

Role of cardiac dyssynchrony and resynchronization therapy in functional mitral regurgitation

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Functional mitral regurgitation (FMR) is a common complication of left ventricle (LV) dysfunction and remodelling. Recently, it has been recognized as an independent prognostic factor in both ischaemic and non-ischaemic LV dysfunctions. In this review article, we discuss the mechanisms through which cardiac dyssynchrony is involved in FMR pathophysiologic cascade and how cardiac resynchronization therapy (CRT) can have therapeutic effects on FMR by reverting specific dyssynchrony pathways. We analyse recent clinical trials focusing on CRT impact on FMR in 'real-world' patients, the limits and future perspectives that could eventually generate new predictors of CRT response in terms of FMR reduction. Finally, we propose a practical diagnostic and therapeutic strategy for the management of symptomatic patients with severe LV dysfunction and concomitant 'prognostic' FMR.

Keywords cardiac resynchronization • mitral regurgitation • ventricular dyssynchrony

Introduction

Functional mitral regurgitation (FMR) is a common complication of left ventricle (LV) dysfunction and remodelling both in ischaemic and non-ischaemic dilated cardiomyopathy.¹ After myocardial infarction, the prevalence of FMR varies from 20 to 50%.^{2,3} The presence of moderate or severe FMR is associated with a 3-fold increased risk of heart failure (HF) and a 1.6-fold increased risk of death at 5-year follow-up.³ In patients with non-ischaemic LV dysfunction, FMR is observed in >50% of cases (from 56 to 65%)⁴ and is associated with an excess cardiac mortality and HF episodes with three- and two-fold increased risks, respectively.⁵ A linear correlation is found between degree of FMR and mortality and morbidity.^{3–5}

Despite many medical and surgical attempts to treat FMR, no radical treatment has been found for the majority of patients. Patients in functional Classes III and IV, despite optimal medical treatment

reduced LV ejection fraction (EF) and QRS duration >120 ms, are good candidates for cardiac resynchronization therapy (CRT) that may reduce the degree of mitral regurgitation (MR).⁶

In this review, we discuss the mechanisms of FMR focusing on the role of mechanical dyssynchrony and CRT as a potential therapeutic option.

Pathophysiology of functional mitral regurgitation

In FMR, mitral leaflets are generally normal and the main determinant of FMR is 'systolic tenting', with displacement of the leaflets coaptation point away from mitral annulus towards the LV cavity. This phenomenon, together with mitral annulus dilation and decreased LV contractility, generates an incomplete mitral valve (MV) closure.

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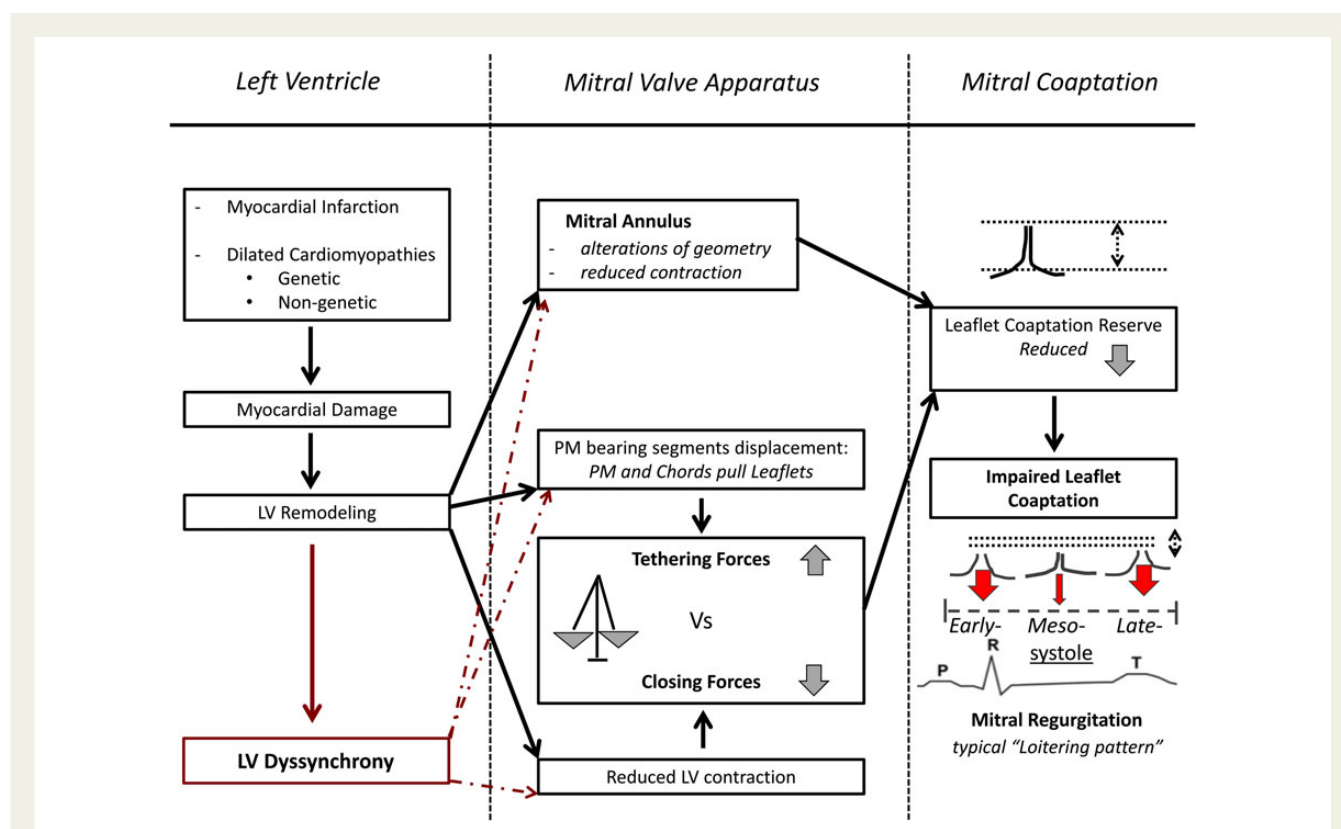


Figure 1 Physiopathologic interaction between LV and MV apparatus resulting in reduction of mitral coaptation reserve. The main determinant is the unbalance of ‘tethering’ vs. ‘closing’ forces. Mitral annulus dilation/dysfunction can be an aggravating factor. LV dyssynchrony is a potential co-determinant impacting on FMR pathophysiologic cascade (red arrows).

Depending on global or local LV remodelling, different tethering patterns occur as a consequence of different tethering vectors. In particular, two typical echocardiographic patterns have been described:⁷ ‘asymmetric’ and ‘symmetric’, on the basis of the disposition of the mitral leaflets with respect to their point of coaptation (moved posteriorly and apically, respectively).

It is therefore clear that FMR is a complex cocktail of pathophysiologic mechanisms generating characteristic echocardiographic patterns of systolic restricted motion of the leaflets.⁸

The balance between tethering and closing forces

Normally, the MV leaflets close in a point (‘coaptation point’) within the annular plane and have a considerable overlap when they face one to the other (‘coaptation reserve’). In FMR, the coaptation reserve is progressively reduced until the loss of coaptation. The main determinant of the reduction of coaptation reserve is the unbalance of ‘tethering’ vs. ‘closing’ forces on MV leaflets in favour of the former (Figure 1).

Tethering forces determined by the papillary muscle (PMs) directly bound through chordae tendineae tend to pull MV leaflets apically and/or posteriorly. On the contrary, closing forces generated by LV contraction tend to push MV leaflets back to the left atrium. These two opposing forces are normally in a balance to obtain proper leaflets coaptation at annular plane level. If closing forces overcome tethering ones, leaflets coaptation occurs away from annular

plane in the left atrium, whereas if tethering forces prevail, then leaflet coaptation occurs away from annular plane in the LV cavity. This restricted motion of MV leaflets due to increased tethering forces and reduced closing ones, is the typical pathophysiologic hallmark of FMR.

It is clear how all the factors increasing or diminishing closing and tethering forces may interact with each other, summing up all together and determining the presence and the degree of FMR (Figure 1).

The main determinant of the *increased tethering force* is the displacement of PM away from the mitral annulus. As a demonstration in animal models,⁹ basal (intermediate) chordal cutting can improve significantly MV leaflet coaptation. PM tethering may be caused by several factors. When myocardium is damaged, a certain degree of LV systolic dysfunction is generated with consequent LV dilatation. LV dilatation *per se* is not able to provoke significant MR, but, when PM bearing segments are directly involved, then significant FMR appears.

The main determinant of the *decreased closing force* is LV contractile dysfunction. Experimental studies *in vivo* showed that pharmacologically induced global LV dysfunction without LV dilatation does not produce significant FMR.¹⁰ In conclusion, LV dilatation was an essential prerequisite for incomplete MV closure.

Role of mitral annulus

Mitral annulus dilation/dysfunction can be considered an aggravating factor that further reduces MV coaptation reserve, thus worsening

FMR (Figure 1). The contraction of atrial fibres in late diastole and LV fibres in systole around the annulus provokes the sphincteric contraction of the posterior annulus. This annular contraction allows a proper coaptation of the free margins of the MV with a normal overlap of ~ 1 cm (i.e. coaptation reserve, Figure 1).¹¹ In FMR patients, LV remodelling generates geometrical distortions of MV apparatus involving mitral annulus. It becomes larger and less contracting due to dysfunction of LV and left atrium fibres. In theory, this condition reduces progressively the MV coaptation reserve until the point of loss of coaptation. However, pure severe mitral annulus dilation and dysfunction are rarely able to generate significant FMR. Therefore, annular dilation/dysfunction plays a minor role in FMR and could be considered an aggravating factor increasing MV tenting area.^{8,11}

Role of mechanical dyssynchrony

Intra- and atrioventricular (AV) dyssynchrony could be a potential co-determinant of FMR (Figure 1). In patients with dilated LV with left bundle branch block (LBBB) or right ventricular pacing, FMR severity correlates with QRS duration.¹² Epidemiologic registries showed that QRS widening is relatively frequent (21–47%) in patients with progressive HF, frequently caused by LBBB.¹³

LV dyssynchrony can precipitate the pathophysiologic cascade of the FMR as follows (Figure 1):

- (A) *Decreased closing force.*⁸ LV dyssynchrony causes a less efficient myocardial fibres contraction reducing the closing forces.
- (B) *Increased tethering force.*⁸ In the context of LV dyssynchrony, two opposing myocardial segments contract with different timing during the same systolic phase. It can generate two effects increasing tethering forces. First, the compensative LV dilation due to dyssynchrony is a major determinant of increased tethering forces, since it displaces away PM with consequent lack of leaflets coaptation. Secondly, when one segment is contracting in advance of the not-yet-contracting opposite segment, it generates important tethering vector forces distorting MV apparatus (Figure 2).
- (C) *Mitral annulus dysfunction and deformation.*^{8,11} When LV dyssynchrony involves the basal LV segments, it can contribute to the loss of mitral annular contraction and can also distort geometry of annulus.
- (D) *AV dyssynchrony.*⁸ During diastole improper timing of AV relaxation, contraction cycles may create a positive pressure gradient through the MV, generating diastolic MR.

FMR is a *dynamic condition*, changing dramatically with loading conditions. The increase in afterload worsens MR through further geometric distortion of the infarcted PM-bearing segments. In fact, diuretics and afterload reducing drugs, general anaesthesia, reduce efficaciously MR severity.^{14,15} FMR presents a typical phasic variation of regurgitant volume where FMR is greater in early and late systoles and lower in the mid-systole, known as the 'loitering pattern'. Beyond intra-beat variability, FMR severity may also have a beat-to-beat variation. This dynamicity of FMR mirrors the phasic changes in the balance between 'tethering forces' and 'closing forces' (maximal in mid-systole when LV pressure is at the top

and minimum in early and late systoles).^{8,16} Therefore, the mechanistic explanation of FMR change during the systolic phase is not to be exclusively attributed to the augmented or diminished closing forces but also to the opposite change in tethering forces. It is reasonable to postulate that during early- and end-systolic phase, PM bearing segments are displaced away from their physiologic position, thus increasing tethering drive on MV apparatus. LV dyssynchrony further aggravates loading-related MR changes. Ennezat *et al.*¹⁷ demonstrated that LV dyssynchrony at rest is related to worsening of FMR during exercise in patients with systolic HF. In this study, two-thirds of the patients who had no significant LV dyssynchrony exhibited a decrease in effective regurgitant orifice (ERO) during exercise, whereas no patients with significant LV dyssynchrony had a decrease in mitral ERO during exercise and 20% developed a large exercise-induced increase in ERO. Lancellotti *et al.* demonstrated that LV synchronicity and dyssynchrony do not remain stable during exercise in HF patients and that exercise-induced changes in LV dyssynchrony strongly correlate both with changes of MR and forward stroke volume.¹⁸ These results have clinical implications since we can correct dyssynchrony by biventricular pacing and hopefully reduce its dynamic component. Lancellotti *et al.*¹⁹ demonstrated that biventricular pacing decreases MR severity not only at rest but also during exercise. D'Andrea *et al.*²⁰ correlated the increase in LV dyssynchrony during exercise with the increase of FMR in patients with HF and narrow QRS. Sixty patients with some degree of FMR in the context of idiopathic dilated cardiomyopathy (EF < 35%), in NYHA Class II–III refractory HF and narrow QRS interval (< 120 ms) were studied by standard Doppler echo and colour Doppler myocardial imaging at rest and during stress. The results showed a significant increase in intra-ventricular delay during stress with systolic dyssynchrony and a concomitant stress-induced increase in FMR. They showed a good correlation between MV ERO and systolic dyssynchrony. Interestingly, they showed that MV remodelling (tenting area) is also increased during exercise, thus enhancing how systolic dyssynchrony may affect MV remodelling and consequently MV regurgitant burden. A subsequent prospective longitudinal study²¹ showed that echocardiographic dyssynchrony during exercise was the strongest predictor of adverse event even in patients with idiopathic dilated cardiomyopathy with narrow QRS.

Therapeutic role of CRT on FMR

Many echocardiographic studies have demonstrated how CRT can contrast all the pathophysiologic determinants of FMR by minimizing LV dyssynchrony by the following (Figure 1):

- (A) increasing 'closing forces' (global synchronization),
- (B) reducing 'tethering forces' (local synchronization),
- (C) reshaping annular geometry and function (local synchronization),
- (D) correcting diastolic MR (AV synchronization).

Increasing 'closing forces' (global synchronization)

CRT is demonstrated to restore AV and LV synchrony. The systolic forces increase global LV contraction efficiency that will be reflected into increased MV coaptation force. Indeed, CRT generates

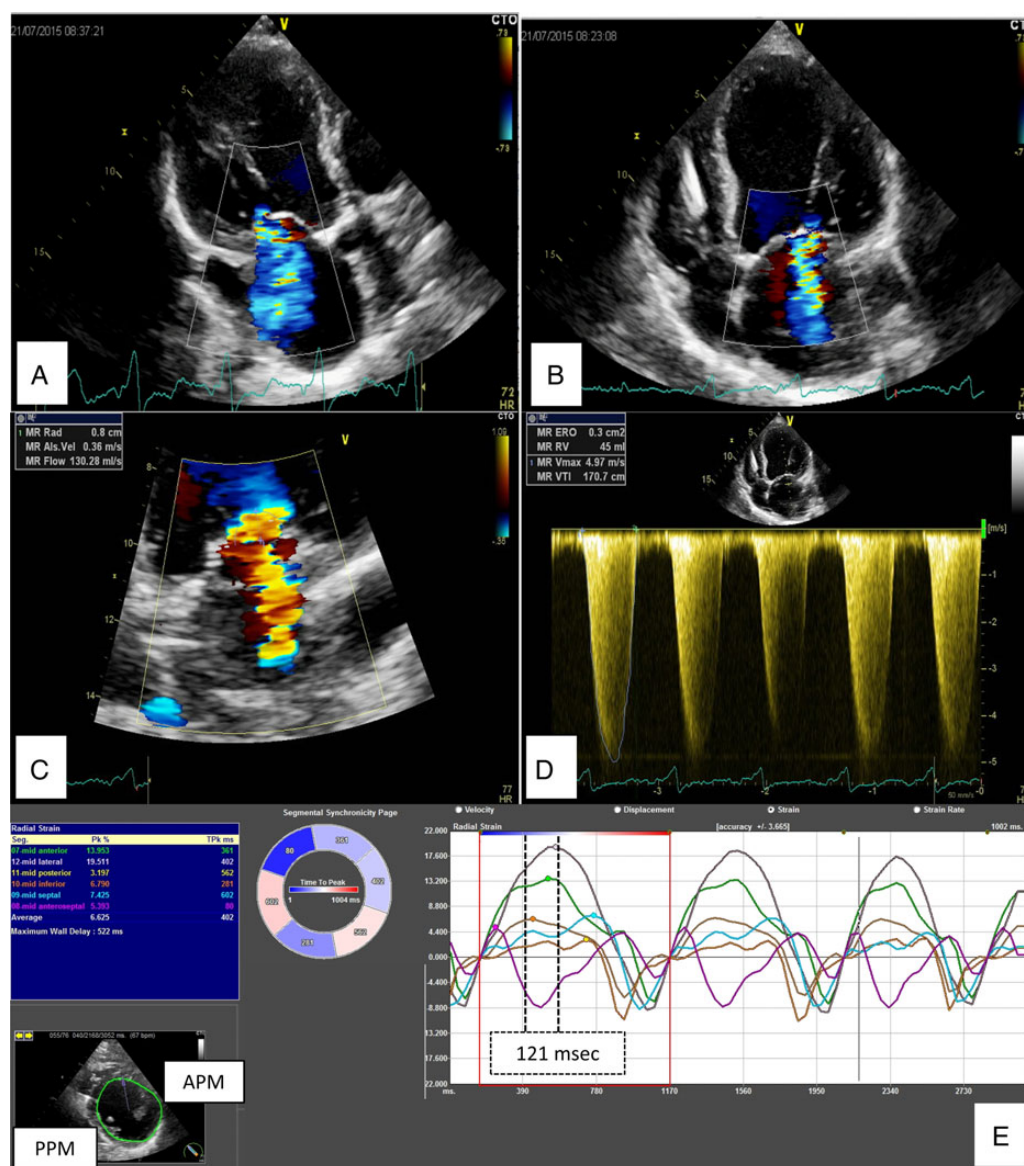


Figure 2 FMR due to symmetric tethering, with demonstration of PM-bearing segments dyssynchrony by 2D radial strain speckle tracking analysis (2DST). (A and B) FMR in three-chamber and four-chamber trans-thoracic views at colour Doppler and continuous Doppler (CW) analyses. (C and D) proximal isovelocity surface area radius and trans-mitral CW analysis. (E) 2DST of LV short axis at PM level. Segments adjacent to PM insertions (mid-inferior bearing posterior PM and mid-lateral bearing anterior PM) have different time to peak radial strain (121 ms), resulting in significant PM dyssynchrony.

a higher pressure gradient through MV with a consequence rise in trans-mitral closing forces counterbalancing the high tethering forces. Breithardt et al.²² performed one of the first studies exploring the cause–effect relationship of increase in dP/dt and decrease in ERO after CRT implantation. They studied 24 HF patients with LBBB and FMR after CRT implantation. Acute changes in FMR were quantified between intrinsic conduction (OFF) and CRT. They concluded that FMR reduction is directly related to the increased closing force (LV dP/dt max) that facilitates effective MV closure through an increase in trans-mitral pressure gradients.

Porciani et al.²³ documented the direct relationship between the restored ventricular synchrony (studied by time to peak systolic velocity with tissue Doppler) and the FMR severity reduction in patients with CRT. They confirmed that the improvement in MR severity was associated with a significant improvement of LV systolic function parameters (EF, myocardial performance index, dP/dt) due to restored ventricular synchrony. Interestingly, in responders to FMR reduction, CRT also induced a resynchronization of global, basal, and mid-LV segments. Therefore, they conclude that the increased contraction efficiency due to global LV resynchronization gives an important contribution to FMR

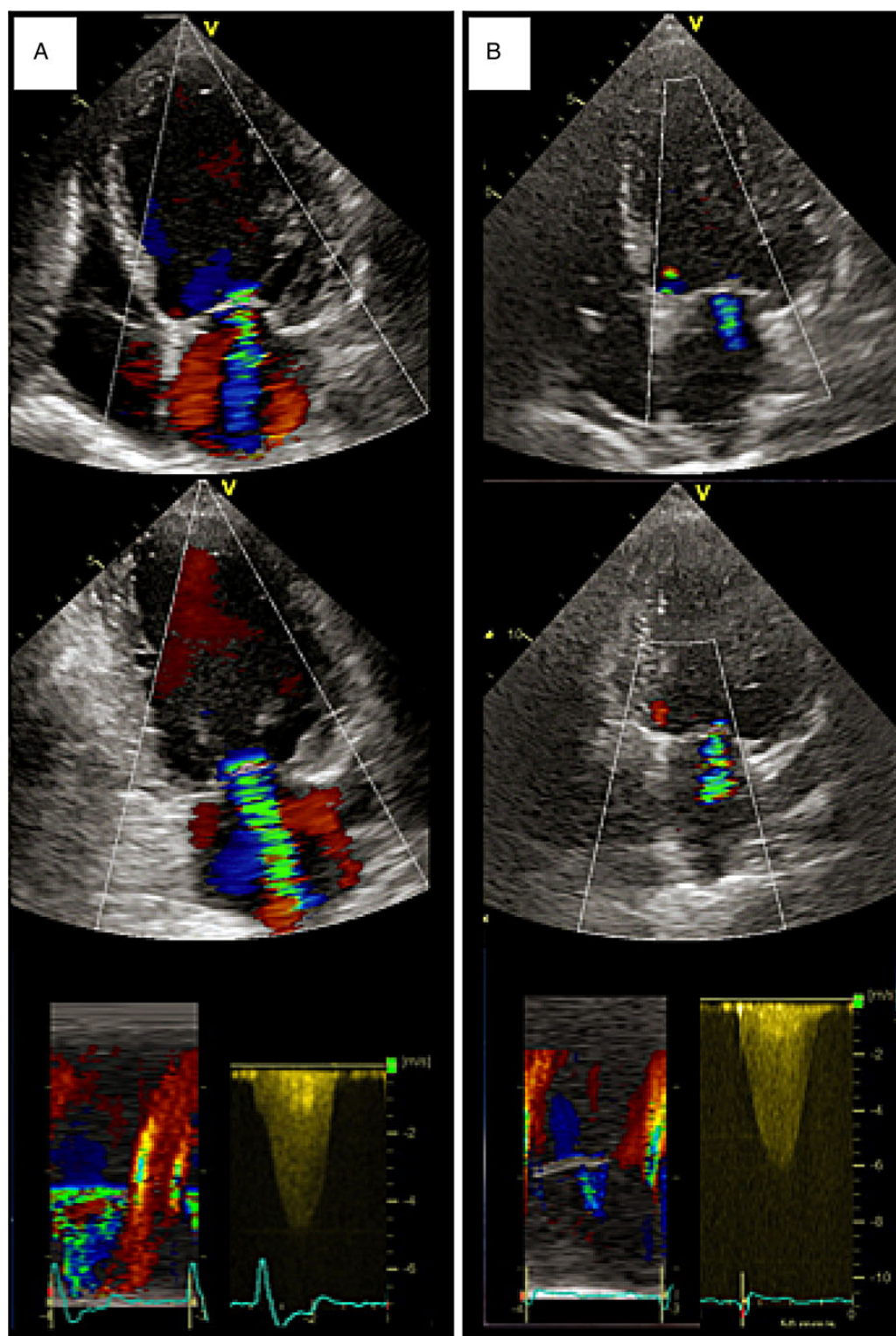


Figure 3 Colour Doppler, colour M-Mode, and CW Doppler changes during off-on CRT effects in the same patient. (A) CRT-off: wide QRS, moderate-to-severe MR with more significant early MR. (B) CRT-on: narrow QRS, mild MR with reduction of both early and late MR.

reduction and postulated that a more 'local' synchronous contraction involving the PMs could play an important role in FMR improvement.

Interestingly, all these described effects are pacing dependent as the interruption of CRT causes an immediate recurrence of MR.²⁴ Solis et al.²⁵ also demonstrated that reduction in MR after

CRT is associated with favourable changes in closing forces on the MV.

Reducing ‘tethering forces’
(local synchronization)

Many studies have shown that CRT reduces FMR not only by increasing closing forces but more importantly through ‘local’ synchronization.

The model of PM dyssynchrony as a crucial factor precipitating FMR began to be investigated.

Kanzaki²⁶ was the first to quantify and associate the immediate reduction in MR after CRT with the coordinated mechanical activation of PM insertion sites. The study identifies the inter-PMs activation time delay as a principal factor related to MR in patients with HF and LBBB, that is, immediately improved with CRT.

Goland et al.²⁷ confirmed that significant time-to-peak delay between inferior and anterior LV segments preserved strain of posterior wall and MR jet area/left atrium area ratio <40% are factors associated with significant MR reduction after CRT implantation.

The presence of myocardial viability is certainly an important predictor of FMR response to CRT, but interesting echocardiographic studies enhanced the importance of local viability.

Onishi et al.²⁸ evaluated the prognostic impact of a MR reduction score, testing the additive value of 3 echocardiographic features associated with MR reduction after CRT and long-term survival: baseline radial dyssynchrony, excessive LV dilatation, and scar at PM insertion site.

Sénéchal et al.²⁹ evaluated myocardial viability by dobutamine-stress echocardiography before CRT implantation with particular attention to local viability in the region of the pacing lead. They concluded that local viability had an excellent sensitivity (96%), but a low specificity (56%) to predict acute response to CRT.

Reshaping annular geometry and function
(local synchronization)

CRT can ameliorate the sphincteric contraction of the posterior mitral annulus through coordinating the contraction of the myocardial segments at the base of the LV.

In spite of the appealing pathogenic postulation, there are some studies that demonstrate no immediate changes in mitral annular dimensions after CRT²⁶ and other studies²³ in which MV annular contraction is correlated to FMR reduction after CRT.

Correcting diastolic MR
(AV synchronization)

AV delay optimization through CRT allows a proper correction of diastolic MR if present thus resulting a further reduction of left atrial pressure.

Timing of MR response after
CRT implantation

A clear distinction is to be defined between two phases of MR reduction after CRT implantation:

Table 1 Trials and studies evaluating MR after CRT implantation with analysis of percentage variation in the baseline value of the specific method of quantification used in the trial

Study (no. of patients)	No. of patients	CRT-on	Method of MR quantification	MR baseline	MR reduction at follow-up after CRT implantation	%MR reduction (P-value)
CARE-HF ^{32,33} (813)	409		Jet area/LA area % (median; IQR)	21.3; 11.6–32.9	14.1 (7.6–24.8) (3 months follow-up)	34% (<0.05)
MIRACLE ³⁴ (373)	172		Jet area, cm ² (mean ± SD)	7.31 ± 6.14	5.21 ± 3.14 (3 months follow-up)	29% (<0.05)
MUSTIC substudy ³⁵ (131)	34		Jet area, cm ² (mean ± SD)	8.1 ± 4.2	6.2 ± 2.9 (6 months follow-up)	23% (<0.05)
Cabrera-Bueno et al. ³⁶ (76)	34	Baseline MR > ++	ERO, cm ²	0.34 ± 0.11	0.28 ± 0.22 (12 months follow-up)	18% (=0.189)
Di Biase ³⁰ (794)	275	Baseline MR > ++	ERO, VC, jet area: multiparametric grading		MR improvement ≥ 1°; 126 patients (46%) No change in MR; 61 patients (22%) MR worsening ≥ 1°; 12 patients (4%)	<0.001 <0.001 <0.001
Verhaert ³⁷ (266)	266		VC, cm (mean ± SD)	3.5 ± 2.4	2.7 ± SD (6 months follow-up)	23% (<0.0001)
Van Bommel ³⁸ (98)	98	Baseline MR > ++	VC, cm (mean ± SD)	0.74 ± 0.15	0.59 ± 0.21	20% (<0.001)
			ERO, cm ² (mean ± SD)	0.51 ± 0.16	0.43 ± 0.18 (6 months follow-up)	16% (=0.001)
Sitges ³⁹ (151)	57	Baseline MR > ++	ERO, mm ² (mean ± SD)	32 ± 16	19 ± 17	41% (<0.01)
			MR volume, ml/beat (mean ± SD)	46 ± 21	28 ± 22 (12 months follow-up)	39% (<0.011)

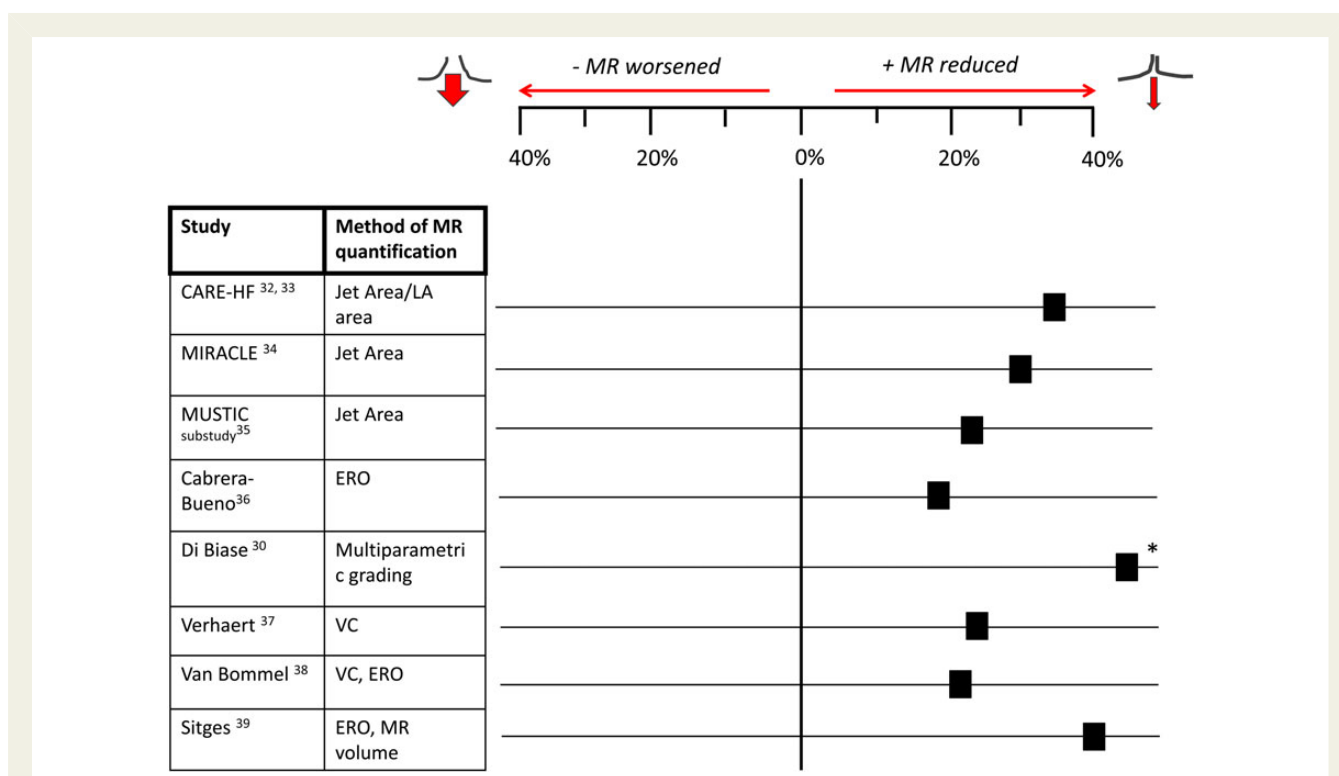


Figure 4 MR reduction after CRT implantation in terms of percentage variation in the baseline value of the specific method of quantification used in the trial. *Di Biase *et al.* results are 'not to scale' as MR grade is a result of multi-parameter grading.

- remote, long-term MR reduction, occurring from weeks to months after CRT implantation,
- immediate, short-term MR reduction, occurring suddenly after CRT implantation

The long-term reduction is secondary to reverse remodelling of the LV with reduction in LV dilation and sphericity, thus minimizing tethering forces on MV apparatus. Reduction of MR in this remote phase is important to stop the vicious circle of wall stress and oxygen consumption of the LV, generated by the chronic volume overload due to FMR. However, reduction of MR in this phase is not strictly attributable to CRT direct effect, but it is the expression of LV healing thanks to CRT-induced better LV contraction. FMR mirrors LV remodelling status.

The immediate MR reduction may be the expression of more coordinated PM bearing segments contraction resulting in acutely diminished tethering vectors. The immediate MR reduction is the major determinant of favourable response to CRT. It is directly involved to the acute reduction in volume overload that certainly contributes favouring reverse remodelling. The immediate MR reduction has demonstrated as a robust prognostic determinant after CRT^{30,31} (Figure 3).

Results from CRT trials

Among the clinical trials, only Cardiac Resynchronization-Heart Failure (CARE-HF),^{32,33} Multicenter InSync Randomized Clinical Evaluation (MIRACLE),³⁴ and Multisite Stimulation in Cardiomyopathy

(MUSTIC)³⁵ trials reported at least the FMR grade before and after CRT implantation demonstrating a small but significant reduction in FMR severity at 3–6 months (Figure 3 and Table 1). In the MUSTIC study,³⁵ the MR jet area decreased from 7.4 ± 6.8 to 5.6 ± 8.3 cm² at 6 months. In the MIRACLE study,³⁴ MR was reduced from a median of 7.31 ± 6.14 to 2.1 cm² at 6 months. In this latter study the magnitude of the MR changes was greater in non-ischaemic than ischaemic HF patients. In the CARE-HF³² study, CRT reduced inter-ventricular mechanical delay, end-systolic volume index, and MR jet area; conversely, the EF increased and symptoms and quality of life improved as compared to medical therapy. Interestingly, on multivariable analysis³² MR severity at 3 months was the strongest predictor of mortality, regardless of the assigned treatment (medical therapy only or CRT on top). These results highlight the prognostic importance of FMR in patients' response to CRT. It is important to underline, however, that in these trials MR evaluation has many limitations regarding the definition of its mechanism and the methods of quantification.

Further insights on FMR in patients undergoing CRT can be derived from studies by Cabrera-Bueno *et al.*,³⁶ Verhaert *et al.*,³⁷ Van Bommel *et al.*,³⁸ Sitges *et al.*,³⁹ and the multicentre study by Di Biase *et al.*³⁰ (Figure 4 and Table 1).

Cabrera-Bueno³⁴ followed 76 patients with dilated cardiomyopathy, assessing MR grade, reverse remodelling, and clinical outcome at baseline and at 6 months after CRT. Almost half of the patients at baseline presented significant MR, and in more than one third of these cases, FMR became non-significant. FMR persistence after CRT was confirmed as a bad prognostic factor with greater incidence of arrhythmic events and less LV reverse remodelling.

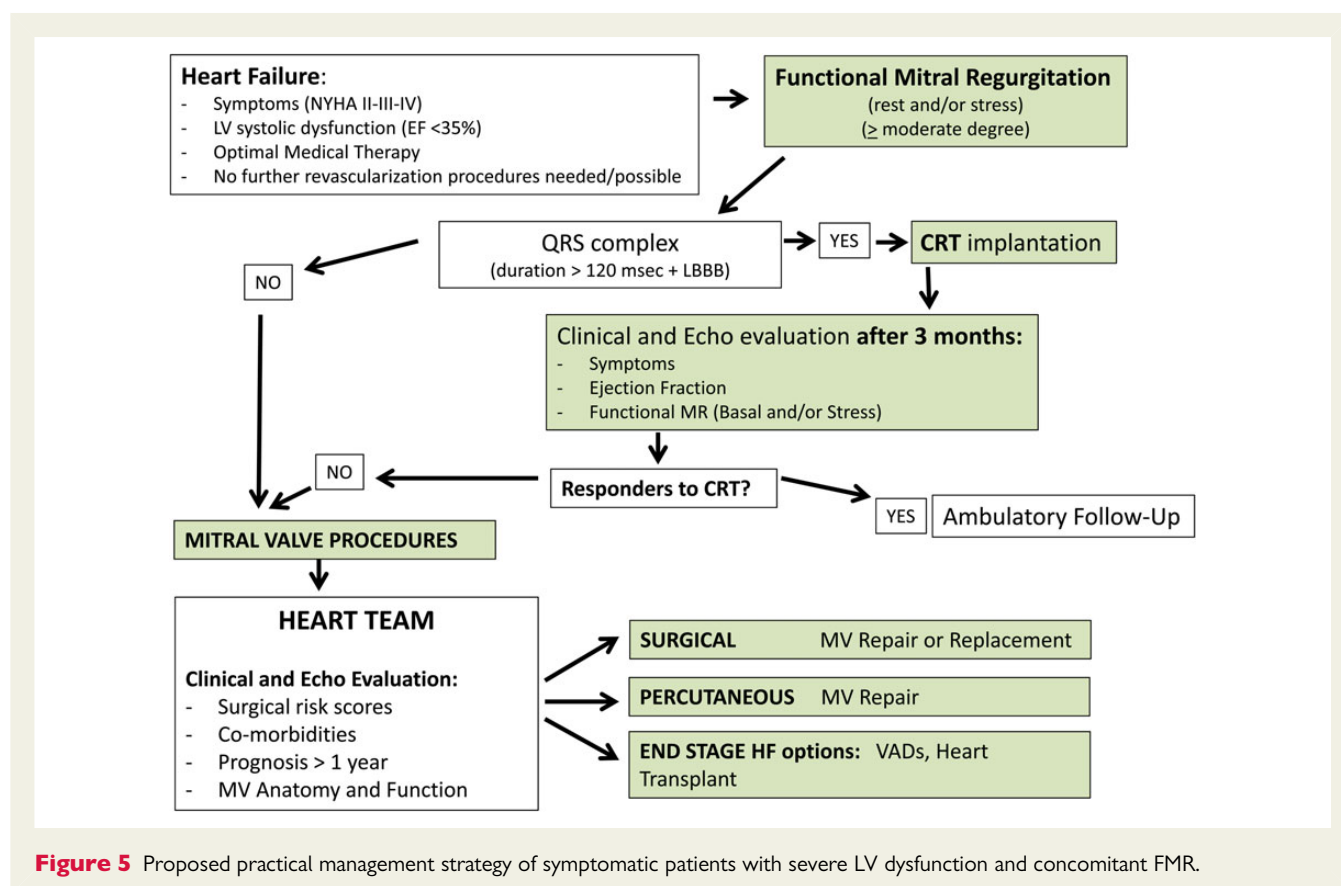


Figure 5 Proposed practical management strategy of symptomatic patients with severe LV dysfunction and concomitant FMR.

In Verhaert³⁷ study, CRT led to an immediate sustained decrease in MR and to reverse remodelling at 12 months follow-up. In Van Bommel³⁸ study, 49% of patients improved >1 grade of MR. Survival was superior in MR improvers compared with MR non-improvers. MR improvement was showed as an independent prognostic factor for survival. Sitges³⁹ confirmed that CRT effectiveness in acutely reducing FMR in almost 50% of patients demonstrating a concomitant acute improvement LV systolic function and dyssynchrony. At 12-month follow-up, an additional reverse global and local LV remodelling was also showed.

The worse clinical outcome of patients with MR persistence after CRT calls for a need for MV correction in non-responders to reduce MR and prevent further LV remodelling. In this scenario, it is crucial to establish the optimal timing for MR correction. The study of Di Biase et al. provided useful data on this issue.³⁰ These authors followed 794 CRT recipients in a multicentre study, assessing MR severity and LV reverse remodelling at baseline and at 3 and 12 months after CRT implantation. At baseline, MR was present in 86% of patients, with 35% prevalence of MR Grades 3 and 4. Improvement of MR ≥1 grade after 12 months occurred in 46% of patients. Di Biase et al. found that advanced MR (Grades 3 and 4) at baseline and improvement in MR at the 3-month follow-up (>1 grade) predicted response to CRT. These results suggest that CRT responders at 3 months do not require any further intervention. Therefore, based on these data, Di Biase et al. proposed to delay the decision for MV surgery at the 3-month follow-up, because at this time some patients could have the MR improved by CRT alone.³⁰ On the other

hand, if no improvement occurred, it is unlikely that a further improvement of MR and MV surgery could be considered.

New percutaneous procedures of MV repair are also an option for FMR uncorrected by CRT. Auricchio et al.⁴⁰ recently demonstrated that, in non-responders to CRT, MitraClip treatment is feasible and safe. Most of the patients (73%) had improved NYHA functional class already at discharge. The first significant improvement in both LV volumes and EF was detected after 6 months with a further improvement at 12 months. Seifert et al.⁴¹ confirmed the safety of MitraClip treatment in the context of both functional and degenerative MR. MR was significantly reduced at follow-up compared with baseline: 60% of patients with baseline Grade 4 + MR and 40% of patients with baseline Grade 3 + MR vs. 0% with Grade 4 + MR and 5% with Grade 3 MR at follow-up. MitraClip treatment was also associated to a significant reduction in N-terminal pro-brain natriuretic peptide median level, pulmonary systolic pressure, and LV end-diastolic volume.

Open questions

There are still many pendent issues talking about the effective evaluation of CRT impact on FMR despite the intrinsic difficulties of quantification of FMR itself. In this regard, the need of integrating multiple echocardiographic parameters was met by Ypenburg et al.³¹ and Matsumoto et al.⁴² They correlated LV synchronization and FMR grading including not only estimation of regurgitant volume, but also to MV deformation parameters.

Considered the intrinsic dynamicity of FMR, there is poor understanding on how CRT impacts regurgitant volume through different phases of the systole, segregating early from late systolic MR. Yu-Jia Liang *et al.*⁴³ provided first data and explored possible mechanisms of such changes.

Conclusion

FMR is a common complication of LV dysfunction and remodelling, and it presents a complex and multifactorial pathophysiology. Despite many studies in the literature, there is not a clear validated strategy for the management of symptomatic patients with severe LV dysfunction and concomitant basal and/or stress-induced 'prognostic' FMR.

In Figure 5, we propose a practical strategy in the light of the evidence discussed in the previous sections. In the presence of severe LV dysfunction (EF < 35%) and wide LBBB-like QRS complex, CRT device is to be implanted as suggested by guidelines.⁷ After 3 months, a clinical and rest/stress echocardiographic re-assessment is recommended. In case of clinical and echocardiographic response, a periodic ambulatory follow-up is advised. On the contrary, in case of non-response to CRT, an interventional procedure on MV should be considered. A Heart Team (involving echocardiographers, interventional cardiologists, anaesthesiologists, and electrophysiologists) should evaluate a tailored therapeutic approach for the single patient, on the basis of clinical, anaesthesiological, and anatomic MV profiles.

Conflict of interest: None declared.

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IMAGE FOCUS

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An unusual case of left bronchial compression caused by a large patent arterial duct in a child with pulmonary atresia with ventricular septal defect

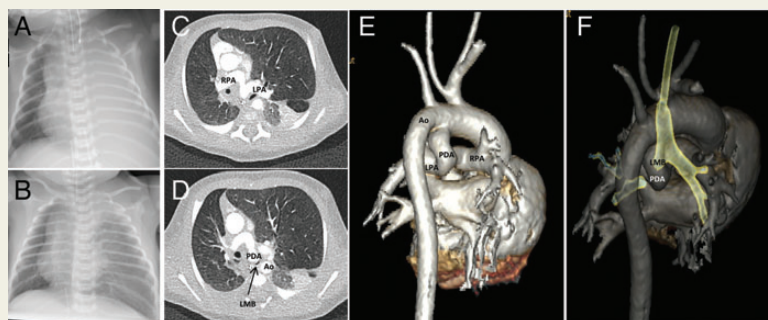
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A 2-day-old term baby was referred to our hospital for an urgent cardiology assessment because of respiratory collapse and complete 'white-out' of a large left lung with mediastinal shift to the right (Panel A). At the time of admission the infant was on high-frequency oscillatory ventilation, inhaled nitric oxide, high-dose inotropes, and Prost-in infusion. Subsequent echocardiographic examination revealed pulmonary atresia with ventricular septal defect and large persistent arterial duct (PDA). A repeat chest X-ray showed persistent over-inflation of the left lung, with some aeration of the left upper lobe but persistent opacification of the remaining lung (Panel B). The baby was weaned to conventional ventilation, however, remained on mild inotropic support. A computed tomography (CT) angio was performed in order to delineate cardiovascular and lung parenchymal anatomy. The CT scan demonstrated a large, tortuous PDA compressing and occluding the left main bronchus (Panels D and F). The compression was particularly exacerbated by the more vertical course of the left-sided PDA. The branch pulmonary arteries originated separately from a very large (7 × 6 mm diameter) PDA arising from the under surface of the aortic arch, with no connection to the right ventricle (Panel E). In addition, there was an overexpansion of the left lung and obstruction of the left main bronchus (Panels C and D). This had resulted in delayed clearance of foetal fluid from the left lung causing the persistent changes seen on the chest X-ray. On the following day, the baby underwent ligation and division of the PDA and a 5 mm RV-PA Gore-tex® conduit insertion. The postoperative course was uneventful.

Panels A and B. Anteroposterior chest radiography; (C and D) axial chest computed tomographic scan; and (E and F) 3D reconstruction from CT scan images. PDA, persistent arterial duct; Ao, aorta; RPA, right pulmonary artery; LPA, left pulmonary artery; LMB, left main bronchus.



Panels A and B. Anteroposterior chest radiography; (C and D) axial chest computed tomographic scan; and (E and F) 3D reconstruction from CT scan images. PDA, persistent arterial duct; Ao, aorta; RPA, right pulmonary artery; LPA, left pulmonary artery; LMB, left main bronchus.