Original article

Prognostic Impact of Chronic Total Occlusion in a Nonculprit Artery in Patients With Acute Myocardial Infarction Undergoing Primary Angioplasty

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A B S T R A C T

Introduction and objectives: The prognostic value of chronic total occlusion in nonculprit coronary arteries in patients with myocardial infarction undergoing primary angioplasty remains controversial. Several publications have described different methodologies and conflicting findings. In addition, causes of death were not reported. Our aim is to analyze the prognostic impact of chronic total occlusion in nonculprit coronary arteries and the role of left ventricular ejection fraction in this analysis.

Methods: Prospective inclusion of consecutive patients with ST-segment elevation myocardial infarction who underwent primary angioplasty. We recorded baseline characteristics, in-hospital clinical course, and mortality and its causes during follow-up. We assessed the impact of chronic total occlusion on mortality using Cox regression analysis.

Results: Chronic total occlusion in nonculprit arteries was present in 125 of 1176 patients (10.6%); in 79 of these 125 patients, chronic total occlusion was present in the proximal segments. The mean follow-up was 339 days; 64 (5.8%) patients died during the first 6 months. Patients with chronic total occlusions had more comorbidities, poorer ventricular function, and higher mortality (hazard ratio=2.79; 95% confidence interval, 1.71-4.56). Chronic total occlusion was also associated with noncardiac death (hazard ratio=3.83; 95% confidence interval, 2.10-7.01). Chronic total occlusion in proximal segments was associated with both cardiac (hazard ratio=3.22; 95% confidence interval, 1.42-7.30) and noncardiac deaths (hazard ratio=3.43; 95% confidence interval, 1.67-7.06). The multivariate analysis performed without including left ventricular ejection fraction showed a significant association between chronic total occlusion and mortality. However, when left ventricular ejection fraction was included in the analysis, this association was nonsignificant (hazard ratio=1.76; 95% confidence interval, 0.85-3.65; P=0.166).

Conclusions: Chronic total occlusion in this clinical setting identified patients at higher risk with more comorbidities and higher mortality, but did not behave as an independent predictor of mortality when left ventricular ejection fraction was included in the analysis.

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Valor pronóstico de la oclusión total crónica de una arteria no responsable en el infarto agudo de miocardio tratado con angioplastia primaria

R E S U M E N

Introducción y objetivos: El valor pronóstico de una oclusión total crónica en arterias no responsables en el infarto de miocardio tratado mediante angioplastia primaria es controvertido. Los artículos publicados presentan importantes diferencias metodológicas y resultados opuestos, sin describir causas de mortalidad. Nuestro objetivo es analizar el impacto pronóstico de la oclusión total crónica de arteria no responsable en la mortalidad y el papel de la fracción de eyeción del ventrículo izquierdo en dicho análisis.

Métodos: Inclusión prospectiva de pacientes consecutivos con infarto agudo de miocardio con elevación persistente del segmento ST sometidos a angioplastia primaria, con registro de características basales, complicaciones, mortalidad y sus causas durante el seguimiento. Se evaluó el impacto de la oclusión total crónica en la mortalidad mediante el análisis de regresión de Cox.

Resultados: Presentaban oclusión total crónica de arteria no responsable 125 (10.6%) de 1.176 pacientes (79 de 125 en segmentos principales). El seguimiento medio fue de 339 días; 64 pacientes (5.8%)

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INTRODUCCIÓN

La oclusión total crónica en este escenario resulta marcador de riesgo, comorbilidades y mayor mortalidad, aunque no se comporta como predictor independiente de mortalidad tras incluir la fracción de eyeción del ventrículo izquierdo en el análisis.

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Fallecieron en los primeros 6 meses. Los pacientes con oclusión total crónica presentaban más comorbilidades, por lo que se propuso un análisis de la fracción de eyeción del ventrículo izquierdo como predictor independiente de mortalidad.

Adjuvante antitrombótico (bivalirudina, glycoprotein IIb/IIIa inhibitors) fue administrado al operador durante la intervención. Las percutanas técnicas de intervención, protocolos de tratamiento o cuestiones de elección de stent son partes importantes de la elección del tratamiento.

La interpretación de resultados se realizó prospectivamente, no interviniendo en el tratamiento de pacientes.

La forma de tratamiento será un punto de interés para futuros análisis. No se consideraron características de pacientes como edad, sexo, comorbilidades, etc., como variables predictoras de mortalidad.

METODOS

Estudio y cuidados de salud

Todos los pacientes con ST-segmentelevation acute myocardial infarction referido a nuestro hospital para PA en el primer 12 h postinfarto de miocardio, incluyendo el período de los meses siguientes, fueron prospectivamente incluidos en el estudio. El análisis se realizó de acuerdo con la definición de la Infarction Code program implementado en la comunidad autónoma de Cataluña en 2009. El criterio utilizado para activar el protocolo fue el dolor de pecho con inicio menos de 12 h previamente con ST-segmentelevation de 1 mm o mayor en 2 segmentos adyacentes o nuevos, con o sin alteraciones de la onda T, en un electrocardiograma de 12 derivaciones.

Los pacientes recibieron tratamiento instituido inicialmente en el servicio de cardiología intervencionista. Los demás pacientes fueron remitidos al servicio de urgencias o traslado a un hospital de referencia para terapia adyuvante.

La valoración clínica se realizó a los 6 meses. Los pacientes con presencia de comorbilidades, por lo que se propuso un análisis de la fracción de eyeción del ventrículo izquierdo como predictor independiente de mortalidad.

La forma de tratamiento será un punto de interés para futuros análisis. No se consideraron características de pacientes como edad, sexo, comorbilidades, etc., como variables predictoras de mortalidad.

La interpretación de resultados se realizó prospectivamente, no interviniendo en el tratamiento de pacientes.
treating physician. The cause of death was determined by the medical practitioner who attended the patient at the time of death. If death occurred outside the hospital setting, the cause was determined by an interview with relatives. If there was more than 1 cause of death, the main cause was established by considering the clinical relevance of each one. Cardiac death was considered to be any death due to myocardial infarction or heart failure and sudden death.

**Statistical Analysis**

PASW Statistics 18 (Chicago, Illinois, United States) was used for the data analysis. The categorical variables are expressed as number and percentage, and the quantitative variables are expressed as mean (standard deviation). Variables with a nonnormal distribution are expressed as median [interquartile range]. The normality of distributions was analyzed by the Kolmogorov-Smirnoff test.

The categorical variables were compared by the chi-square test or Fisher’s exact test when applicable. The quantitative variables were compared by the Student t test. Survival curves were obtained by the Kaplan-Meier method.

**Analysis of the Relationship Between Chronic Total Occlusion in Nonculprit Artery and Mortality**

Mortality related to CTOnr was analyzed by the Cox regression method, and the proportional hazard model assumption was confirmed by the Kalbfleisch and Prentice method. Potential confounders included in the multivariate analysis had to meet the following requirements: statistically significant association (P<.2) with both exposure (CTOnr) and effect (mortality); clinically reasonable potential confounding effect between CTOnr and mortality, and not an intermediate variable in the relationship between CTOnr and mortality.

The variables of LVEF and Killip class on admission were handled in a specific manner, as they could be considered, at least partly, as intermediate variables between CTOnr and mortality. However, because they are clinically relevant, multivariate analyses were performed with and without these 2 variables to study the association between CTOnr and mortality.

The association between CTOnr and mortality in the final model was considered statistically significant if the hazard ratio (HR) resulted in P<.05 and its 95% confidence interval (95%CI) did not include the value of 1.

**Analysis of the Relationship Between Chronic Total Occlusion in Nonculprit Artery in Proximal Arteries and Mortality**

To analyze the relationship between CTOnr in proximal arteries and mortality, the same statistical procedure was followed as with all CTOnr.

**RESULTS**

During the period analyzed, 1176 patients were referred to our hospital for PA; of these, 125 (10.6%) had CTOnr in at least 1 coronary artery, 79 of whom had a CTOnr in at least 1 proximal artery.

The patients’ baseline characteristics, procedures, and clinical course according to the presence of CTOnr are listed in Table 1. Patients with CTOnr were older and had a higher burden in terms of cardiovascular risk factors and other comorbidities. They were also more likely to show signs of heart failure, more massive coronary disease, and worse ventricular function at discharge. Their requirements for invasive procedures during hospitalization (intraventricular balloon pump, invasive mechanical ventilation, Swan-Ganz catheter) were significantly higher than those of patients without CTOnr.

There were no significant differences in ischemia time or TIMI (Thrombolysis In Myocardial Infarction) flow in the culprit artery at the end of the interventional procedure. In-hospital mortality was significantly greater in the patients with CTOnr, but no significant differences were observed in the in-hospital incidence of infectious and hemorrhagic complications. No differences were observed in the incidence of reinfarction (3.5% vs 3.4%; P=.977) or the need for new revascularization (7.8% vs 8.9%; P=.693) during follow-up. In 4 (3.2%) patients, the CTOnr was revascularized during follow-up.

The comparative analysis of patients with CTOnr in proximal arteries compared with all others showed similar findings to those observed in all patients with CTOnr (Table 2); although these patients had higher comorbidity burdens, more severe coronary disease, worse ventricular function at discharge, and higher in-hospital mortality, no significant differences were found in the incidence of infectious and hemorrhagic complications. The ischemia time was slightly higher in patients with CTOnr in proximal segments, although this different was not statistically significant.

**Association Between Chronic Total Occlusion in Nonculprit Artery and Mortality**

Follow-up data were collected from 1112 (94.6%) patients, 122 (97.6%) in the group with CTOnr and 990 (94.1%) in the group without CTOnr. The mean follow-up was 339 days. Total mortality during follow-up was significantly higher among patients with CTOnr (HR=2.79; 95%CI, 1.71-4.56; P<.001; 6-month mortality among patients with CTOnr, 16 of 122 [13.1%]; 6-month mortality among patients without CTOnr, 48 of 990 [4.8%]). When the causes of death were analyzed separately, a statistically significant association was observed between CTOnr and noncardiac mortality (HR=3.83; 95%CI, 2.10-7.01; P<.001). The association between CTOnr and cardiac mortality was not statistically significant (HR=1.86; 95%CI, 0.82-4.21; P=.138; 6-month cardiac mortality among patients with nonculprit, 6 of 122 [4.9%]; 6-month cardiac mortality among patients without CTOnr, 29 of 990 [2.9%]). Figure 1 shows the trend for total cumulative mortality according to the presence of CTOnr.

**Association Between Chronic Total Occlusion in Nonculprit Artery in Proximal Segments and Mortality**

The results of this analysis were very similar to the previous results. Total mortality during follow-up was significantly higher among patients with CTOnr in proximal segments (HR=3.18; 95%CI, 1.82-5.55; P<.001). However, unlike the previous analysis, the association between CTOnr and mortality was statistically significant for both cardiac (HR=3.22; 95%CI, 1.42-7.30; P=.005) and noncardiac causes (HR=3.43; 95%CI, 1.67-7.06; P<.001). Figure 2 shows the trend for total cumulative mortality according to the presence of CTOnr in proximal segments.

**Multivariate Analysis**

**Relationship Between Chronic Total Occlusion in Nonculprit Artery and Mortality**

The multivariate analysis performed without including LVEF or Killip class on admission showed a significant association
### Table 1
Baseline Clinical Characteristics, Procedures, and Complications According to the Presence of Chronic Total Occlusion in Nonculprit Artery

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CTOotr (n=125)</th>
<th>No CTOotr (n=1051)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>65.3 (12.2)</td>
<td>61.6 (13.3)</td>
<td>.002</td>
</tr>
<tr>
<td>Men</td>
<td>103 (82.4)</td>
<td>827 (78.7)</td>
<td>.335</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>40 (32.0)</td>
<td>243 (23.1)</td>
<td>.028</td>
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<td>Hypertension</td>
<td>84 (67.2)</td>
<td>555 (52.8)</td>
<td>.002</td>
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<td>Dyslipidemia</td>
<td>75 (60.0)</td>
<td>564 (53.7)</td>
<td>.179</td>
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<tr>
<td>Active smoker</td>
<td>63 (50.4)</td>
<td>493 (47.4)</td>
<td>.526</td>
</tr>
<tr>
<td>Creatinine clearance, ml/min</td>
<td>81.8±36.4</td>
<td>95.1±51.4</td>
<td>.005</td>
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<tr>
<td>History of stroke</td>
<td>15 (12.4)</td>
<td>59 (5.8)</td>
<td>.010</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>25 (20.0)</td>
<td>71 (6.8)</td>
<td>.001</td>
</tr>
<tr>
<td>History of AMI</td>
<td>32 (25.6)</td>
<td>93 (8.8)</td>
<td>.001</td>
</tr>
<tr>
<td>History of PCI</td>
<td>19 (15.2)</td>
<td>81 (7.7)</td>
<td>.005</td>
</tr>
<tr>
<td>History of CAGB</td>
<td>5 (4.0)</td>
<td>5 (0.5)</td>
<td>.002</td>
</tr>
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<td>Hemoglobin on admission, g/dL</td>
<td>13.8 (1.8)</td>
<td>13.8 (1.7)</td>
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<td>Leukocytes, cells/µL</td>
<td>12152±4140</td>
<td>12236±5506</td>
<td>.869</td>
</tr>
<tr>
<td>Blood glucose on admission, mg/dL</td>
<td>10.2 (5.2)</td>
<td>9.0 (4.0)</td>
<td>.021</td>
</tr>
<tr>
<td>History of AMI</td>
<td>65 (52)</td>
<td>451 (43)</td>
<td>.054</td>
</tr>
<tr>
<td>Number of affected leads</td>
<td>4.3±1.8</td>
<td>4.3±1.7</td>
<td>.846</td>
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<td>Maximum ST-segment elevation, mm</td>
<td>3.6±2.1</td>
<td>3.4±2.1</td>
<td>.457</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>127±26.1</td>
<td>127±25.9</td>
<td>.959</td>
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<td>Heart rate, bpm</td>
<td>82.8±18.9</td>
<td>80.5±17.0</td>
<td>.158</td>
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<td>Affected vessels</td>
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<td></td>
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</tr>
<tr>
<td>1</td>
<td>0</td>
<td>619 (58.9)</td>
<td>.001</td>
</tr>
<tr>
<td>2</td>
<td>58 (46.4)</td>
<td>276 (26.3)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>67 (53.6)</td>
<td>124 (11.8)</td>
<td></td>
</tr>
<tr>
<td>Killip class on admission</td>
<td></td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>I</td>
<td>79 (63.2)</td>
<td>880 (84.0)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>32 (25.6)</td>
<td>120 (11.5)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>6 (4.8)</td>
<td>21 (2.0)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>8 (6.4)</td>
<td>27 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Ischemia time, min</td>
<td>245±192</td>
<td>222±160</td>
<td>.111</td>
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<tr>
<td>Thrombus aspiration</td>
<td>82 (64.6)</td>
<td>815 (78.0)</td>
<td>.001</td>
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<td>Direct stenting</td>
<td>64 (50.4)</td>
<td>702 (67.2)</td>
<td>.001</td>
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<tr>
<td>Drug-eluting stent</td>
<td>25 (23.4)</td>
<td>239 (25.6)</td>
<td>.616</td>
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<td>No-reflow phenomenon</td>
<td>9 (7.1)</td>
<td>69 (6.6)</td>
<td>.836</td>
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<td>TIMI 3 flow after PCI</td>
<td>113 (95.0)</td>
<td>932 (93.1)</td>
<td>.445</td>
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<td>LVEF, %</td>
<td>43.9±11.8</td>
<td>52.0±9.8</td>
<td>.001</td>
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<td>Intraventricular balloon pump</td>
<td>15 (12.0)</td>
<td>35 (3.4)</td>
<td>.001</td>
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<td>Orotracheal intubation</td>
<td>13 (10.4)</td>
<td>59 (5.6)</td>
<td>.029</td>
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<tr>
<td>Swan-Ganz catheter</td>
<td>8 (6.4)</td>
<td>25 (2.4)</td>
<td>.016</td>
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<td>Hemodialysis</td>
<td>2 (1.6)</td>
<td>4 (0.4)</td>
<td>.123</td>
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<tr>
<td>Temporary pacemaker</td>
<td>4 (3.2)</td>
<td>46 (4.4)</td>
<td>.647</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>3 (2.4)</td>
<td>8 (0.8)</td>
<td>.104</td>
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<td>Infections</td>
<td>9 (7.1)</td>
<td>40 (3.8)</td>
<td>.094</td>
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<td>In-hospital mortality</td>
<td>8 (6.4)</td>
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<td>.047</td>
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<td>In-stent thrombosis</td>
<td>1 (0.8)</td>
<td>16 (1.6)</td>
<td>.512</td>
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<td>6-month mortality</td>
<td>16 (13.1)</td>
<td>48 (4.8)</td>
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<td>6-month cardiac mortality</td>
<td>6 (4.9)</td>
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<td>.207</td>
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<tr>
<td>6-month noncardiac mortality</td>
<td>10 (8.2)</td>
<td>19 (1.9)</td>
<td>.001</td>
</tr>
</tbody>
</table>

AMI, acute myocardial infarction; CAGB, coronary aortic bypass graft; CTOotr, chronic total occlusion in nonculprit artery; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; TIMI, Thrombolysis In Myocardial Infarction.

The data are presented as no. (%) or mean±standard deviation.
Table 2
Baseline Clinical Characteristics, Procedures, and Complications According to the Presence of Chronic Total Occlusion in Nonculprit Artery in Proximal Segments

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CTOnrp (n=79)</th>
<th>No CTOnrp (n=1097)</th>
<th>P</th>
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<tr>
<td>Age, years</td>
<td>64.1±12.5</td>
<td>61.8±13.2</td>
<td>.132</td>
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<td>Men</td>
<td>66 (83.5)</td>
<td>864 (78.8)</td>
<td>.313</td>
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<td>Diabetes mellitus</td>
<td>30 (38.0)</td>
<td>253 (23.1)</td>
<td>.003</td>
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<td>Hypertension</td>
<td>52 (65.8)</td>
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<td>Dyslipidemia</td>
<td>46 (58.2)</td>
<td>593 (54.1)</td>
<td>.472</td>
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<td>Active smoker</td>
<td>43 (54.4)</td>
<td>513 (47.2)</td>
<td>.217</td>
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<tr>
<td>Creatinine clearance, mL/min</td>
<td>84.8±35</td>
<td>94.3±51</td>
<td>.105</td>
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<td>History of stroke</td>
<td>9 (11.7)</td>
<td>65 (6.1)</td>
<td>.057</td>
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<tr>
<td>Peripheral vascular disease</td>
<td>17 (21.5)</td>
<td>79 (7.2)</td>
<td>.001</td>
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<td>History of AMI</td>
<td>23 (29.1)</td>
<td>102 (9.3)</td>
<td>.001</td>
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<td>History of PCI</td>
<td>10 (12.5)</td>
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<td>.027</td>
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<td>History of CABG</td>
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<td>.141</td>
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<td>Hemoglobin on admission, g/dL</td>
<td>13.8±1.9</td>
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<td>Blood glucose on admission, mg/dL</td>
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<td>.006</td>
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<td>History of AMI</td>
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<td>477 (43.5)</td>
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<td>Number of affected leads</td>
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<td>4.3 (1.7)</td>
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<td>Maximum ST-segment elevation, mm</td>
<td>3.3 (1.8)</td>
<td>3.4 (2.1)</td>
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<td>SBP, mmHg</td>
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<td>655 (57)</td>
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<td>47 (59.5)</td>
<td>141 (12.9)</td>
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<td>Killip class on admission</td>
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<tr>
<td>I</td>
<td>49 (62.0)</td>
<td>910 (83.2)</td>
<td>.001</td>
</tr>
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<td>II</td>
<td>20 (25.3)</td>
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<tr>
<td>IV</td>
<td>5 (6.3)</td>
<td>30 (2.7)</td>
<td></td>
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<tr>
<td>Ischemia time, min</td>
<td>256 [181-395]</td>
<td>223 [165-325]</td>
<td>.052</td>
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<tr>
<td>Thrombus aspiration</td>
<td>60 (64.1)</td>
<td>842 (77.5)</td>
<td>.007</td>
</tr>
<tr>
<td>Direct stenting</td>
<td>42 (53.8)</td>
<td>719 (66.2)</td>
<td>.027</td>
</tr>
<tr>
<td>Drug-eluting stent</td>
<td>18 (26.1)</td>
<td>245 (25.4)</td>
<td>.894</td>
</tr>
<tr>
<td>No-reflow phenomenon</td>
<td>6 (7.7)</td>
<td>72 (6.6)</td>
<td>.717</td>
</tr>
<tr>
<td>TIMI 3 flow after PCI</td>
<td>74 (94.9)</td>
<td>971 (93.2)</td>
<td>.566</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>43±12</td>
<td>52±10</td>
<td>.001</td>
</tr>
<tr>
<td>Intravascular balloon pump</td>
<td>12 (15.2)</td>
<td>38 (3.7)</td>
<td>.001</td>
</tr>
<tr>
<td>Orotracheal intubation</td>
<td>8 (10.7)</td>
<td>64 (6.2)</td>
<td>.141</td>
</tr>
<tr>
<td>Swan-Ganz catheter</td>
<td>5 (6.7)</td>
<td>28 (2.7)</td>
<td>.066</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2 (2.7)</td>
<td>4 (0.4)</td>
<td>.056</td>
</tr>
<tr>
<td>Temporary pacemaker</td>
<td>0</td>
<td>50 (4.8)</td>
<td>.044</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1 (1.3)</td>
<td>9 (0.8)</td>
<td>.498</td>
</tr>
<tr>
<td>Infections</td>
<td>6 (7.7)</td>
<td>43 (3.9)</td>
<td>.132</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>6 (7.6)</td>
<td>30 (2.7)</td>
<td>.029</td>
</tr>
<tr>
<td>6-month mortality</td>
<td>12 (15.8)</td>
<td>52 (5.1)</td>
<td>.001</td>
</tr>
<tr>
<td>6-month cardiac mortality</td>
<td>5 (6.6)</td>
<td>30 (2.9)</td>
<td>.053</td>
</tr>
<tr>
<td>6-month noncardiac mortality</td>
<td>7 (9.2)</td>
<td>22 (2.1)</td>
<td>.001</td>
</tr>
</tbody>
</table>

AMI, acute myocardial infarction; CABG, coronary aortic bypass graft; CTOnrp, chronic total occlusion in nonculprit artery in proximal segments; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; TIMI, Thrombolysis In Myocardial Infarction.

The data are presented as no. (%), mean± standard deviation or median [interquartile range].
between CTONr and mortality (HR = 2.09; 95%CI, 1.16-3.77; P=0.014). When both variables were included in the analysis, the statistical model showed a nonsignificant association (HR = 1.76; 95%CI, 0.85-3.65; P=0.166). Table 3 lists the results of the univariate and multivariate analyses, including all potential confounders.

Table 3
Analysis of the Relationship Between Chronic Total Occlusion in Nonculprit Artery and Mortality

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>P</td>
</tr>
<tr>
<td>CTONr</td>
<td>2.79 (1.71-4.56)</td>
<td>.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>1.08 (1.06-1.10)</td>
<td>.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.50 (0.96-2.35)</td>
<td>.077</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.01 (1.27-3.18)</td>
<td>.003</td>
</tr>
<tr>
<td>Creatinine clearance, mL/min</td>
<td>0.97 (0.96-0.97)</td>
<td>.001</td>
</tr>
<tr>
<td>History of stroke</td>
<td>3.39 (1.97-5.84)</td>
<td>.001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>2.31 (1.30-4.08)</td>
<td>.004</td>
</tr>
<tr>
<td>History of AMI</td>
<td>1.84 (1.06-3.21)</td>
<td>.031</td>
</tr>
<tr>
<td>History of PCI</td>
<td>1.74 (0.92-3.27)</td>
<td>.086</td>
</tr>
<tr>
<td>Blood glucose on admission</td>
<td>1.10 (1.06-1.13)</td>
<td>.001</td>
</tr>
<tr>
<td>Anterior infarction</td>
<td>2.34 (1.45-3.79)</td>
<td>.001</td>
</tr>
<tr>
<td>Heart rate</td>
<td>1.04 (1.02-1.05)</td>
<td>.001</td>
</tr>
<tr>
<td>Number of vessels</td>
<td>1.88 (1.46-2.41)</td>
<td>.001</td>
</tr>
<tr>
<td>Killip class on admission</td>
<td>2.47 (2.06-2.95)</td>
<td>.001</td>
</tr>
<tr>
<td>Ischemia time</td>
<td>1.001 (1.001-1.003)</td>
<td>.079</td>
</tr>
<tr>
<td>Direct stenting</td>
<td>0.67 (0.42-1.06)</td>
<td>.088</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.92 (0.90-0.94)</td>
<td>.001</td>
</tr>
</tbody>
</table>

95%CI, 95% confidence interval; AMI, acute myocardial infarction; CTONr, chronic total occlusion in nonculprit artery; HR, hazard ratio; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Univariate analysis of the association of each potential confounder with mortality. The multivariate analysis includes all potential confounders (variables with statistical association P<.2 with exposure [chronic total occlusion in nonculprit artery; Table 1] and effect [mortality; univariate analysis in this same table], including left ventricular ejection fraction and Killip class on admission).

Relationship Between Chronic Total Occlusion in Nonculprit Artery in Proximal Segments and Mortality

The results of this analysis were very similar to those of the previous analysis. The multivariate analysis performed without including LVEF or Killip class on admission showed a significant
**Table 4**
Analysis of the Relationship Between Chronic Total Occlusion in Nonculprit Artery in Proximal Segments and Mortality

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<thead>
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<td>HR (95%CI)</td>
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</tr>
<tr>
<td>Diabetes mellitus</td>
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<td>History of stroke</td>
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<td>History of AMI</td>
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</tr>
</tbody>
</table>

95%CI, 95% confidence interval; AMI, acute myocardial infarction; CTOnr, chronic total occlusion in nonculprit artery in proximal segments; HR, hazard ratio; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Univariate analysis of association of each potential confounder with P<.2 with mortality. The multivariate analysis includes all potential confounders (variables with statistical association [P<.2] with exposure [chronic total occlusion in nonculprit artery in proximal segments; Table 2] and effect [mortality; univariate analysis in this same table], including left ventricular ejection fraction and Killip class on admission).

The association between CTOnr in proximal segments and mortality (HR = 2.53; 95%CI 1.29-4.96; P<.007). Again, when both variables were included, the association observed was no longer statistically significant (HR = 1.78; 95%CI 0.83-3.80; P=1.41). Table 4 lists the results of the univariate and multivariate analyses, including all potential confounders.

**DISCUSSION**

The main findings of our study were: a) CTOnr represented a special-risk subgroup, with more comorbidities and poorer clinical course; b) this worse prognosis was mainly due to noncardiac mortality in all patients with CTOnr, and c) the presence of CTOnr did not behave in our series as an independent predictor of mortality when LVEF was included in the analyses.

The prevalence of CTOnr in our series was similar to that of previously published series, which reported levels of 8% to 13%. The characteristics of patients with CTOnr were also similar to those of earlier series, with older ages and greater comorbidity burdens, severity of coronary disease, ventricular dysfunction, and medium-term mortality.

The prognostic implication of CTOnr in patients who undergo PA is controversial. The observation of a worse prognosis attributable to the CTOnr in this setting could further justify early and careful reperfusion of the culprit artery as well as more intensive therapeutic management in the acute phase, in order to manage potential complications earlier and while the patient is more clinically stable.

Although many articles that have addressed this question describe an independent prognostic value of the presence of CTOnr, recent data do not support this hypothesis. The populations analyzed are different (in some cases, from clinical trials) and there may be major methodological differences, as most authors do not include LVEF in the analyses. In addition, the severity of the coronary disease was coded differently.

Recently, Bataille et al. analyzed a population of 2020 consecutive patients who underwent PA, concluding that the worse prognosis of patients with CTOnr was mainly caused by the higher comorbidity burden and severity of coronary disease, rather than by the actual presence of CTOnr. The main difference between this study and earlier studies is the inclusion of LVEF and baseline glomerular filtration rate in the analysis of the association between CTOnr and mortality.

The inclusion of LVEF in this analysis is controversial. The presence of CTOnr in an artery contralateral to the culprit artery in patients with ST-segment elevation acute myocardial infarction could lead to worse collateralization in the acute phase and, consequently, larger infarction and worse residual LVEF. In fact, the presence of CTOnr has been correlated with worse ventricular function after infarction. Likewise, the presence of CTOnr could explain a worse Killip class on admission in this clinical setting. Consequently, it could be considered that both variables are, at least partly, intermediate in the relationship between CTOnr and mortality, and their inclusion in the analyses could contribute to an underestimation of the association between exposure and effect (type II statistical error).

On the other hand, noninclusion of LVEF because it is part of the CTOnr-mortality causal chain could result in an opposite bias. Patients with CTOnr clearly had more adverse characteristics (older age, more severe coronary disease, more frequent history of infarction) that could explain some degree of preexisting ventricular dysfunction. Therefore, excluding LVEF could theoretically magnify the association between chronic total occlusion and mortality. This reasoning, along with the fact that LVEF inclusion in the analyses is the main difference between the negative result obtained by Bataille et al. and the positive results obtained in previous studies, was what led the authors to perform analyses with and without these 2 variables, in an attempt to further analyze the relationship between CTOnr and mortality.

The results do not clearly indicate a prognostic implication of the CTOnr in this setting. The statistical significance of the association between CTOnr and mortality was observed only after...
exclusion of powerful mortality predictors such as LVEF or Killip class. Although both factors may be part of the causal chain between exposure and effect, excluding variables of such clinical relevance and such clear prognostic implications (largely unrelated to the presence of CTOs) could be hard to justify. 

An analysis of the causes of mortality (not available in previous series) also provides relevant information. Higher noncardiac mortality in patients with CTOnr as a whole would support the hypothesis of CTOnr as a marker of total and comorbidity risk, rather than as a predictor of cardiac mortality per se. A CTOnr in a proximal artery could have a somewhat different prognostic implication. The larger myocardial area at risk could explain the higher cardiac mortality in these patients. Earlier series are also inconsistent in these aspects, as some restrict their analysis to CTOnr in arteries of a certain size, with technically feasible revascularization, or affecting a significant myocardial area, while other series include all patients with CTOnr.

The possible benefit of CTOnr revascularization in this clinical setting is controversial. Some data might support this strategy. A recent nonrandomized study pointed out the benefits of successful revascularization of the CTOnr in 136 patients 7 to 10 days after PA for ST-segment elevation acute myocardial infarction. None-theless, the paucity of information means that randomized trial data are needed to answer this question adequately.

Limitations

Our study has several limitations. Firstly, the study consisted of a single-center observational registry with a relatively low number of patients with CTOnr. The low rate of events limits the power of the predictive model. In patients who died before day 3, the last LVEF before death was recorded, but the authors felt that any resulting bias would be irrelevant. Because of the low rate of revascularization of CTOnr in our patients (findings also described in the literature26), it was impossible to analyze the possible contribution of this variable to the clinical course. Nevertheless, earlier series also did not include this variable in their analyses. Lastly, because this is a relatively recent series, some patients had a somewhat shorter follow-up time than that reported in some of the published series.

CONCLUSIONS

In unselected patients with ST-segment elevation acute myocardial infarction who underwent PA, a CTOnr identified a group with a higher risk profile and more comorbidities. These patients had higher total-medium-term mortality, particularly due to noncardiac causes. When LVEF was included in the analyses, CTOnr did not behave as an independent predictor of mortality in this setting.

CONFLICTS OF INTEREST

None declared.

REFERENCES


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