Percutaneous mitral commissurotomy in pregnant women: Immediate and long-term outcomes

Commissurotomie mitrale percutanée chez la femme enceinte: Résultats immédiats et à long terme

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Abstract

Background: Rheumatic mitral stenosis (MS) is prevalent in developing countries. Poorly tolerated during pregnancy, MS is often requiring urgent intervention.
Objectives: This study aimed to evaluate immediate and long-term outcomes after percutaneous (PMC) in pregnant women.
Methods: Observational retrospective study of pregnant women who underwent PMC for severe MS between January 2008 and December 2018. Primary endpoint was procedural success (mitral valve area > 1.5 cm²) without complications.
Results: 39 patients. Mean age 34.2±5.1 years. Mean gestational age 28.2±4.9 weeks. PMC was successful in 37 patients (94.8%). There was no maternal mortality. Two procedures failed (1 transseptal puncture failure and 1 severe traumatic mitral regurgitation requiring emergent surgery). If successful, PMC allowed the pursue of pregnancy until full term and vaginal delivery in 36 (92.3%) and 20 (51.3%) patients, respectively. One in utero foetal demise and one neonatal death occurred. At 56.1-month, after exclusion of three patients with prompt surgical valve replacement, there were 7 cases of mitral restenosis (19.4%) with Wilkins score >8, suboptimal result (valve area between 1.5 and 1.8 cm²) and incomplete bicommissural splitting as predictive factors. All babies maintained normal growth and development.
Conclusion: This study confirmed effectiveness and safety of PMC during pregnancy when performed by an experienced team with a procedural success of 94.8% but at the cost of a restenosis rate of 19.4% at 56.1 months. These were predicted, in addition to Wilkins score, by a suboptimal but accepted immediate result of the procedure, still allowing a step forward.
Key words: Mitral stenosis, Pregnancy, Mitral valvuloplasty

Résumé

Introduction : Le rétrécissement mitral rhumatismal est fréquent dans les pays en développement. Mal toléré pendant la grossesse, il nécessite souvent une intervention urgente.
Objectifs : Cette étude visait à évaluer les résultats immédiats et à long terme après une commissurotomie mitrale percutanée (CMP) chez les femmes enceintes.
Méthodes : Étude rétrospective observationnelle entre janvier 2008 et décembre 2018. Le critère de jugement principal était le succès procédural (surface mitrale >1.5 cm² sans complications).
Résultats : 39 patientes. Âge 34,2±5,1 ans. Âge gestationnel 28,2±4,9 semaines. Un succès procédural a été observé chez 37 patientes (94,8%). Aucun décès maternel n'a été observé. Deux procédures ont échoué. En cas de succès, la CMP a permis la poursuite de la grossesse à terme et l'accouchement par voie basse chez respectivement 36 (92,3%) et 20 (51,3%) patientes. Un décès fœtal in utero et un décès néonatal sont survenus. À 56,1 mois (en excluant trois patientes ayant bénéficié d'un remplacement valvulaire chirurgical rapide), 7 cas de resténose (19,4%) ont été notés avec un score de Wilkins >8, un résultat sous-optimal et une ouverture bicommissurale incomplète comme facteurs prédictifs. Tous les bébés ont conservé une croissance et un développement normaux.
Conclusion : Cette étude a confirmé l'efficacité et la sécurité de la CMP pendant la grossesse, avec un succès procédural de 94,8%, mais au prix d'un taux de resténose de 19,4% à 56,1 mois. Ces resténoses étaient prédites entre autres par un résultat immédiat sous-optimal mais accepté de la procédure, permettant néanmoins de passer un cap.
Mots clés: Sténose mitrale, Grossesse, Valvuloplastie mitrale

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Introduction

Rheumatic mitral stenosis (MS) remains prevalent in developing countries, especially among women of childbearing age. It's the most common valvulopathy encountered during pregnancy and may first manifest or worsen secondary to gestation hemodynamic changes (1). Cardiovascular adaptation during pregnancy is marked by an increase in cardiac output, early arterial vasodilation, and secondary activation of the renin-angiotensin-aldosterone system, leading to fluid retention, further amplified by pregnancy-related hyperestrogenism (2). This approximately 50% rise in cardiac output increases trans-mitral gradient and may unmask previously asymptomatic MS (3,4).

Such hemodynamic stress can precipitate acute pulmonary oedema, cardiogenic shock, or even maternal-foetal death, necessitating optimal medical therapy and, in some cases, urgent relief of the mitral obstruction (1).

Percutaneous mitral commissurotomy (PMC), first described by Japanese surgeon Kanji Inoue in 1984, has become the treatment of choice for severe MS (5,6,7). During pregnancy, it allows to stabilize acute episodes and optimize hemodynamics for delivery, though sometimes at the cost of suboptimal results and a higher risk of restenosis (3,6). Despite its benefits, foetal radiation exposure remains a concern, with limited data on long-term effects.

This study aimed to assess short- and long-term outcomes of PMC during pregnancy and evaluate potential adverse effects on children.

Methods

Study design

This was a retrospective, descriptive, and analytical single-center cohort study led between 25 January 2008 and December 2018.

Study population

All pregnant women who underwent PMC were included. PMC were performed in patients with severe MS (mitral valve area (MVA) ≤ 1.5 cm²), with or without mild to moderate mitral regurgitation (MR) (≤ grade II), symptomatic dyspnoea (NYHA class ≥ 2), and a left atrium free of thrombus 72 hours prior to the procedure were included. Cases with left atrial appendage thrombus, significant valvular or subvalvular calcifications, or other surgical valvulopathies were discussed individually by local multidisciplinary Heart Team.

Patient data were collected by reviewing clinical records, echocardiography databases and catheterization lab logs. No patients meeting selection criteria were excluded, and complete follow-up data were available for all included patients.

Echocardiographic evaluation

All patients underwent transthoracic echocardiography (TTE) with measurement of MVA before procedure, immediately afterwards, and at 48 hours post procedure. MVA assessment was based on planimetry and pressure half-time parameters. Planimetry, performed in parasternal short axis during mid-diastole, was considered as the reference method due to its better correlation with anatomical MVA. In case of discrepancy, planimetry value was retained.

Mean transmitral gradient was measured by continuous-wave Doppler from the apical view. A mean gradient >10 mmHg was considered indicative of severe MS. Gradient interpretation was contextualized, considering factors such as heart rate, cardiac output, atrial fibrillation (AF), and associated MR. Wilkins score was calculated to assess suitability for PMC. This score evaluated four parameters: leaflet mobility, leaflet thickening, subvalvular apparatus thickening, and leaflet calcification. A threshold of >8 distinguished severe mitral disease predicting less favourable results for PMC (6). Transesophageal echocardiography (TEE) was mandated prior to the procedure to rule out thrombus in the left atrium and left atrial appendage unless hemodynamic instability or poor tolerance in patients with sinus rhythm.

Percutaneous mitral commissurotomy procedure

PMC, described by Inoue in 1984 (7), replicates the surgical procedure by allowing the opening of one or both fused mitral commissures through balloon inflation at the mitral orifice. This technique currently represents the first-line treatment for symptomatic rheumatic MS with favorable anatomical or clinical characteristics (6, 19).

Procedure was generally performed under local anesthesia via femoral venous approach.

Pre- and post-procedural measurements of right atrial, right ventricular, main pulmonary artery, and pulmonary capillary wedge pressures were obtained during right heart catheterization.

Transseptal puncture was routinely fluoroscopy guided using standard views without any need for a pigtail catheter in the non-coronary sinus nor TEE avoiding general anesthesia. Balloon size selection was primarily based on patient height. Sequential low-pressure inflations were performed to achieve commissural opening, with the procedure terminating upon achieving a MVA more than 1.5 cm², assessed via echocardiography using planimetry. Procedure was immediately halted if significant MR developed during the process.

PMC is an irradiating technique for both the mother and foetus. To minimize radiation exposure, it was imperative to provide abdominal protection using a lead apron. Unnecessary abdominal radiation was avoided through collimation and distance reduction between patient and imaging sensor. Minimizing time and storing fluoroscopy getting rid of cineangiography were also recommended for dose reduction.

Follow up

In hospital follow up consisted of clinical and echocardiographic assessments immediately after and 48 hours following the procedure.
Thereafter, clinical follow up was provided for all patients as well as for their infants: closely monitored until delivery, then followed up in outpatient consultations every six months, and additionally via referring physicians or, if unavailable, by telephone contact.
In addition to clinical follow up, echocardiographic surveillance was carried out every six months during the first year, then annually thereafter in the absence of symptoms.
Neonatal follow up included a comprehensive initial examination at birth, followed by monitoring of growth charts and psychomotor development.

Study endpoints

Primary endpoint was immediate procedural success rate. This was defined by a MVA ≥ 1.5 cm², provided no complications occurred.
When successful, the outcome was categorized as optimal result if MVA ≥ 1.8 cm², and intermediate or sub-optimal result if 1.5 < MVA < 1.8 cm².
Secondary endpoints included peripartum period evaluation, specifying delivery mode and any cesarian section indication, newborn's status including birth weight, and any neonatal complications.
Maternal complications included significant MR due to commissural tear or chordal rupture during Inoue balloon inflation, cardiac tamponade, systemic embolism and death.
Foetal and neonatal complications included in utero foetal demise, prematurity, intrauterine growth restriction, neonatal distress, neonatal intensive care admission and neonatal death.

Statistical analysis

SPSS software, version 22 was used. Simple and relative frequencies were calculated for qualitative variables and means, medians, standard deviations, and ranges for quantitative variables. Comparison of means was performed using the Student's t-test and comparison of proportions was carried out using Pearson's chi-squared test for independent samples.
Factors associated with mitral restenosis were investigated, focusing on prior PMC, age at the time of PMC, immediate post-procedure mitral valve area, commissural splitting, and the Wilkins anatomical score. Event-free survival was analyzed using the Kaplan-Meier method, and the log-rank test was used to compare survival distributions in univariate analysis.
A p-value < 0.05 was considered statistically significant for all tests.

Ethical considerations

Medical confidentiality was respected for all patients. No conflicts of interest were declared by all authors.

Results

During the study period, 469 PMC procedures were performed. Thirty-nine PMC procedures were conducted on pregnant women, representing 8.3% of the total PMC volume (Figure 1).

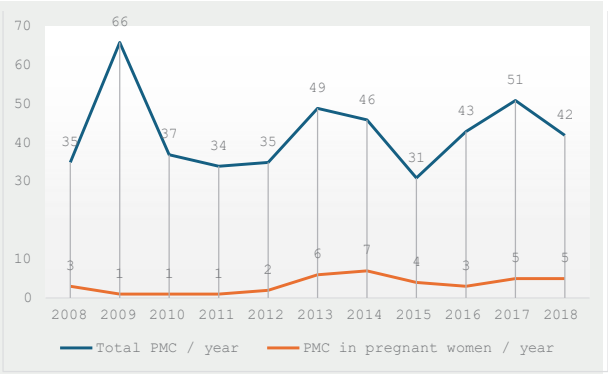


Figure 1. Total and among pregnant women percutaneous mitral balloon valvuloplasty procedures volume evolution from January 2008 to December 2018.

Baseline characteristics

Mean age was 34.2±5.1 years, with extremes ranging from 24 to 44 years.
Mean gestational age at the time of PMC was 28.2±4.9 weeks of amenorrhea (17–37 weeks).
PMC was performed during second trimester in 10 patients (25.6%) and during third trimester in 29 patients (74.4%). Two procedures only were performed before 20 weeks of amenorrhea(17 and 19 weeks).
Twenty-six parturient patients (66.6%) were housewives with low intellectual and socioeconomic status, predominantly with a primary education level (66.6%). Thirteen patients were of rural origin (33.4 %).
MS etiology was rheumatic in all the patients. Rheumatic fever prophylaxis based on benzathine benzylpenicillin was initiated in five patients only despite an established disease diagnosis from the young age in all cases. Eleven patients had previously undergone PMC in their medical history. Two patients underwent multiple PMC procedures (2 and 3 interventions, respectively). All patients desired the studied pregnancy. None of them were using contraception method at the time of conception and no pre-pregnancy cardiological evaluation was performed for any of them. All patients presented with dyspnea. Of them, twelve (30.8 %) presented with acute pulmonary edema and one presented in a state of cardiogenic shock with low cardiac output related to very severe MS (MVA of 0.8 cm² and a transmitral gradient of 22 mmHg). Thirty-seven patients were in sinus rhythm before PMC (94.8%), and only two were AF (5.2%).

Echocardiographic data

Baseline MVA was 0.98±0.22 cm², ranging from 0.40 to 1.40 cm². Valvular and subvalvular structures were mildly

to moderately altered in all patients. Wilkins score was ≤ 8 in 74.4% of cases (n=29) and between 9 and 11 in 25.6% of cases (n=10). No patients had severely altered subvalvular structures or valvular calcifications (Wilkins score ≥ 12). The average sPAP was 61.1±16.4 mmHg, with extremes ranging from 30 to 120 mmHg. No contraindications to PMC were noted in 38 parturients. One patient had severe aortic stenosis (aortic valve area 0.7 cm²), making the procedure theoretically contraindicated. After multidisciplinary discussion, decision was to proceed with PMC during pregnancy to allow its continuation under better conditions, followed by planned double valve replacement after delivery. Baseline echocardiographic characteristics were summarized in table 1.

Table 1. Baseline echocardiographic characteristics.

Variable	Pregnant women (N=39)
LVEF (%)	62.6±5.1
MVA (cm²)	0.98±0.22
Trans-mitral gradient (mmHg)	16.6±5.8
Indexed LA volume (ml/m²)	64±12.8
Wilkins score ≤ 8	29 (74.4%)
LAA thrombus	1 (2.5%)
Spontaneous contrast in LA or LAA	35 (89.7%)
Mild mitral regurgitation	24 (61.5%)
Aortic stenosis / Severe aortic stenosis	4 (10.2%) / 1 (2.5%)
Aortic regurgitation	6 (15.4%)
Tricuspid regurgitation	37 (94.9%)
sPAP (mmHg)	61.1±16.4
TAPSE (mm)	19±2.6
S' wave (cm/s)	11.6±1.1

LA: Left atrium; **LAA**: Left atrial appendage; **LVEF**: Left ventricular ejection fraction; **MVA**: mitral valve area; **sPAP:** Systolic pulmonary artery pressure; **TAPSE**: Tricuspid annular pansystolic excursion.

TEE was performed in all patients. Only one patient had an intra-auricular thrombus and was placed on anticoagulation therapy with a vitamin K antagonist. PMC was delayed and performed after effective thrombus resolution confirmed by repeat TEE two weeks later.

After the procedure, average MVA was 1.88±0.25 cm², ranging from 1.5 to 2.5 cm². Average sPAP was 42±14.9 mmHg, ranging from 25 to 100 mmHg. Nine patients had no MR post- procedure. In 13, mild regurgitation remained stable; 15 showed new or worsened regurgitation (not exceeding grade 2). Two developed moderate regurgitation during the procedure, and one had severe regurgitation due to chordal rupture (Figure 2).

Excluding two patients, one with failed transseptal puncture and one with severe acute MR, changes in echocardiographic parameters before and after the procedure are presented in table 2.

Table 2. Comparison of echocardiographic parameters before and after percutaneous mitral commissurotomy.

Variable	Before PMC	After PMC*	P
MVA (cm^2)	0.98±0.22	1.88±0.25	<0.01
Mean transmitral gradient (mm Hg)	16.6±5.8	9.1±4.2	<0.01
sPAP (mm Hg)	61.1±16.4	42.0±14.9	<0.01

MVA: Mitral valve area; **sPAP**: systolic pulmonary artery pressure. *Excluding two patients (1 failed transseptal puncture, 1 acute severe mitral regurgitation).

Procedural data

Procedures were conducted under local anesthesia in 38 cases. General anesthesia was mandatory in only one case in a cardiogenic shock setting.

Transseptal puncture was performed under fluoroscopic guidance only in all cases.

Hemodynamic parameters before and after PMC are summarized in table 3.

Table 3. Evolution of hemodynamic parameters before and after percutaneous mitral commissurotomy.

Parameter	Before PMC	After PMC	p
LA (mmHg), N=37*	30.0±8.5 (12-50)	16.4±7.6 (7-50)	<0.01
RA (mmHg), N=22†	10.2±6.4 (3-30)	6.8±3.6 (2-15)	<0.01
RV (mmHg), N=22†	55.7±24.4 (20-120)	42.1±14.2 (25-90)	<0.01
PA (mmHg), N=22†	51.5 ± 17.1 (20-120)	44 ± 17.7 (27-100)	<0.01

LA: Left atrium; **PA**: Pulmonary artery; **PMC**: Percutaneous mitral commissurotomy; **RA**: Right atrium; **RV**: right ventricle. *Excluding two patients (1 failed transseptal puncture, 1 acute severe mitral regurgitation). †Evaluated in 22 patients only (not available data being retrospectively collected).

Primary outcome: Immediate procedural results

A procedural success, defined by a MVA of at least 1.5 cm² without complications, was achieved in 37 patients (94.8%). Immediate result was optimal, with a MVA ≥ 1.8 cm² in 29 patients (74.3%). Immediate result was intermediate (1.5 cm² < MVA < 1.8 cm²) in 8 patients (20.5%) (Figure 2). Procedure failed in 2 patients (5.2%).

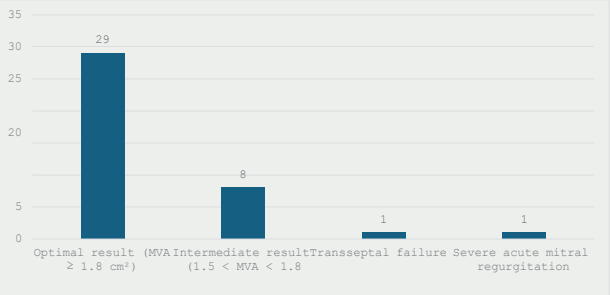


Figure 2. Primary outcome: immediate procedural results.

MVA: Mitral valve area.

First failure occurred in a 35-year-old patient treated at 28 weeks' gestation for a MS of 0.9 cm² in AF. Failure was due to two unsuccessful transseptal puncture attempts (rigid and calcified interatrial septum). This patient was managed medically (initial oxygen therapy, beta-blocker and diuretic) with extended maternal–foetal monitoring and hospitalization.

Second failure involved a 30-year-old patient admitted at 26 weeks' gestation for a MS of 1.1 cm², with minimal MR and minimally altered valvular and subvalvular apparatus (Wilkins score of 8). Procedure was complicated during first balloon inflation by acute severe MR due to chordae rupture. An emergent mechanical prosthetic valve replacement was performed, leading to straightforward maternal postoperative course but resulting in intrauterine foetal death (Figure 3).



Figure 3. Severe acute mitral regurgitation due to chordal rupture after the first inflation of the Inoue balloon, not predicted by the valvular or subvalvular anatomy.

Secondary outcome

Pregnancy Follow-up (Maternofoetal and neonatal morbidity and mortality)

A pregnancy was complicated by intrauterine foetal death. This was the case in relation with the patient who developed acute severe MR necessitating emergency surgical valve replacement at 26 weeks of gestation.

Mean term of delivery was 38.3±2.1 weeks of gestation, with a range from 29 to 40 weeks. Two preterm deliveries were noted: the first occurred in the patient whose transseptal puncture failed at 28 weeks. Pregnancy was later complicated by a retro-placental hematoma at 29 weeks, leading to hemorrhagic shock. According to the consulting gynecologists, this obstetric complication was explained by her primiparity and advanced age (35 years). The second preterm delivery occurred at 32 weeks, in the patient who had undergone PMC in the setting of cardiogenic shock under mechanical ventilation, with an intermediate immediate procedural result and residual pulmonary arterial hypertension.

Among patients with immediate procedural success (n=37, 94.9%), hemodynamic and clinical improvement following PMC allowed 36 patients (92.3%) to carry the pregnancy to term.

Vaginal delivery was possible in 20 patients (51.3%) while cesarian section was needed in 19 patients (48.7%). Indication for cesarian was purely obstetric in 13 patients, purely hemodynamic in 4 patients, and a mixed obstetric and hemodynamic indication in 2 patients.

One patient experienced hemorrhagic shock during a cesarian delivery, due to a retro-placental hematoma with a favorable outcome. No other obstetric, hemodynamic, thromboembolic, or infectious complications were observed in other parturients.

Mean birthweight was 2979.5±439.1 g, ranging from 1.300 to 3.500 g. Two newborns were growth-restricted with low birthweight (1.300 g and 1.500 g). No malformations were identified in any of the newborns.

Apart from the case of in utero foetal demise observed in the patient undergoing emergent surgical mitral valve replacement due to acute traumatic severe MR, there was one neonatal death. This occurred 48 hours after a preterm delivery and was attributed to acute respiratory distress secondary to hyaline membrane disease. The newborn was preterm (32 weeks' gestation), growth-restricted (1.500 g), and born to a mother who underwent PMC under extreme emergency conditions (cardiogenic shock requiring intubation, mechanical ventilation, and catecholamine support), with a suboptimal procedural outcome (MVA of 1.5 cm^2 and residual pulmonary arterial hypertension).

Long term follow-up

Median follow-up duration was 56.1 months ranging from 5 to 121 months. No deaths were observed during follow-up period.

Patient for whom the PMC procedure failed (due to unsuccessful trans-septal puncture) underwent mechanical MV replacement, 11 months after delivery.

One patient, in whom PMC led initially to moderate MR, subsequently underwent MV replacement, 12 months after delivery due to progression to severe MR.

Patient who had been scheduled by the Heart Team for dual mitral and aortic valve replacement after delivery (given associated aortic stenosis) was lost to follow-up, returning for consultation 18 months later due to worsening dyspnea. She had mitral restenosis (MVA of 1 cm^2) and severe aortic stenosis (aortic valve area of 0.7 cm^2). She then underwent double valve replacement (mitral and aortic) along with tricuspid annuloplasty.

All the patients were classified as NYHA functional class I or II at the end of follow-up. New AF onset was noted in two patients who were in sinus rhythm immediately after PMC. One of these cases was associated with a revealing ischemic stroke.

Mitral restenosis was identified in seven cases (7 out of 36 patients, 19.4%), excluding the two initial PMC failures and one patient who promptly underwent mitral valve replacement due to rapidly worsening MR. Of these, five patients required mechanical mitral valve replacement, while two patients underwent a repeat PMC.

Median time to restenosis was 32.4 months, ranging from 12 to 71 months.

According to the Kaplan–Meier estimate, restenosis rate was 6.2% at 1 year, 20.2% at 5 years, and 27.4% at 8.75 years (Figure 4).

At the end of follow up, mean age of the children (n=37) born from the studied pregnancies was 4.1±2.4 years, ranging from 5 months to 10 years. All the children demonstrated normal growth and normal intellectual and psychomotor development. Fourteen were school aged with normal school performance.

Factors associated with mitral restenosis

After excluding the three patients who underwent prompt MV replacement (one patient with severe traumatic MR, one patient with trans-septal failure and one patient whose moderate traumatic MR worsening quickly to severe), we analyzed the predictive factors for mitral restenosis in a univariate statistical analysis among the remaining 36 patients with initially successful procedures.

Three factors associated with mitral restenosis were identified: the intermediate immediate result (p<0,0001),

incomplete commissural splitting (p=0.002). Indeed, a significant difference was observed in post-PMC MVA between patients who developed restenosis during follow-up and those who did not (1.67±0.1 vs 1.96±0.2, p=0.01). An unfavorable valvular and subvalvular anatomy (Wilkins score > 8) was also associated with restenosis (p<0,0001) (Figure 4). A history of PMC was associated with a trend to more restenosis (p=0.185).

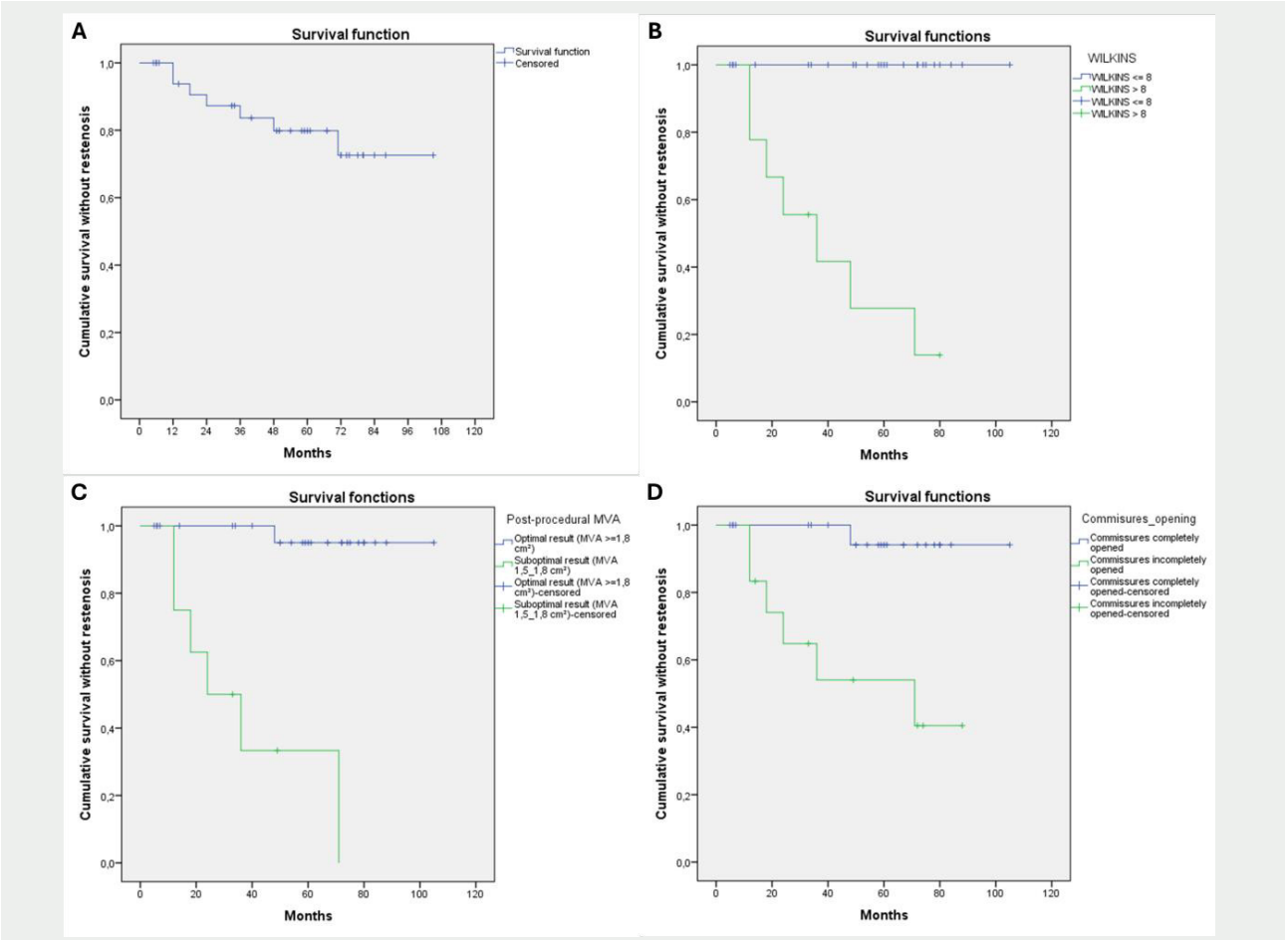


Figure 4. Mitral restenosis and associated factors according to Kaplan Meier estimates.

Panel A: Mitral restenosis–free survival, according to the Kaplan–Meier estimate (n = 36), after exclusion of patients who underwent prompt mitral valve replacement (n = 3). **Panel B**: Restenosis-free survival function according to the Wilkins echocardiographic score. **Panel C**: Restenosis-free survival function according to initial procedural result: intermediate (between 1.5 and 1.8 cm²) vs. optimal (≥1.8 cm²); **Panel D**: Restenosis-free survival function according to complete or incomplete bicommissural splitting.

Discussion

This study represents one of the largest published series from a reference Tunisian center examining PMC during pregnancy. It confirmed that PMC yielded excellent immediate hemodynamic and clinical improvement — substantial increase in MVA, reduction in trans-mitral gradient and pulmonary pressures — leading to marked relief of symptoms in women often in NYHA class III–IV. Despite being performed relatively late in gestation (around 28 weeks), procedural success was very high in selected patients. Short- and long-term obstetric and neonatal outcomes were reassuring: most women deliver at term with normal birth-weights, without congenital malformations, and fatal / neonatal mortality was rare.

Over a median follow-up of ~ 56 months, there was no maternal death although there was a significant risk of mitral restenosis, particularly beyond 5 years, especially in patients with higher Wilkins scores, incomplete commissural opening, or suboptimal post-procedure valve area. Children born from these pregnancies showed normal growth, intellectual and psychomotor development in the long term.

Heart disease during pregnancy incidence has remained stable between 1–2% since the 1930s, with more recent estimates ranging from 0.1% to 1.4% (8). Despite its relatively low prevalence, it remains a significant cause of maternal and foetal morbidity and mortality, posing complex diagnostic, therapeutic, and perinatal management challenges. Cardiovascular causes are the leading non-obstetric cause of maternal death in developed countries, accounting for 15% of maternal deaths in France. In these settings, hypertension is the primary cause of maternal cardiovascular complications, followed by congenital heart disease (9,10). In contrast, in developing countries, rheumatic heart disease—which predominantly affects women—is the most common cardiovascular condition during pregnancy, representing 56–89% of all cardiac conditions and contributing to 25% of all maternal deaths (11).

During pregnancy, early arterial vasodilation leads to a significant increase in cardiac output— by about 50%—

due to both increased heart rate (by 15% from estrogen release) and stroke volume (by 30%) (12,13). In parallel, blood volume expands due to sodium and water retention (mediated by estrogens and aldosterone), systemic vascular resistance decreases until 26–28 weeks of gestation, and structural and mechanical changes also affect the mitral valve (12,13,14).

During pregnancy, the increased heart rate reduces left ventricular diastolic filling time, raising left atrial pressure and the transvalvular gradient, which can cause dyspnea even in previously asymptomatic patients (15). MS also limits the heart's ability to increase cardiac output, potentially reducing uteroplacental blood flow and leading to foetal growth restriction, preterm birth, and low birth weight (16).

Pierlot CM et al. (14) showed that pregnancy causes major changes in mitral valve collagen, with loss of fiber crimp, a 53% increase in fibrosis, and a 16% rise in total collagen. This adaptive response is absent in rheumatic MS, leading to reduced valve mobility and a higher risk of decompensation during pregnancy (14).

Thus, severe MS in pregnant women is considered very high risk for maternal morbidity and mortality, with an estimated risk of cardiac events between 40% and 100% (mWHO IV).

In pregnant women with symptomatic MS and/or pulmonary hypertension >50 mmHg, strict rest and medical treatment with beta-blockers preferably bisoprolol or metoprolol—are the first-line approach (39,40). Diuretics are indicated in cases of congestion, and PMC is recommended after 20 weeks of gestation if symptoms persist (NYHA class III–IV) despite optimal medical therapy, provided there are no contraindications (class IIa, level of evidence C) (6,17).

Inoue first proposed PMC in 1984 (7). Since its introduction, this technique has replaced both open and closed heart surgical commissurotomy, becoming the treatment of choice for symptomatic severe rheumatic MS, including during pregnancy (6,18).

Surgical treatment under cardiopulmonary bypass is associated with a foetal mortality rate of 15–30% (19) and should be reserved for rare, life-threatening conditions for the mother.

For women with severe MS (MVA ≤ 1.5 cm^2) desiring pregnancy, preconception treatment—either PMC or mitral valve replacement—is recommended (6). In our series, no patient received preconception counseling, despite 11 being known to have rheumatic MS and having undergone PMC at a younger age. This lack of counseling was due to irregular follow-up, insufficient education, and denial of the disease.

Population characteristics: Average age was 34.2±5.1 years, which aligns with other Tunisian series (20,21). However, this average age is relatively high compared to international series (22–24). This trend is likely due to the delayed age at first marriage in Tunisia (25).

All patients had rheumatic MS, which is the most prevalent etiology in various studies (20–24).

Clinical presentation of pregnant women with severe MS correlates with maternal and foetal outcomes. Maternal mortality increases from less than 1% in NYHA classes I–II to 7% in classes III–IV, reaching 17% in cases of AF. Foetal mortality is 30% in NYHA class IV (26,27).

In this series, the most common presentation was NYHA class III dyspnea (61.5%).

Echocardiography was crucial to evaluate MS severity and PMC suitability. Wilkins anatomical score is helpful for selecting cases with favorable anatomy for PMC (6,28,29). In this series, 29 patients had favorable anatomy (Wilkins score ≤ 8), while 10 had unfavorable anatomy. PMC was performed in these 10 patients in order to complete pregnancy. Additionally, experienced operators were performing PMC on valves with unusual and unfavorable anatomy in this reference investigating center (30).

Follow-up: Clinical improvement was observed in 37 patients (94.8%) representing all patients with successful procedure. This clinical improvement aligns with findings from Tunisian, North African, and international series, where most patients experienced at least a one-grade improvement in dyspnea following PMC (21,31,32).

Short- and mid-term prognosis is closely correlated with immediate results post-PMC. Post- procedural parameters associated with clinical events and a more severe prognosis include MVA, severity of residual MR, trans-mitral gradient, and pulmonary artery pressures (18).

In this series, PMC significantly improved MVA. These immediate post-PMC results were consistent with data from other published series (21,33) (Table 4).

Table 4. Mitral valve area after percutaneous mitral commissurotomy during pregnancy in published series.

Authors	Year	Region	N	MVA before PMC (cm2)	MVA after PMC (cm2)
Ben Farhat M [44]	1997	Monastir (Tunisia)	44	1,07±0,21	2,32±0,36
De Souza JA [64]	2001	Brasil	21	0.96±0,15	1.84±0,3
Bennis A [61]	2006	Marocco	70	0,9±0,14	2,17±0,3
Gamra H [63]	2006	Monastir (Tunisia)	61	1,1±0,2	2,2±0,3
Esteves C [65]	2006	Brasil	71	0,9±0,14	2,17±0,3
Abdi S [62]	2012	Iran (Teheran)	33	0,83±0,13	1,88±0,29
Salehi R [46]	2013	Iran (Tabriz)	24	0,92±0,15	1,57±0,16
Zairi I [45]	2016	Tunis (Tunisia)	12	1,03±0,15	2±0,35
Rathakrisnnan SS [24]	2017	India	38	0,8±0,3	1,7±0,4
This series	2021	Tunis (Tunisia)	39	0,98±0,22	1,88±0,25

MVA: mitral valve area; **N**: Number of patients; **PMC**: Percutaneous mitral commissurotomy.

This study also confirmed data in the literature concerning improvement of hemodynamic parameters, an outcome that is expected after relief of the mitral obstruction (32, 34, 35). (Table 5).

Table 5. Hemodynamic parameters after percutaneous mitral commissurotomy during pregnancy in various published series.

Authors	Year	Region	N	Mitral gradient before PMC (mmHg)	Mitral gradient after PMC (mmHg)	sPAP before PMC (mmHg)	sPAP after PMC (mmHg)
Ben Farhat M [44]	1997	Tunisia (Monastir)	44	22±8	5±3	41±18	25±12
De Souza JA [64]	2001	Brazil	21	15.9±8.6	4.7±3.3	38.2±15.6	21.2±8.3
Bennis A [61]	2006	Morocco	70	29.1±7.4	13.3±8	NP	NP
Gamra H [63]	2006	Tunisia (Monastir)	61	22.5±8.6	5.4±3.5	NP	NP
Esteves C [65]	2006	Brazil	71	18±7	3.9±3.1	38±15	24±11
Abdi S [62]	2012	Iran (Tehran)	33	15.5±7.4	2.3±2.3	65.24±17.9	50.4±15.3
Zairi I [45]	2016	Tunisia (Tunis)	12	18.5±5.1	4.4±1.1	39.5±8.7	23.2±9.1
Rathakrisnnan SS [24]	2017	India	38	18±8	5±2	50±12	36±10
This study	2021	Tunisia (Tunis)	39	16.6±5.8	9.1±4.2	60.8±16.2	42±14.9

N: Number of patients; **PMC**: Percutaneous mitral commissurotomy; **sPAP**: systolic pulmonary artery pressure.

Procedural failure and complications: Two failures were observed (trans-septal puncture failure and severe acute MR due to chordal rupture, respectively) and eight suboptimal outcomes. No failures were reported in Gamra's series (33), which included 61 pregnant women. This discrepancy could be explained by two factors: first, the younger age of the patients included in that series (28.5±5 vs 34.2±5.1), and second—and consequently—their relatively more favorable anatomy (mean Wilkins score of 7.1±2.1 in that series). Thus, young age and favorable anatomy are predictive parameters of both immediate and long-term procedural outcomes (33, 36).
Mild MR onset or worsening, without exceeding moderate grade, was observed in 15 patients.
In two patients, MR progressed to a moderate grade intra-procedurally. Only one patient experienced significant acute traumatic MR due to chordal rupture. These findings align with published series, where minimal MR development or worsening was common and hemodynamically insignificant. In Zairi's study (21), trivial MR worsened by one grade in three out of twelve patients and newly appeared in two patients; no severe MR occurred. In Gamra's series (33), a new trivial MR was seen in 15 patients, with no cases of aggravated MR. Similarly, in the large Esteves's series (37), 17 patients progressed from MR grade I to II.
Mode of delivery: In this series, 20 pregnant women delivered vaginally (51%) and 19 by cesarian section (49%). Indication for cesarian was purely hemodynamic in four patients (significant pulmonary hypertension and suboptimal result of PMC). Other Tunisian studies (21, 33) reported lower cesarean rates compared to ours. This difference may be explained by obstetric indications in this cohort: patients were often older, multiparous, and had scarred uteri—factors contraindicating vaginal delivery.
Median follow-up: In this series, median follow-up was 56.1 months. No maternal deaths occurred. One patient experienced an ischemic stroke related to a first episode of AF. All patients maintained clinical improvement, remaining in NYHA class I or II, throughout follow- up, consistent with other studies: Zairi (21), Gamra (33), and Mangione (38).
Mitral restenosis: Defined as MVA ≤ 1.5 cm², this definition is commonly used across studies (33, 38, 39). Mechanisms of rheumatic mitral restenosis include commissural fusion due to progressive fibrosis, as well as turbulent flow-induced trauma and inflammatory remodeling (40–42). Early restenosis (≤1 year) may be due to elastic recoil (41).
In this cohort, 7 patients (19.4%) developed restenosis after a median follow-up of 32.4 months.
Among them: All had Wilkins scores >8, six (85.7%) displayed absent or partial commissural
splitting and post- procedure MVA in these patients was significantly lower (1.67±0.1 cm² vs 1.96±0.2 cm²; p = 0.001). Five underwent mechanical mitral valve replacement; two had repeat PMC.
Predictors of restenosis: As per the literature beyond pregnancy, age, AF, Wilkins score, and MVA before and after PMC are strong predictors (39). In Hernandez et al. (43), older age, low anatomical score, and larger post-procedure mitral area predicted lower restenosis at 7 years.
Nunes MC emphasized that procedural MVA, residual MR, and hemodynamics are key predictors of long-term event-free survival (18). In this cohort, three long-term predictors were identified:
• Wilkins score, aligning with Ben Farhat's findings that a score ≤8 corresponded to 77% restenosis-free survival at 10 years, versus 46% for scores 9–11 and 50% for ≥12 (86). It also matched observations in pregnant cohorts (21, 44).
• Immediate post-PMC mitral area, where MVA ≥1.8 cm² had good negative predictive value for restenosis (45); Zairi found 3 of 5 restenosis cases had MVA <1.8 cm² post-procedure (21).
• Partial commissural splitting, also a significant predictor in Zairi's series (21).
Long-term follow-up of children: Potential risks include mental retardation, malformations, or cancer (46, 47). In this cohort, children's mean age at follow-up was 4.1±2.4 years; all had normal physical growth and neuro-psychomotor development. This aligns with other studies: Kinsara AJ (48) observed no mental retardation among 20 children; Gamra H (33) found no
severe retardation, though 8 children had IQ <70, with no predictive factors identified; Gulraze A (49) reported

normal intellect in children followed up to 17 years post-procedure.

Study strengths: To our knowledge, this study represents one of the largest single-center cohorts in Tunisia, with a patient population size comparable to that reported in the literature.

It was conducted at a center staffed by an experienced multidisciplinary medical team.

Involvement of a local Heart Team enabled collaborative medical–surgical decision-making for each patient. Moreover, both mothers and their offspring benefited from comprehensive long- term follow-up: survival analysis using the Kaplan– Meier method provided prognostic insight regarding restenosis in women, while children born from these pregnancies were also monitored long term.

Study limits: This study was limited by its single-center, retrospective design, with data collection relying primarily on patients' medical records. Absence of a non-pregnant control group undergoing PMC restricted ability to compare outcomes across different populations.

Despite efforts to mitigate follow-up loss by recontacting all patients, some bias related to missing data may still persist.

Conclusion

This study demonstrated that PMC was an effective procedure for severe MS, often poorly tolerated, in pregnant women. When performed by an experienced team, it contributed to reducing maternal and foetal risks.

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