Atrial Fibrillation After Surgical Correction of Mitral Regurgitation in Sinus Rhythm
Incidence, Outcome, and Determinants

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Background—The incidence, determinants, and outcome of postoperative atrial fibrillation (AF) after surgery for mitral regurgitation (MR) are poorly defined but may have important implications for timing of mitral valve surgery.

Methods and Results—In 762 patients in sinus rhythm with no AF history undergoing MR surgical correction, we examined the rates and prognostic implications of postoperative AF for early AF (within 2 weeks postoperatively) and late AF (>2 weeks after surgery). During postoperative follow-up, 180 patients (24%) experienced new AF (early AF in 136 and late AF in 111). Isolated early AF without recurrence was observed in 69 patients characterized by high angina class and lower left ventricular ejection fraction but no significant left atrial (LA) enlargement. However, overall early AF predicted late AF: 62±5% of patients with early AF had late AF at 10 years compared with 9±1% of patients without early AF (P<0.0001). Large LA size strongly and independently predicted early AF (P=0.01) and late AF (P=0.003). For late AF, the predictive value of an enlarged LA was cumulative to that of early AF. Postoperative AF was associated with an increased subsequently higher risk of stroke or congestive heart failure (adjusted risk ratio=1.46 [1.04 to 2.05], P=0.03).

Conclusions—Postoperative AF is common after surgical correction of MR in patients with no prior history of AF and is associated with increased subsequent morbidity. LA enlargement is independently predictive of postoperative AF and as such, should be integrated into the clinical decision-making process in patients with MR. (Circulation. 2004;110:2320-2325.)

Key Words: echocardiography ▪ atrial flutter ▪ fibrillation ▪ valves ▪ stroke

Atrial fibrillation (AF) is a frequent complication after cardiac surgery, with a reported incidences as high as 65%.1 Postoperative AF is associated with increased mortality and morbidity,2 longer hospital stay,3 and increased hospitalization cost.4 Consequently, preventive strategies with β-blockers or amiodarone have been proposed.5,6 AF is also a common complication of mitral regurgitation (MR) when conservatively managed.7 Its incidence increases with age and left atrial (LA) dimension. Importantly, the occurrence of AF under conservative management is associated with subsequent excess mortality and morbidity. However, the incidence and determinants of AF after mitral valve surgery are poorly defined for several reasons. First, postoperative AF has been mainly evaluated after coronary artery bypass surgery (CABG), and few patients undergoing mitral valve surgery (for mitral stenosis or MR) were included.2,4,8–11 Second, these studies included mostly post–valve replacement patients, and in an era of mitral valve repair dominance, the incidence of postoperative AF remains undefined. Third, early postoperative AF has been mainly evaluated, and the long-term incidence of AF after mitral valve surgery is seldom reported. Consequently, the relation between early postoperative AF and late recurrence is unknown, and the impact of postoperative AF on outcome is not defined. The lack of data on the incidence, predictors, and long-term clinical implications of AF after MR surgery hinders management of patients with MR and the potential development of preventive strategies.

The aims of this study were, in patients undergoing mitral valve surgery repair or replacement, to (1) evaluate the incidence of AF immediately and late after mitral valve surgery, (2) assess the determinants of postoperative AF, (3) investigate the consequences of early postoperative AF in terms of recurrence of AF, and (4) assess the impact of postoperative AF on outcome.
Methods

Patient Population
All patients who underwent mitral valve surgery for MR (repair or replacement) at the Mayo Clinic, Rochester, Minnesota, from January 1980 through December 1995 were potentially eligible for the present study. Exclusion criteria were (1) nonsinus rhythm at entry (2) history of paroxysmal or chronic AF, (3) previous cardiac surgery, (4) associated mitral stenosis of more than a trivial degree, (5) associated aortic valve disease of more than a trivial degree, and (6) cardiac congenital or pericardial surgery. Associated CABG at the time of mitral valve surgery was not an exclusion criterion. Medical records of eligible patients were comprehensively reviewed for clinical data. Significant coronary artery disease (CAD) was defined by the presence of stenosis \( \geq 70\% \) (50% for left main) on preoperative angiograms. Patients denying access to their medical records for research were excluded.

All patients were followed up clinically by their personal physicians. Follow-up information was obtained by review of ECGs and consultations performed at our institution and at outside physicians’ institutions. We contacted prospectively and repeatedly the outside physicians and institutions participating in the patient’s care and obtained copies of their records after authorization. All episodes of AF reported herein were confirmed by investigator’s review of ECGs or prints of telemetry monitoring. No unsubstantiated episode of palpitation was considered to be AF. Early AF was defined as AF occurring within the first 2 postoperative weeks. Late AF, defined as AF occurring between 2 weeks after surgery and last follow-up, was analyzed by censoring at time of death or last follow-up, and late AF as AF occurring \( \geq 2\) weeks after surgery. Postoperative stroke and congestive heart failure (CHF) complications were confirmed by physician or hospital records.

Echocardiographic Assessment

Comprehensive 2-dimensional (2D) echocardiography was performed before MR surgery,12,13,15 all echocardiographic variables were collected prospectively, and for subsequent analyses, all values were used unaltered from the original echocardiographic report. The etiology of MR was defined according to valve alterations and confirmed by surgical observations14 and was classified as ischemic or nonischemic. Left ventricle (LV) and left atrium (LA) dimensions were measured by 2D-directed, M-mode echocardiography. LV ejection fraction (LVEF), visually estimated,15 was averaged with the calculated values16 when available.

Statistical Analysis

Continuous variables are expressed as mean\( \pm \)SD, and categorical variable as percentages. Comparisons between groups were performed with standard \( t \) tests or \( \chi^2 \) test as appropriate. Identification of predictors of early AF was performed by logistic regression. The incidences of late AF and other events (stroke or CHF) were estimated by the Kaplan-Meier method, expressed as mean\( \pm \)SE and compared between groups by the log-rank test. Occurrence of late AF was analyzed by censoring at time of death or last follow-up, and the time analyzed was that between surgery and occurrence of AF or last follow-up. Identification of predictors of late AF was based on univariate and multivariate Cox proportional-hazards analyses. To determine the impact of follow-up AF on subsequent outcome (occurrence of death or the combined end point of stroke or CHF as major potential complications of AF), a time-dependent AF variable (specifying the time of occurrence with respect to surgery and to complications) was tested (as an independent variable) in univariate and multivariate Cox proportional-hazards models including other baseline predictors of outcome. \( P<0.05 \) was considered significant.

Results

Baseline Characteristics

During the study period, 1344 patients underwent isolated mitral surgery for MR at our institution, of whom 544 were in AF preoperatively and 38 had a history of AF, so that 762 patients fulfilled the eligibility criteria. Baseline characteristics are summarized in the Table, left. Age was 62\( \pm \)13 years, 62% were male, 48% were in New York Heart Association (NYHA) class III/IV, and 23% were in Canadian Cardiovascular Society (CCS) angina class III/IV. Mitral valve repair was performed in 72% and replacement in 28% by a standard left atriotomy and caval cannulation through the right atrial appendage in all patients. Forty percent had concomitant CABG. LVEF was 59\%\( \pm \)13% and was \( <50\% \) in 19% of patients. LA diameter was 51\( \pm \)8 mm.

Incidence of Postoperative AF

Follow-up was obtained in 98% until the time of death or 2000 (mean duration, 5.5\( \pm \)4.8 years; up to 19.4 years). AF occurred in 180 patients (24%). One hundred thirty-six patients (18%) developed early AF (within the first 2 postoperative weeks). Among these patients, AF remained confined to the 2 weeks postoperatively (isolated early AF) in 69 patients (9%), whereas 67 patients (9%) had recurrence of AF (early plus late AF). Another subset of 44 patients (6%) experienced AF only after the 2 postoperative weeks (late AF only). Thus, a total of 111 patients (15%) experienced late AF. The incidence of late AF at 5 and 10 years was 12\% and 19\%\( \pm \)2, respectively (Figure 1).

Predictors of Postoperative Early AF

Overall Early AF

Comparisons between patients with early AF and no AF with regard to baseline characteristics are presented in the middle panel of the Table. Early AF patients were older (\( P=0.0008 \)), had significantly larger LA (\( P=0.001 \)), and had more frequent mitral valve replacement than repair (\( P=0.03 \)). There were no differences with regard to CAD status, associated CABG, or etiology of MR. By logistic regression analysis, after adjustment for age, sex, and NYHA class, independent predictors of early AF were lower LVEF (odds ratio [OR]=1.03 [1.01 to 1.05] per percent decline in EF; \( P=0.006 \)), larger LA size (OR=1.04 [1.02 to 1.08] per 1-mm LA diameter increase; \( P=0.006 \)), mitral valve replacement (OR=1.81 [1.18 to 2.77]; \( P=0.006 \)), and nonischemic etiology of MR (OR=2.40 [1.33 to 4.35]; \( P=0.004 \)). After adjusting for these predictors, it was found that early AF has not decreased after compared with before 1990 (\( P=0.21 \)). Early AF was more frequent in patients with than without LA size \( \geq 50 \) mm (20% versus 13%, \( P=0.05 \)). The predictive value of LA size was superior to that of LA size normalized to body surface area, which was not statistically significant.

Isolated Early AF

Patients with isolated early AF were older (\( P=0.004 \)), were more frequently symptomatic for angina (\( P=0.006 \)), had lower LVEF (\( P=0.004 \)), had higher serum creatinine (\( P=0.001 \)), and more frequently underwent mitral valve replacement (\( P=0.04 \)) than did patients with no AF. LA size was not different (\( P=0.54 \)) between the 2 groups. By logistic regression analysis, predictors of isolated early AF were lower LVEF (OR=1.04 [1.01 to 1.06] per percent decline in EF; \( P=0.0002 \)), shorter bypass time (OR=1.01 [1.00 to 1.02]; \( P=0.03 \)), CCS angina class III/IV (OR=2.28 [1.18 to
Baseline Characteristics in the Overall Population and According to the Occurrence of AF

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall, N=762</th>
<th>No AF, n=582</th>
<th>Early AF, n=136</th>
<th>P vs No AF</th>
<th>Isolated Early AF, n=69</th>
<th>P vs No AF</th>
<th>Late AF, n=111</th>
<th>P vs No AF</th>
</tr>
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<tbody>
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<td>Clinical</td>
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<td></td>
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<td>Age, y</td>
<td>62±13</td>
<td>62±14</td>
<td>66±10</td>
<td>0.0008</td>
<td>67±12</td>
<td>0.004</td>
<td>64±10*</td>
<td>0.49</td>
</tr>
<tr>
<td>Male, %</td>
<td>62</td>
<td>62</td>
<td>66</td>
<td>0.37</td>
<td>72</td>
<td>0.09</td>
<td>58*</td>
<td>0.42</td>
</tr>
<tr>
<td>NYHA class III/IV, %</td>
<td>48</td>
<td>49</td>
<td>46</td>
<td>0.63</td>
<td>48</td>
<td>0.90</td>
<td>44</td>
<td>0.39</td>
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<td>History of diabetes, %</td>
<td>9</td>
<td>9</td>
<td>10</td>
<td>0.77</td>
<td>9</td>
<td>0.99</td>
<td>11</td>
<td>0.49</td>
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<td>History of smoking, %</td>
<td>48</td>
<td>48</td>
<td>51</td>
<td>0.47</td>
<td>48</td>
<td>0.98</td>
<td>45</td>
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<td>History of hypertension, %</td>
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<td>37</td>
<td>32</td>
<td>0.27</td>
<td>28</td>
<td>0.11</td>
<td>38</td>
<td>0.94</td>
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<td>SBP, mm Hg</td>
<td>128±20</td>
<td>127±19</td>
<td>130±22</td>
<td>0.14</td>
<td>127±21</td>
<td>0.99</td>
<td>133±21</td>
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<td>DBP, mm Hg</td>
<td>74±11</td>
<td>74±11</td>
<td>75±12</td>
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<td>73±11</td>
<td>0.98</td>
<td>77±12</td>
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<td>BSA, kg/m²</td>
<td>1.8±0.2</td>
<td>1.8±0.2</td>
<td>1.9±0.2</td>
<td>0.19</td>
<td>1.8±0.2</td>
<td>0.56</td>
<td>1.9±0.3</td>
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<tr>
<td>CCS angina class III/IV</td>
<td>23</td>
<td>21</td>
<td>26</td>
<td>0.21</td>
<td>36</td>
<td>0.006</td>
<td>20*</td>
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<td>CAD, %</td>
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<td>49</td>
<td>41</td>
<td>0.14</td>
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<td>0.92</td>
<td>34</td>
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<tr>
<td>LVEF, %</td>
<td>59±13</td>
<td>59±13</td>
<td>57±13</td>
<td>0.12</td>
<td>53±15</td>
<td>0.004</td>
<td>62±11*</td>
<td>0.16</td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>51±8</td>
<td>50±8</td>
<td>54±19</td>
<td>0.001</td>
<td>51±8</td>
<td>0.54</td>
<td>55±8*</td>
<td>&lt;0.001</td>
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<tr>
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<tr>
<td>Total cholesterol, mg/dL</td>
<td>213±48</td>
<td>215±49</td>
<td>212±45</td>
<td>0.58</td>
<td>217±44</td>
<td>0.48</td>
<td>205±43</td>
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<td>Serum creatinine, mg/dL</td>
<td>1.2±0.6</td>
<td>1.2±0.7</td>
<td>1.3±0.4</td>
<td>0.74</td>
<td>1.4±0.5</td>
<td>0.001</td>
<td>1.2±0.3*</td>
<td>0.61</td>
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<tr>
<td>Surgical</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Bypass time, min</td>
<td>97±50</td>
<td>97±51</td>
<td>94±41</td>
<td>0.46</td>
<td>96±37</td>
<td>0.46</td>
<td>95±50</td>
<td>0.63</td>
</tr>
<tr>
<td>MVR, %</td>
<td>28</td>
<td>26</td>
<td>35</td>
<td>0.03</td>
<td>38</td>
<td>0.04</td>
<td>31</td>
<td>0.31</td>
</tr>
<tr>
<td>Mechanical MVR, % of MVR</td>
<td>49</td>
<td>50</td>
<td>56</td>
<td>0.48</td>
<td>46</td>
<td>0.74</td>
<td>47</td>
<td>0.78</td>
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<tr>
<td>Associated CABG, %</td>
<td>40</td>
<td>41</td>
<td>37</td>
<td>0.32</td>
<td>43</td>
<td>0.74</td>
<td>31</td>
<td>0.03</td>
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<tr>
<td>Ischemic etiology, %</td>
<td>21</td>
<td>23</td>
<td>16</td>
<td>0.10</td>
<td>25</td>
<td>0.71</td>
<td>16*</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values are mean±SD or percent. SBP indicates systolic blood pressure; DBP, diastolic blood pressure; BSA, body surface area; and MVR, mitral valve replacement. All other abbreviations are as defined in text.

*P<0.05 vs isolated AF.

4.39]; P=0.01), and mitral valve replacement (OR=2.31 [1.29 to 4.14]; P=0.005).

Predictors of Postoperative Late AF

There were no demographic differences between patients with late AF and those with no AF (right panel of the Table).

However, patients with late AF had higher blood pressures (P<0.05), less frequent CAD, less frequent ischemic MR or associated CABG (all P<0.05), and significantly larger LA size (P<0.0001). The incidence of late AF at 5 and 10 years was significantly higher in patients with an LA size ≥50 mm than in those with LA size <50 mm (18±3% versus 7±2%, and 24±3% versus 11±3%, respectively; P=0.006; Figure 2). Patients with late AF also had more frequent early AF, and 49% of patients with early AF subsequently developed late AF compared with only 7% of those without early AF. The incidence of late AF in patients with versus without early AF was 42±5% versus 5±1% (at 5 years) and 62±5% versus 9±1% (at 10 years; P<0.0001; Figure 3). Of note, the difference in AF between patients with and without recurrent MR did not reach statistical significance (21% versus 14%, P=0.063).

By multivariate Cox proportional-hazards regression analysis, after adjustment for age, sex, and NYHA class, independent predictors of late AF were early AF (relative risk [RR]=9.3 [6.2 to 13.9]; P<0.0001), LA size (RR=1.04 per mm increment [1.02 to 1.08]; P=0.003), and diastolic blood pressure (RR=1.03 per mm Hg increment [1.02 to 1.05]; P=0.0002). After adjusting for these predictors, we found that late AF has not decreased after compared with
before 1990 ($P=0.30$). Early AF and LA enlargement (LA diameter $\geq 50$ mm) exerted a cumulative influence on the occurrence of late AF (10-year rate of late AF was $6\pm 2\%$ with none of these risk factors, $10\pm 3\%$ with LA enlargement only, $41\pm 11\%$ with early AF only, and $70\pm 7\%$ with both; $P<0.001$).

**Impact of AF on Outcome**

During follow-up, stroke occurred in 98 patients (13%) and CHF in 183 (24%) patients. Incidence rates of stroke, of CHF, and of stroke or CHF were $18\pm 2\%$, $28\pm 2\%$, and $39\pm 2\%$, at 10 years, respectively. After adjustment for age, sex, and other confounding factors (NYHA class, cardiac risk factors, creatinine, LVEF, type of surgery [replacement or repair], CAD, and associated CABG), postoperative AF remained an independent predictor of subsequent stroke or CHF ($RR=1.23$ [0.94 to 1.61]; $P=0.12$).

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**Incidence of Postoperative AF**

The incidence of postoperative AF has mainly been reported after CABG, and cumulative data on $>20,000$ patients have been published.$^{2,4,8–11}$ Limited studies report this complication after mitral valve surgery, and available data include patients with both mitral stenosis and MR undergoing predominantly mitral valve replacement or patients undergoing double-valve surgery.$^{1,17}$ Therefore, the occurrence of AF after modern surgical correction of MR is poorly defined. The present study shows that postoperative AF is frequent, involving $24\%$ of operated patients, $18\%$ for early AF and $19\pm 2\%$ at 10 years for late AF. Differences between current incidences and higher ones reported in previous studies are likely related to stringent AF criteria, patient differences, and higher utilization of mitral valve repair, as the present study suggests that the incidence of postoperative AF is lower after mitral valve repair. Nevertheless, these rates remain high, suggesting that defining predictors of postoperative AF is essential.

**Predictors of Postoperative AF**

This study provides the opportunity to assess for the first time the incidence of late postoperative AF, its determinants, and its relation to early postoperative AF.

**Influence of Early AF**

The present study clearly demonstrates that early AF is a major predictor of recurrence of AF. The incidence of late AF in patients with early AF was $62\pm 5\%$ at 10 years compared with only $9\pm 1\%$ in patients without early AF. Therefore, AF that occurs early after mitral valve surgery should not be
considered an isolated phenomenon related to perioperative factors but as a high-risk marker for further recurrences. In contrast, the absence of early AF is reassuring, because >90% of patients remained free of AF at 10 years.

**Influence of LA Size**
Recent outcomes studies in widely varied populations emphasize the role of LA size as a major marker of adverse cardiovascular events. The role of LA enlargement as a harbinger of subsequent AF has been reported in patients without valve disease as well as in patients with MR treated medically. The influence of LA size after cardiac surgery is less clear, because it was not evaluated in most of the largest studies after CABG, and conflicting results have been published in others. In this study, LA size was a strong predictor of both early AF and late AF postoperatively, even after adjusting for various factors such as age, sex, type of surgery, bypass time, LV systolic function, and the presence or absence of CAD. LA size remained an independent predictor of late AF even after adjusting for early AF. The critical importance of LA size was further demonstrated in the subgroup of patients with isolated early AF. These patients were characterized by high CCS angina class and lower LVEF but with a small LA size; comparable to patients without AF, they experienced only transient postoperative AF without recurrence. The power of LA size as a predictor of AF may not be fully measured by LA diameter, and development of criteria for surgery based on LA volume will be of great importance.

**Clinical Implications**
First, AF after successful MR surgery is frequent early and late and should be taken seriously, as it is associated with an excess risk of morbid events, irrespective of the mode of correction of MR. Patients with early AF are at high risk of recurrence and should be closely monitored.

Second, LA enlargement in MR is associated with a high postoperative AF risk, despite the surgical correction of MR. Increased LA size is also associated with a higher AF incidence in MR conservatively managed and with increased morbidity and mortality. Thus, the present data suggest that LA enlargement should raise awareness about the risk of subsequent AF and that MR surgery should be considered in patients with enlarged atria, especially when the probability of successful repair is high. In view of present and previous results, LA diameter ≥50 mm should be considered an indicator of marked LA enlargement. Future enhancements of LA dilatation assessment by echocardiography should help refine this criterion.

**Study Limitations**
AF was considered present only when objectively documented but may be transient, and all episodes may not be detected. However, it is currently impossible to constantly monitor for “silent” AF occurrences. Hence, it is essential to define the incidence and consequences of detectable AF, the only form of this arrhythmia that presently may lead to therapeutic intervention. The prognostic implications of detectable AF underscore the importance of this finding. Approximately 40% of our patients underwent CABG at the time of mitral valve surgery, but this associated procedure does not add to the high rate of AF linked to mitral surgery. Furthermore, LA size, which reflects the severity of MR, independently determined AF, demonstrating the link between MR and postoperative AF.

The present study is not a clinical trial and cannot provide information of potential preventive measures with medical treatment (such as β-blockers or amiodarone) or surgical atrial interventions, which should be assessed in future controlled studies now that the high incidence and serious prognosis of postoperative AF have been demonstrated by the present study.

**Conclusions**
Postoperative AF is a common complication after mitral valve surgery for MR in patients with no prior history of AF at baseline and carries important prognostic implications, even after adjustment for other confounding factors. Early postoperative AF is not an incidental isolated finding and is a harbinger of recurrent AF. LA enlargement is a major predictor of both early and late AF. Therefore, in addition to the important prognostic information provided by LA size and AF occurrence under conservative management in patients with MR, these data further suggest that LA size should be integrated into the decision-making process of patients with MR and that surgery may be considered earlier in the course of the disease.

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**References**


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