Anesthesia for high-risk patients undergoing percutaneous mitral valve repair with the MitraClip system in the catheterization laboratory

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Background
MitraClip system implantation is a new technique for high-risk patients with severe mitral regurgitation and patients risky for surgical repair or replacement of mitral valve through cardiopulmonary bypass.
Aim
The aim of this study was to evaluate the anesthetic experience in high-risk patients undergoing MitraClip implantation.
Setting
Madinah Cardiac Center, Saudi Arabia.
Patients and methods
The study included 34 patients scheduled for MitraClip implantations in the catheterization laboratory. An arterial line and a central venous line were inserted before induction. Epinephrine was started before induction and milrinone infusion was started after induction. The anesthetic technique for induction and maintenance was the same for all patients. Monitors included the heart rate, the arterial blood pressure, the central venous pressure, arterial blood gases, the temperature, and the urine output.
Results
All patients were hemodynamically stable intraoperatively and postoperatively. The intervention was successful in 33 cases and aborted in one case because of severe posteromedial leaflet tethering. Epinephrine and milrinone were weaned, and all patients were extubated, except for one mortality case that happened within the first 8 h postoperatively.
Conclusion
Percutaneous mitral valve repair with MitraClip implantation is a successful alternative in high-risk patients with symptomatic severe mitral regurgitation. Proper preoperative evaluation of the patients by an anesthetist and a cardiologist is very important. Starting epinephrine before anesthetic induction and milrinone infusion after induction resulted in a decreased pulmonary artery pressure, an increased ejection fraction, and maintained the arterial blood pressure during the procedure.

Keywords:
epinephrine, general anesthesia, milrinone, MitraClip system implantation, mitral regurgitation, three-dimensional transesophageal echocardiography

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Introduction

Mitral regurgitation is the second most common clinically significant form of valvular disease in adults [1,2]. Causes of severe mitral regurgitation include primary valvular disease or left ventricular dilatation [3–5]. Medical treatment in symptomatic mitral valve disease may not be effective for improvement in clinical symptoms [6–10]. A large percentage of patients for valve reconstruction or replacement do not undergo surgery because of a high perioperative risk [10–12].

The MitraClip system is a new percutaneous approach for treating mitral regurgitation that involves mechanical edge-to-edge coaptation of mitral leaflets, which is analogous to the surgical Alfieri technique [13]. General anesthesia is required for these procedures for the following reasons:

(1) To facilitate the use of transesophageal echocardiography (TEE) to guide the precise placement of the MitraClip;

(2) To allow the use of controlled breath holding at a critical time of the procedure such as positioning a clip or implantation of a second clip; and
(3) To ensure that the patient does not move during the procedure [14].

Many studies were reviewed regarding the anesthetic technique for high-risk patients who underwent mitral clipping, and there was only one study that reported the anesthetic experience for these patients, but the preoperative ejection fraction was higher in this study [14]. The present study was conducted to record the anesthetic experience and considerations for high-risk patients undergoing mitral clipping during laboratory catheterization under general anesthesia.

Patients and methods

After obtaining informed consent and approval of the local ethics and research committee at Madinah Cardiac Center, Almadinah Almunarwarrah, Saudi Arabia, this prospective study included 34 adult patients scheduled for MitraClip (Abbott Laboratories, Abbott Park, Illinois, USA) in the Catheterization Laboratory (September 2012 to July 2014). The inclusion criteria were patients with severe mitral regurgitation and ejection fraction less than or equal to 30%. The mitral regurgitation was ischemic, functional, degenerative, or failed repair after surgery and the second surgery was contraindicated through cardiopulmonary bypass. Patients were evaluated by the referring cardiologist, the interventional cardiologist, cardiac surgeons, and cardiac anesthesiologists. The exclusion criteria included patients with acute myocardial infarction within the previous 8 weeks, primary stenotic valvular disease, a malfunctioning artificial heart valve, mitral valve area of less than 4.0 cm^2, obstructive cardiomyopathy, pericardial disease, and primary pulmonary disease. The preoperative evaluation included the reviewing of the medical and surgical history, echocardiography, and coronary angiography. Renal hemodialysis was performed for patients with renal failure on the night before the surgery.

Monitoring of patients

Monitoring included the heart rate, the mean arterial blood pressure, the central venous pressure, the temperature, arterial blood gases, the urine output, and the activated clotting time (ACT). The pulmonary artery pressure was measured by Doppler echocardiography (by a cardiologist). Hemodynamic values were collected serially at the following time points: at baseline, after induction of anesthesia, and then every 5 min during the intervention, on admission to the ICU, and at the sixth and the 24th hour after ICU admission. After anesthetic induction, a TEE probe was inserted to assess ventricular and valvular functions by a cardiologist (full study before, during, and after the intervention).

The anesthetic technique

A radial arterial cannula and a central venous catheter were inserted under local anesthesia before the procedure to allow continuous hemodynamic monitoring, and administration of inotropic support. Two external adhesive pads were attached to the patient for early management of arrhythmias. Epinephrine was started at 0.03 μg/kg/min before induction and continued at an infusion of 0.03–0.1 μg/kg/min to maintain hemodynamics during anesthesia. Induction was performed with intravenous ketamine 1–2 mg/kg, fentanyl 1–2 μg/kg, and rocuronium 0.8 mg/kg. After tracheal intubation, the anesthesia was maintained with oxygen, sevoflurane (1–3%), fentanyl infusion (1–2 μg/kg/h), and cisatracurium (1–2 μg/kg/min). Milrinone was started without a loading dose (0.4 μg/kg/min) and maintained during anesthesia to decrease the pulmonary hypertension. During the procedure, heparin was given upon crossing of the interatrial septum with the trans-septal needle and catheter to maintain ACT more than 250 s. Breath holding (transient endotracheal tube disconnection) was needed to allow the precise placement of the device. Careful and cautious monitoring of hemodynamics is required for crossing the device and the mitral valve. At the end of each grasp and before the release of the device, the blood pressure was increased pharmacologically to be around the same preoperative values. This allows the evaluation of the extent, the location, and the severity of any residual mitral regurge and the determination of whether the clip should be deployed and/or whether another clip is needed. At the end of the intervention, the patients were transferred to the cardiac ICU with full monitoring and were managed by the intensivist, where the epinephrine and the milrinone were weaned gradually and completely in all patients. The patients were weaned and extubated easily.

The MitraClip technique

The procedure was performed with three-dimensional TEE and fluoroscopic guidance. Vascular access was obtained with an 8-Fr sidearm sheath in the right and the left femoral veins and a 6-Fr sheath in the left femoral artery; the vein was probed with a wire, and right-heart catheterization was first performed to document right-heart pressures, and through a puncture in the atrial septum, a catheter can be introduced from the right into the left atrium under TEE guidance. After changing to a harder wire, a 24-Fr guide catheter with a dilator is placed in the

left atrium. Various TEE views guide the positioning of the clip across the regurgitant jet to show the site of maximum regurgitation, and then introduced in the open position into the left ventricle. Once the positioning is ideal, the mitral leaflets are grasped under real-time TEE guidance and the clip is closed; the mitral leaflets can be caught and fixed with the clip arms. The clip is then released from the delivery catheter and the mitral valve is interrogated by TEE for the adequacy of leaflet capture, the degree of residual mitral regurge, and evidence of mitral stenosis. In some patients with very wide regurgitation surfaces, the placement of a second clip may be necessary. Right-heart and left-heart catheterization is then repeated to document final hemodynamic parameters. The guide catheter is then removed, and the femoral punctures are repaired percutaneously with Proglide devices (Abbott Vascular, Abbott Park, Illinois, USA) [15].

Statistical analysis

Data were described statistically in terms of mean ± SD. A comparison between the different time points was performed using repeated-measure analysis of variance through the general linear model. *P* values less than 0.05 were considered to be statistically significant. All statistical calculations were performed using computer program statistical package for the social sciences (SPSS, version 15 for Microsoft Windows; SPSS Inc., Chicago, Illinois, USA).

Results

Preoperative data of patients

Table 1 shows the demographic data, comorbidities, the ejection fraction, the Euroscore, the New York Heart Association functional class, and previous surgery.

Table 1 Preoperative data of patients

Variables	Mean ± SD/*n*
Age (years)	62.53 ± 12.05
Weight (kg)	81.09 ± 9.97
Sex (male/female)	22/12
Smoking	5
Hypertension	26
Diabetes mellitus	24
Hyperlipidemia	11
Ischemic heart diseases	23
Previous coronary surgery	4
Previous coronary stent	17
Heart failure	2
Renal diseases	
Impairment	12
Failure	5
Hepatic (liver enzymes >3 folds)	6
Cerebrovascular accident	2
NYHA	
III	6
III–IV	11
IV	17
Euroscore	18.76 ± 3.13

NYHA, New York Heart Association functional class.

Intraoperative data of patients

Table 2 shows the data of patients during the procedure. The mean duration of procedures was 188.91 ± 22.75 min. The mean urine output was 279.71 ± 54.41 ml. Blood gases were within normal values during the procedure; some patients received packed red blood cells intraoperatively, and the mean was 0.82 ± 0.75 U and the mean hemoglobin concentration was 12.31 ± 1.69 g/dl. The mean preoperative ACT was 135.15 ± 9.01 s; it was 305.59 ± 31.17 s during the procedure after heparin and 154.65 ± 17.56 s after reversal by protamine. The mean dose of heparin was 138.24 ± 36.01 U/kg and protamine was 1.23 ± 0.24 mg/kg (Table 2).

Table 2 Intraoperative data of patients

Variables	Mean ± SD
Hemoglobin (g/l)	12.31 ± 1.69
Temperature (°C)	36.66 ± 0.40
SPO_2 (%)	99.18 ± 0.79
$PaCO_2$ (mmHg)	33.88 ± 1.59
Heparin (U/kg)	138.24 ± 36.01
Protamine (mg/kg)	1.23 ± 0.24
ACT baseline (s)	135.15 ± 9.01
ACT after heparin (s)	305.59 ± 31.17
ACT after protamine (s)	154.65 ± 17.56
Packed red blood cells (U)	0.82 ± 0.75
Urine output (ml)	279.71
Duration (min)	188.91 ± 22.75

ACT, activated clotting time; $PaCO_2$, arterial partial pressure of carbon dioxide; SPO_2, arterial oxygen saturation.

Hemodynamic data of patients

Table 3 shows the hemodynamic changes. There was no significant change in the heart rate before, during, and after the procedure ($P = 0.668$). The preoperative mean arterial blood pressure was 79.65 ± 5.443, and it

Table 3 Hemodynamic data of patients

Variables	Baseline	During procedure	After procedure	*P*-value
Heart rate (bpm)	83.06 ± 6.14	86.82 ± 5.86	85.24 ± 4.38	0.668
CVP (mmHg)	13.00 ± 2.04	11.35 ± 1.30	10.06 ± 1.74	0.022
MAP (mmHg)	79.65 ± 5.44	87.62 ± 5.36	91.24 ± 5.43	0.013
PAP (mmHg)	49.53 ± 8.69	38.32 ± 8.41	33.68 ± 6.51	0.001
EF (%)	25.74 ± 2.65	33.29 ± 2.88	37.09 ± 3.50	0.001

Data are presented as mean ± SD; CVP, central venous pressure; EF, ejection fraction; MAP, mean arterial blood pressure; PAP, systolic pulmonary artery pressure.

increased during and after the procedure to 87.62 ± 5.36 and 91.24 ± 5.43, respectively (P = 0.013). The baseline central venous pressure was 13.00 ± 2.04 and decreased during and after the procedure to become 11.35 ± 1.30 and 10.06 ± 1.74, respectively (P = 0.022). The systolic pulmonary artery pressure was higher before anesthesia; the mean was 49.53 ± 8.69 and it decreased during and after the procedure to 38.32 ± 8.41 and 33.68 ± 6.51, respectively (P < 0.001). The preoperative ejection fraction was 25.74 ± 2.65 and increased during and after the procedure to 33.29 ± 2.88 and 37.09 ± 3.50 (P < 0.001), respectively.

Perioperative complications

Table 4 shows the postoperative outcome and complications. Five patients had supraventricular tachycardia and were managed by intravenous adenosine. There were attacks of atrial fibrillation in seven patients during the procedure: five cases recovered spontaneously and two cases required DC shock. There was femoral artery dissection in two patients: one case required vascular repair and the second case required vascular stent inserted by the cardiologist. There was one mortality case through 8 h in the ICU. The patient was tracheostomized and ventilator-dependent for 3 months before the procedure and after intervention; the patient was stable for the first 4 h and started to deteriorate and stopped responding to medical support and expired after 8 h postoperatively (Table 4).

Postoperative outcomes

The MitraClip implantation was successful in 33 patients and failed in one case because of severe posteromedial leaflet tethering. Table 5 shows the preoperative grading of mitral regurge and the improvement after MitraClip implantation. All patients were extubated in the ICU, except one patient. The mean time of extubation was 1.76 ± 0.85 h. The mean ICU length of stay was 1.21 ± 0.41 days and the hospital length of stay was 5.03 ± 1.01 days (Table 4).

Table 4 The postoperative outcome and complications

Variable	Mean ± SD
Time of extubation in ICU (hour)	1.76 ± 0.85
ICU length of stay (day)	1.21 ± 0.41
Hospital length of stay (day)	5.03 ± 1.01
Supraventricular tachycardia	5
Atrial fibrillation during procedure	7
Femoral artery injury	2
Mortality	1

ICU: Intensive care unit

Table 5 Data of mitral regurge of patients

Causes of regurge	*N*	Preintervention MR		Postintervention MR	
		Grade	*N*	Grade	*N*
Ischemic	3	Grade IV	32	Grade I	23
Functional	26	Open	2	Grade II	6
Cleft (after surgery)	1	—	—	Grade III	4
Degenerative	4	—	—	Grade IV	1

MR, mitral regurge.

Discussion

Hemodynamic stability and the prevention of potential life-threatening complications are the main objectives of anesthetic management during the MitraClip implantation. The present study shows the anesthetic experience and considerations for 34 high-risk patients who underwent percutaneous MitraClip implantation in a catheterization laboratory. Challenges pertaining to anesthesia during the procedure are similar to those of conventional cardiac surgery, and patients were prepared as they would be for cardiac surgery (vasopressors, resuscitation medications, and operative room). The patients were critical and risky for many reasons: a low ejection fraction (≤30%), a dilated left ventricle, severe mitral regurge, severe pulmonary hypertension, and associated comorbidities (ischemic heart diseases, congestive heart failure in some patients despite proper treatment, hypertension, renal impairment or failure, and old age). Therefore, anesthetists should be cautious during these procedures, and perform proper preoperative evaluation, monitoring, and management of the hemodynamics.

Before induction, epinephrine was started to maintain the arterial blood pressure during anesthesia. Ketamine was used for induction to minimize changes in hemodynamics during induction. After induction and stabilizing the hemodynamics, the milrinone infusion was started to decrease the pulmonary hypertension and minimize the after load of the right and the left ventricles. The loading dose of milrinone was not given to avoid the possibility of hypotension in critical patients. Intravenous fluid administration was titrated and controlled carefully according to the central venous pressure, the mean arterial blood pressure, the blood loss, and the urine output.

The present study showed that the mean arterial blood pressure and the ejection fraction increased during and after the procedure. Also, the pulmonary artery pressure decreased after MitraClip and postoperatively. These changes in hemodynamics were related to three reasons: the first was the inotropic effect of epinephrine, which improved the myocardial contractility; the second was the decrease in the after load by milrinone infusion; and the third was the decrease in the regurgitant fraction as a result of mitral regurgitation repair by

MitraClip. Some patients suffered from hypotension during intervention and were managed by increasing the dose of epinephrine and increasing the rate of fluid administration. While placing the MitraClip in position, five patients had supraventricular tachycardia and were managed with intravenous adenosine (6–12 mg) without any side effect related to adenosine. Seven patients had atrial fibrillation, five cases recovered spontaneously, and two cases required DC shock. The extubation of all patients was performed in the cardiac ICU according to the preoperative plan between the anesthetist and the cardiologist to wean the patients smoothly from ventilation, epinephrine, and milrinone in the ICU.

Kothandan *et al*. [14] reported their anesthetic experience in a study including 21 patients who underwent mitral clipping. They inserted the arterial line and the central venous line before the induction of anesthesia. The preoperative ejection fraction was 47 ± 15% and the mean arterial pulmonary blood pressure was 76.2 mmHg. They used propofol, midazolam, etomidate, or dexmedetomidine in addition to fentanyl or morphine during induction and sevoflurane or desflurane during maintenance. The hypotension during anesthesia was managed with phenylephrine in 15 patients and with ephedrine in five patients. For patients with persistent hypotension, a norepinephrine infusion was used in five patients and an adrenaline infusion was used in two patients. Twelve patients were extubated in the operative room and the other patients were ventilated electively. All patients tolerated general anesthesia. The grade of mitral valve regurge decreased significantly from 3.5 ± 0.5 to 1.4 ± 0.6 postoperatively. Despite findings similar to our result, the type of medications used during induction or the timing of the administrated vasopressors differed from the present study. First, their preoperative ejection fraction was higher (47 ± 15%) compared with the present study (≤30%). Second, they used phenylephrine and norepinephrine with a preoperative mean pulmonary artery pressure of 76.2 mmHg, and there was no information about the intraoperative or the postoperative pulmonary pressure in their study, and these medications may increase the grade of mitral regurge as a result of the increased after load. Third, despite the significant decrease in the mitral valve grade, the ejection fraction was not improved or even decreased slightly postoperatively. Fourth, the mean arterial blood pressure decreased slightly or did not improve postoperatively, despite using vasopressors in their patients.

Practice and learning points

(1) Proper preoperative evaluation of high-risk patients undergoing MitraClip implantation by the assessment of noninvasive and invasive cardiac investigations in addition to a general anesthetic assessment of other body systems (cerebral, respiratory, hepatic, and renal), to optimize the medical condition of the patients and reduce the morbidity and the mortality associated with MitraClip.
(2) Proper preparation of the patients as for cardiac surgery [14].
(3) Proper monitoring of hemodynamics using invasive and noninvasive methods.
(4) Proper control of electrolytes, the acid–base balance, and the temperature.
(5) Proper use of inotropic, inodilator, or vasopressors agents [16].
(6) Minimizing the after load for the left and the right ventricles.
(7) Proper choice of the anesthetic agent by selecting drugs that maintain cardiovascular stability.
(8) The anesthesiologist should be aware of the complications associated with MitraClip implantation:
    (a) Hypothermia, hypovolemia, and hemorrhage.
    (b) Severe hemodynamic instability and cardiac arrest.
    (c) Various procedure-related complications (worsening of mitral regurge, mitral stenosis, vascular injuries, retroperitoneal bleeding, arrhythmia, ventricular and atrial perforation, with a possibility of cardiac tamponade, partial dehiscence of the clip after initial seating, leaflet or chordal tears) [17,18].
(9) The anesthesiologist should be aware of the hazards of radiation, as this intervention was performed under fluoroscopy [19].
(10) Long-time and frequent movement of the TEE probe may lead to inadvertent dislodgement of the endotracheal tube [14].

Conclusion

Percutaneous mitral valve repair with MitraClip implantation is a successful alternative in high-risk patients with symptomatic severe mitral regurgitation. Proper preoperative evaluation of patients by an anesthetist and a cardiologist is very important. Administration of epinephrine before anesthetic induction and milrinone infusion after induction resulted in a decreased pulmonary artery pressure, an increased ejection fraction, and maintained the arterial blood pressure during the procedure.

Limitations

Our study recognizes some limitations such as being a single-center study and the small number of patients.

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Conflicts of interest

There are no conflicts of interest.

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