In COAPT, there were more often 2 clips implanted per patient, but more often 3 clips in MITRA-FR and procedural success was similar: 98% for COAPT and 95% for MITRA-FR.

- The roll-in procedures before first patient inclusion was low in both the COAPT and the MITRA-FR (3 and 5, respectively), and we agree that the learning phase requires more cases.
- In COAPT, there were more often 2 clips implanted per patient, but more often 3 clips in MITRA-FR and procedural success was similar: 98% for COAPT and 95% for MITRA-FR.
- Enrollment rate was lower in COAPT (1.7 patient/center/year) than in MITRA-FR (2.6 patient/center/year).
- The decreased complication rate in COAPT was mainly due to different definitions.
- The 5% mitral regurgitation recurrence in COAPT at 1 year (the lowest ever published for FMR) is probably due to a combination of patient selection and the technique itself. Mitral regurgitation recurrence, the Achilles’ heel of surgical repair, is usually higher even than the 17% observed in MITRA-FR. The edge-to-edge technique may be better suited to treat FMR than surgical downsizing annuloplasty.

Therefore, differences in technical expertise do not explain the divergent trials results. Differences in baseline characteristics have generated an intense debate.

- The larger regurgitant orifice in COAPT is undoubtedly a key element. Conversely, the finding of larger left ventricular (LV) volumes in MITRA-FR is more subtle. LV volumes, assessed by the Simpson method in both studies, matched well with regurgitant volume measured using the proximal isovelocity surface area method in MITRA-FR but not in COAPT. Larger LV volumes observed in MITRA-FR are possibly due to differences in Corelab evaluations (Table 1). Post hoc analyses including the proportionate/disproportionate theory are attractive but rely on fragile evidence.

- COAPT echocardiographic selection criteria were not mentioned in the initial protocol.

The COAPT central eligibility committee was also key for COAPT success but hard to reproduce in clinical practice. Conversely, MITRA-FR was a pragmatic trial reflecting real-life practice.

Interpreting medical management is difficult, leading to more questions than answers. Guideline-directed medical therapy was compulsory for at least 3 months in both protocols, so that patients were supposed to be stable at randomization. Mitral regurgitation decreased in both study control groups: 46.9% in the COAPT and 32.5% in the MITRA-FR. After randomization, any modification of medical treatment was discouraged in the COAPT, which may have highlighted the difference between the 2 COAPT groups. Conversely, guideline-directed medical therapy was encouraged during the follow-up in MITRA-FR with more than 80% of adaptation (data not published).

Taken together, COAPT and MITRA-FR suggest that percutaneous mitral valve repair is safe and effective and encourage the local teams to be selective. As concluded by the Cardiothoracic Surgical Trials Network panelists, there is a critical need for additional research to identify

<table>
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<tr>
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<th>MITRA-FR</th>
<th>COAPT</th>
<th>COAPT EDV recalculation</th>
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<tbody>
<tr>
<td>EDV</td>
<td>245 mL</td>
<td>193 mL</td>
<td>290 mL</td>
</tr>
<tr>
<td>EF</td>
<td>31%</td>
<td>31%</td>
<td>31%</td>
</tr>
<tr>
<td>Total LVSV</td>
<td>(EDV × 0.31)</td>
<td>(EDV × 0.31)</td>
<td>(Regular volume + efficiency stroke volume)</td>
</tr>
<tr>
<td></td>
<td>= 76 mL</td>
<td>= 59 mL</td>
<td>90 mL 88</td>
</tr>
<tr>
<td>Regular volume (PISA method)</td>
<td>45 mL</td>
<td>60 mL</td>
<td>60 mL</td>
</tr>
</tbody>
</table>
Obadia reports personal fees from Abbott, Delacroix-Chevalier, Landanger, and Medtronic. Iung reports personal fees from Edwards Lifesciences, Boehringer Ingelheim, and Novartis. Messika-Zeitoun received consultant fees from Edwards. The MITRA-FR Trial is an academic study supported by the French Ministry of Health (Programme Hospitalier de Recherche Clinique - Identifier: NCT01920698) and partially by Abbott Vascular, United States.

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potential subsets who may benefit from an intervention, but for the time being, we should avoid fast and simple conclusions about this complex disease.

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3. Asch FM, Grayburn PA, Siegel RJ, Kar S, Lim DS, Zaroff JG, et al. Echocardiographic outcomes after transcatheter leaflet approximation in patients with secondary mitral regurgitation: a COAPT oriented study, it is tempting to focus on technical aspects and patient selection as possible sources of differences in outcomes, yet medical adjuncts deserve equal attention. As outlined by the Obadia and colleagues,1 it seems that technical expertise is unlikely to account for the discordant result of the trials, and the concept of “disproportionate” versus “proportionate” functional MR provides a helpful conceptual framework5 but few firm conclusions in an attempt to reconcile the data on the basis of differential relationships of mitral insufficiency and chamber size in the 2 studies. It is noteworthy that the rate of recurrent MR in both trials was superior to randomized surgical results with ring repair in patients with ischemic MR and less advanced myocardial dysfunction.

Although leaflet approximation may represent repair superior to isolated annular reduction, medical management of these ill patients should not be ignored. More than half of patients eligible for randomization in the COAPT trial were excluded during the run-in period, many because medical optimization had caused these patients to no longer meet inclusion criteria. Furthermore, at 1 year, 46.8% patients in the control group had moderate or less MR, suggesting significant improvement from baseline with medical therapy alone. Medical therapy in the COAPT trial was tightly controlled through the Clinical Endpoint Committee, and medication adjustments were tracked throughout the study period (Appendix Table S6 in the original COAPT article1). Medical therapy in the MITRA-FR trial was provided at randomization (Appendix Table S2 in the original MITRA-FR article1) but subsequently left to the discretion of the local treating physician. Both β-blocking and afterload-reducing agents appeared to be used with similar frequencies at randomization in the studies. In the COAPT study, however, the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor/neprilysin inhibitors was significantly lower in the control group than in the device group at baseline and at 1- and 2-year follow-ups. Whether this difference in afterload reduction contributed to the divergence in clinical outcomes in the study is feasible, although speculative. It is tempting to conjecture that less protocol-driven medical adjustment in the MITRA-FR trial resulted in its negative outcomes, but that trial also better reflects reality of clinical medicine.