoperatively, intraoperatively and postoperatively – measures able to encourage the production of red blood cells and reduce their loss.

All our patients agreed to the administration of erythropoietin. Rate and amount of Hb increase with erythropoietin are subject to individual patient variation, with an average of 1.44 g/dl of Hb per week [10]. Noteworthy is that erythropoietin is more effective when preoperative Hb is less than 13 g/dl [9].

Preoperative indications are to suspend all medications that might contribute to postoperative bleeding and, in the case of anticoagulation, it is preferable to replace low-molecular-weight heparin with fractioned heparin 24 h before surgery [9].

All our patients consented to cell-saver, which is widely used in cardiac surgery [11], whereas normovolaemic haemodilution is not provided by our protocol. Normovolaemic haemodilution is utilized in less than 20% of cardiac surgery centres [12] and does not seem to actually improve results or confer an additional benefit when compared with cell-saver only [13].

Careful monitoring of postoperative blood loss and, in cases of excessive bleeding, prompt surgical revisions are mandatory. In our series these measures were not needed because accurate intraoperative haemostasis was performed – either with the use of an electrosurgical knife

or with topical haemostatic agents (Bioglue Cryolife Inc, Kennesaw, Georgia, USA) allowed by Jehovah's witnesses because they do not contain human derivatives.

Prompt surgical revision is indicated if bleeding exceeds 250 ml in the first hour or 400 ml in the first two postoperative hours; in these patients aggressive treatment is needed [14] due to the impossibility of performing transfusions, and in such cases, removal of mediastinal clots, resulting in marked fibrinolysis, can significantly reduce bleeding. Moreover, it is essential to have both a good control of hypertension in the surgical field and in the postoperative period, maintaining a relative hypotension to prevent excessive bleeding [15–18].

After surgery, all our patients were given iron and folic acid, to implement the production of red blood cells (as provided by the so-called 'bloodless surgery') [18,19].

The decision to use biological or mechanical prostheses may be difficult in such patients, given the risk of bleeding during the course of anticoagulant therapy. The criterion we followed depended mainly on the age of the patient, individual compliance with the anticoagulation and the clinical conditions.

Nevertheless, we tend to prefer valve replacement with mechanical prostheses in an attempt to avoid a subsequent reintervention; the age limit is 70 years since, as revealed by Cannegieter and colleagues [20], the risk of thromboembolism and bleeding is higher in older patients.

Some authors prefer to treat the disease of ascending aorta associated with aortic valve regurgitation using a modified Bentall procedure rather than Tirone–David remodelling, considering the need for lifetime anticoagulation [9] at lower risk than reintervention [21], which in this case is associated with high mortality [22].

In our experience, replacement of the supracoronary ascending aorta was performed in two patients: in one case for poststenotic aneurismatic dilatation and in the other for iatrogenic dissection. In such cases, we set out to make a definitive corrective procedure able to avoid any need for reintervention. Pasic *et al.* [17] recommended in this patient population – in cases of acute type A aortic dissection – to replace the ascending aorta and aortic arch in normothermia to avoid deterioration of the coagulative system resulting from hypothermia, whereas other authors, despite everything, prefer to perform the intervention in deep hypothermia and circulatory arrest [9,21].

The development of mini-invasive techniques and the ability to perform off-pump CABG have allowed new opportunities to avoid the use of blood products [23].

In patients undergoing CABG, the conduits we use are the left internal mammary artery for revascularization of the anterior descending and the saphenous vein magna for other coronary vessels, thus avoiding complete arterial revascularization. In one of the largest series of patients operated for CABG with bloodless surgery [18], we saw the same intervention strategy, due to a higher risk of bleeding when double mammary and other arterial conduits are used.

The mini-ECC is very useful in this patient population, as it significantly reduces blood cell damage, coagulation cascade changes and tissue damage when compared to conventional ECC [24,25].

Patients with chronic renal failure, treated with dialysis, are usually anaemic, have platelet dysfunction and are at higher risk of bleeding in case of surgery; preoperative and intraoperative techniques for blood conservation and miniaturized circuits for ECC and microplegia allow cardiac surgery to be performed on Jehovah's witnesses on dialysis [26,27].

Successful transplant cardiac interventions [27,28] and correction of complex congenital heart disease have also been performed [29].

Reintervention and intervention in urgency and emergency are feasible with acceptable surgical risks, due to the strategies available at present to reduce bleeding and increase production of red blood cells, as demonstrated by Reyes *et al.* [14], who reported a study in which 30% of patients were reinterventions with morbidity and mortality comparable to the control group.

Estioko *et al.* [30], in their series of reintervention measures designed to reduce intraoperative bleeding (already known and tested), also recommend, whenever possible, avoiding re-sternotomy in favour of an anterior thoracotomy approach associated with femoral vessel cannulation. Complex interventions in cases of aortic dissection, bacterial endocarditis [21,33] and thoracoabdominal aneurysm [9,31] have been performed with good results; in such cases, it is essential to have an accurate surgical strategy that uses cell-saver, reduced time of CPB, careful intraoperative haemostasis with the use of an electrosurgical knife and pharmacological agents such as tranexamic acid [32,33] and aprotinin [9,34] (the latter no longer available in Italy).

Strict adherence to protocols avoiding the need for blood transfusions and high doses of erythropoietin allowed Casati *et al.* [33] to treat successfully even anaemic Jehovah's witnesses patients requiring urgent complex surgery.

In our limited experience it was possible to carry out a heterogeneous group of interventions with reduced cardiac morbidity and no mortality.

The fact that up to 92% of patients undergoing cardiac interventions receive blood transfusions is known [35]. The side-effects of transfusion are the risk of blood-carried infections, increased susceptibility to infection – especially for sternotomy – risk of myocardial infarction [32,37–45], multiorgan failure (MOF) [36], acute lung injury [46] and increased incidence of certain cancers [35]. Consequently, avoiding the use of blood products should always be considered mandatory not only for Jehovah's witnesses, but for the entire population.

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