

**UNIVERSIDADE FEDERAL DE UBERLÂNDIA**  
**PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE**  
**FACULDADE DE MEDICINA**

**Impacto da ruptura da placa aterosclerótica na mortalidade em  
longo prazo após infarto agudo do miocárdio**

**Adriadne Justi Bertolin**

Mestrado profissional

**2020**

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**Impacto da ruptura da placa aterosclerótica na mortalidade em longo prazo após infarto agudo do miocárdio**

Dissertação apresentada ao Programa de Pós-Graduação em Ciências da Saúde da Faculdade de Medicina da Universidade Federal de Uberlândia, como requisito parcial para obtenção do título de Mestre em Ciências da Saúde.

Área de concentração: Ciências da Saúde.

Orientador: Elmiro Santos Resende

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**Uberlândia**

**2020**

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B546 2021	<p>Bertolin, Adriádne Justi, 1987- Impacto da ruptura da placa aterosclerótica na mortalidade em longo prazo após infarto agudo do miocárdio [recurso eletrônico] : Impacto da ruptura da placa aterosclerótica na mortalidade em longo prazo após infarto agudo do miocárdio / Adriádne Justi Bertolin. - 2021.</p> <p>Orientador: Elmiro Santos Resende. Coorientador: Luciano Moreira Baracioli. Dissertação (Mestrado) - Universidade Federal de Uberlândia, Pós-graduação em Ciências da Saúde. Modo de acesso: Internet. Disponível em: <a href="http://doi.org/10.14393/ufu.di.2021.33">http://doi.org/10.14393/ufu.di.2021.33</a> Inclui bibliografia.</p> <p>1. Ciências médicas. I. Resende, Elmiro Santos, 1953-, (Orient.). II. Baracioli, Luciano Moreira, 1970-, (Coorient.). III. Universidade Federal de Uberlândia. Pós-graduação em Ciências da Saúde. IV. Título.</p> <p style="text-align: right;">CDU: 61</p>
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Bibliotecários responsáveis pela estrutura de acordo com o AACR2:

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**Adriadne Justi Bertolin**

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**Presidente da banca (orientador): Prof. Dr. Elmiro Santos Resende**

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**ATA DE DEFESA - PÓS-GRADUAÇÃO**

Programa de Pós-Graduação em:	Ciências da Saúde				
Defesa de:	Dissertação de Mestrado Profissional do PPCSA, 008/2020				
Data:	27 de novembro de 2020	Hora de início:	14:00	Hora de encerramento:	17:00
Matrícula do Discente:	11812PSC001				
Nome do Discente:	Adriádne Justi Bertolin				
Título do Trabalho:	Impacto da ruptura da placa aterosclerótica na mortalidade em longo prazo após infarto agudo do miocárdio				
Área de concentração:	Ciências da Saúde				
Linha de pesquisa:	Promoção da Saúde				
Projeto de Pesquisa de vinculação:	Epidemiologia clínica em doenças degenerativas do aparelho cardiovascular				

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Documento assinado eletronicamente por **Remo Holanda de Mendonça Furtado, Usuário Externo**, em 22/12/2020, às 15:03, conforme horário oficial de Brasília, com fundamento no art. 6º, § 1º, do [Decreto nº 8.539, de 8 de outubro de 2015](#).



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## DEDICATÓRIA

Aos meus pais, Luiz Carlos e Maria de Lourdes, por sempre acreditarem em mim e por terem abdicado de suas vidas em prol das realizações e da felicidade de suas filhas.

À minha irmã Ariadne, por sua preocupação, carinho e incentivo.

Ao meu esposo Willterson, por todo amor e incentivo.

Aos demais familiares e amigos pela compreensão.

Nada disso teria sentido se vocês não existissem na minha vida.

## AGRADECIMENTOS

A Deus, pela oportunidade de crescimento e por me permitir realizar tantos sonhos nesta existência.

Ao Prof. Dr. Elmiro Santos Resende, Prof. Dr. Luciano Moreira Baracioli e Prof. Dr. José Carlos Nicolau, pela orientação, competência, profissionalismo e dedicação.

Aos membros da banca examinadora, Prof. Dr. João Lucas O'Connell e Prof. Dr. Remo H. M. Furtado, que gentilmente aceitaram participar e colaborar com esta dissertação.

Às amigas Talia Dalçóquio e Rocio Salsoso, pelo comprometimento, preocupação e apoio constantes.

À Profa. Dra, Flávia Bittar, pela competência e respeito.

À Francis e Claudia, por todo auxílio e pela gentileza diária.

À Prof. Dra. Yara Cristina de Paiva Maia, pelo empenho e incentivo à pesquisa.

Aos funcionários da secretaria do Programa de Pós-graduação em Ciências da Saúde pela receptividade e disponibilidade.

A todos os demais amigos e amigas do Instituto do Coração (InCor), e da Faculdade de Medicina da Universidade Federal de Uberlândia, obrigado pelo convívio, amizade e apoio demonstrado.

Agradeço, especialmente, aos meus pais, por todo amor, companheirismo, amizade, dedicação e compreensão. Sinto-me orgulhosa e privilegiada por ter pais tão especiais. E à minha querida irmã, sempre pronta a me apoiar em tudo nesta vida.

Ao meu esposo, por todo amor, carinho, compreensão e apoio em tantos momentos difíceis desta caminhada.

Por fim, a todos aqueles que contribuíram, direta ou indiretamente, para a realização desta dissertação, o meu sincero agradecimento.



## EPÍGRAFE

*“A mente que se abre a uma nova ideia  
jamais volta ao seu tamanho original”. Albert  
Einstein*

## RESUMO

**Introdução:** A presença de ruptura da placa aterosclerótica (PR +) é o substrato mais frequente das síndromes coronárias agudas (SCA). No curto prazo pós-SCA, a PR + está associada a piores desfechos, incluindo mortalidade. No entanto, a influência da PR + no desfecho em longo prazo após o infarto agudo do miocárdio (IAM) é mal compreendida.

**Objetivos:** Testar a hipótese de que, em pacientes com IAM, a PR + detectada na cineangiocoronariografia durante a internação hospitalar devido ao evento índice, se correlaciona com o aumento da mortalidade por todas as causas no seguimento a longo prazo após a alta hospitalar. **Métodos:** Pacientes com IAM (n = 500) incluídos prospectiva e consecutivamente em um banco de dados, foram acompanhados por até 17 anos (média  $10,3 \pm 5,3$  anos). Variáveis angiográficas foram coletadas no início do estudo, antes de qualquer intervenção coronária, e todos os angiogramas coronários foram revisados por um único cardiologista experiente. A população foi dividida, conforme o aspecto angiográfico, em PR + (113, 52%) ou PR- (126, 48%). Pacientes com fluxo TIMI 0 (n = 195) foram excluídos das análises. Curvas de Kaplan-Meier foram construídas para cada um dos grupos e comparadas pelo teste de log-rank. O modelo multivariável de riscos proporcionais de Cox foi usado para ajustar os fatores de confusão. **Resultados:** As taxas de mortalidade estimadas pelo método de Kaplan Meier foram 49,6% no grupo PR + e 28,0% no grupo PR-  $p = 0,0085$  (HR 1,84; 95% IC 1,16 a 2,93;  $p = 0,010$ ). Na análise multivariada, a RP + correlacionou-se independentemente com maior risco de mortalidade em longo prazo (HR ajustado = 1,83; 95% IC 1,08 a 3,11;  $p = 0,024$ ). **Conclusões:** Em pacientes com IAM, a presença de aspecto angiográfico sugestivo de PR + na artéria coronária culpada foi independentemente associada à redução da sobrevida em longo prazo.

**Palavras-chave:** Ruptura de placa, infarto agudo do miocárdio, cineangiocoronariografia, mortalidade.

## ABSTRACT

**Background:** The presence of atherosclerotic plaque rupture (PR+) is the most frequent substrate of acute coronary syndromes (ACS). In the short-term post-ACS PR+ is associated with a trend toward worse outcomes, including mortality, when compared with ACS without plaque rupture (PR-). However, the influence of PR+ in the long-term outcome after acute myocardial infarction (AMI) is poorly understood. **Aims:** To test the hypothesis that, in patients with AMI, the presence of PR+ detected at coronary angiography during the index event hospitalization, was correlated with increased all-cause mortality in the long-term follow-up after hospital discharge. **Methods:** AMI patients (n=500) included prospectively and consecutively in a databank, were followed for up to 17 years (mean 10.3±5.3 years). Angiographic variables were collected at baseline, prior to any coronary intervention, and all coronary angiograms were reviewed by a single experienced intervention cardiologist. The population were divided according their angiographic aspect in PR+ (113, 52%) or PR- (126, 48%). Patients with TIMI flow 0 (n=195) were excluded from the analyses. Kaplan-Meier curves were constructed for each of the groups and compared by the log-rank test. Multivariable Cox proportional hazards model was used in order to adjust for confounders. **Results:** The mortality rate at 15 years, estimated by Kaplan Meier method, was higher in the PR+ cohort (49.6% vs. 28.0%, respectively;  $p = 0.0085$  by long-rank), as shown in Figure 2 (HR 1.84; 95% CI 1.16-2.93;  $p = 0.010$  by the Cox model). In the multivariate analysis, PR+ correlated independently with a higher risk of long-term mortality (adjusted HR=1.83; 95% CI 1.08 to 3.11;  $p=0.024$ ). **Conclusions:** In AMI patients, the presence of angiographic aspect suggestive of PR+ at the culprit coronary artery was independently associated with decreased long-term survival.

**Keywords:** Plaque rupture, acute myocardial infarction, coronary angiography, mortality.

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## LISTA DE ABREVIATURAS E SÍMBOLOS

<b>CCA</b>	artéria coronária culpada
<b>DCVs</b>	doenças cardiovasculares
<b>DIC</b>	doença isquêmica do coração
<b>IAM</b>	infarto agudo do miocárdio
<b>OCT</b>	tomografia de coerência óptica
<b>PR+</b>	ruptura da placa aterosclerótica
<b>SCA</b>	síndrome coronariana aguda
<b>TIMI</b>	Thrombolysis in myocardial infarction

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## ***1 Introdução***

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## 1 Introdução

As doenças cardiovasculares (DCVs) constituem a principal causa de mortalidade global (1) e a maioria dessas mortes são atribuídas às doenças isquêmicas do coração ou cerebrovasculares (2), sendo que, o infarto agudo do miocárdio (IAM) é considerado a principal causa de morte entre as doenças isquêmicas do coração (3).

A trombose coronariana secundária à ruptura da placa aterosclerótica (4) constitui-se no mecanismo fisiopatológico mais comum no desenvolvimento das síndromes coronárias agudas (SCA) (5), sendo a erosão, o segundo em frequência, sendo encontrado em, aproximadamente, 20% dos casos. (6). Ambos os fenômenos desencadeiam um processo trombótico de evolução imprevisível no qual a formação e a degradação dos trombos tendem a ocorrer simultaneamente, causando alterações no fluxo sanguíneo coronariano tornando-o intermitente (7) ou interrompido (6).

Já foi previamente demonstrado que a presença de ruptura da placa coronariana na angiografia se correlaciona positivamente com a formação de trombos e com o grau de obstrução residual da artéria coronariana culpada (CCA) (8). Estudos que avaliaram as características da placa por tomografia de coerência óptica (OCT), evidenciaram que pacientes com SCA e capa fibrosa intacta apresentaram menos eventos cardíacos adversos maiores, em comparação com aqueles com PR + (14% vs. 39%,  $p = 0,001$ ) (9). A ausência de PR + também foi indicativa de maior sobrevida livre de eventos cardiovasculares (10).

Apesar da importância prognóstica das características da placa culpada no IAM, muito pouco se sabe sobre o papel prognóstico da PR + diagnosticada por cinecoronariografia sendo este o objetivo principal do presente estudo.

## 1.1. Revisão da Literatura

As doenças cardiovasculares (DCVs) constituem a principal causa de mortalidade global e são o principal contribuinte para a redução da qualidade de vida (1). De acordo com os padrões globais e regionais de mortalidade cardiovascular identificados entre 1990 e 2013, as DCVs foram responsáveis por 32% de todas as mortes em todo o mundo e a maioria destas foram atribuídas à doença isquêmica do coração (DIC) ou à doença cerebrovascular (2). Além disso, o infarto agudo do miocárdio (IAM) é a principal causa de morte entre as DICs (3). Estudos epidemiológicos, como o ARIC, estimou que, em 2019, aproximadamente 720.000 americanos teriam um novo evento coronariano, definido como sendo o primeiro IAM ou morte por doença cardíaca coronária (DAC), e, aproximadamente, 335.000 teriam um evento recorrente (4). No Brasil, ocorreram 96.215 óbitos por SCA em 2017(5).

A causa mais comum de IAM é o fluxo sanguíneo inadequado para o miocárdio, relacionado à ruptura ou à erosão aguda da placa aterosclerótica e à formação de trombo (6).

A ruptura da placa é a causa mais frequente de trombose coronariana (7) e é a lesão mais comum, subjacente às síndromes coronarianas agudas (SCA) (8). Entretanto, a erosão da placa pode desencadear a trombose coronariana em até 20% dos eventos de SCA (9). Ambos os fenômenos desencadeiam um processo trombótico de evolução imprevisível. Fenômenos de trombose e trombólise tendem a ocorrer simultaneamente, causando fluxo sanguíneo coronariano intermitente (10). Portanto, a lesão culpada na SCA é frequentemente dinâmica, causando obstrução e turbulência de fluxo sanguíneo (9).

Aspectos angiográficos indicativos da ruptura da placa aterosclerótica foram correlacionados, de forma independente, com a maior presença de trombos e com o maior grau de obstrução residual da artéria coronariana culpada. A PR + também é mais comum em pacientes de etnia branca (11). Já foi demonstrado previamente que pacientes com capa fibrosa íntegra (14,0%) têm menos eventos cardíacos adversos maiores quando comparados com aqueles com ruptura de placa (39,0%). Estes eventos podem ser mais frequentes e registrados em até 3 anos de acompanhamento (12). Além disso, os pacientes com capa fibrosa íntegra na lesão

culpada, evidenciada pela tomografia de coerência óptica (OCT), apresentaram melhor sobrevida livre de eventos, quando comparados aos pacientes com ruptura de placa ou com trombose maciça, em seguimento médio de 576 dias (13).

Em ambos os estudos a lesão culpada foi classificada como apresentando ruptura de placa ou com capa fibrosa íntegra (incluindo erosão de placa) pelos critérios da OCT. A OCT de coronárias é uma modalidade de exame de imagem que permite avaliar as características da placa e medir a espessura da capa fibrosa do ateroma (14). Recentemente, estudos observaram o potencial desse exame para diferenciar entre erosão da placa, presença de nódulos calcificados e ruptura, sugerindo que a OCT pode representar a melhor modalidade de imagem para examinar a patogênese da síndrome coronariana aguda *in vivo* (15,16).

Outro método de imagem que permite a análise da característica da placa é a angiografia coronariana. Conforme demonstrado previamente, a análise da morfologia da placa aterosclerótica pelas suas características angiográficas em pacientes com SCA, apresenta uma boa correlação entre placa classificada como excêntrica do tipo II de Ambrose (estenose assimétrica, geralmente com obstrução de forma convexa, lisa com o colo estreito ou com as bordas irregulares) e a presença de ruptura na mesma lesão (17–20).

Apesar da importância prognóstica das características angiográficas da lesão culpada no IAM, poucos são os estudos disponíveis que avaliaram as associações entre as características angiográficas da lesão culpada no IAM e a mortalidade em longo prazo.

## ***2 Objetivo***

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## **2 Objetivo**

Estimar o impacto da presença de aspectos sugestivos de RP + na artéria culpada no IAM, encontrados na cineangiocoronariografia na mortalidade em longo prazo (até 17 anos).

**Artigo 1.** “Impact of atherosclerotic plaque rupture on long-term mortality after acute myocardial infarction”

Impact of atherosclerotic plaque rupture on long-term mortality after acute myocardial infarction

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## Abstract

**BACKGROUND:** The presence of atherosclerotic plaque rupture (PR+) is the most frequent substrate of acute coronary syndromes (ACS). In the short-term post-ACS PR+ is associated with a trend toward worse outcomes, including mortality, when compared with ACS without plaque rupture (PR-). However, the influence of PR+ in the long-term outcome after acute myocardial infarction (AMI) is poorly understood.

**AIMS:** To test the hypothesis that, in patients with AMI, the presence of PR+ detected at coronary angiography during the index event hospitalization, was associated with increased all-cause mortality in the long-term follow-up after hospital discharge.

**METHODS:** AMI patients (n=500) included prospectively and consecutively in a databank, were followed for up to 17 years (mean 10.3±5.3 years). Angiographic variables were collected at baseline, prior to any coronary intervention, and all coronary angiograms were reviewed by a single experienced intervention cardiologist. The population were divided according their angiographic aspect in PR+ (113, 52%) or PR- (126, 48%). Patients with TIMI flow 0 (n=195) were excluded from the analyses. Kaplan-Meier curves were constructed for each of the groups and compared by the log-rank test. Multivariable Cox proportional hazards model was used in order to adjust for confounders.

**RESULTS:** The mortality rate at 15 years, estimated by Kaplan Meier method, was higher in the PR+ cohort (49.6% vs. 28.0%, respectively; p = 0.0085 by long-rank), as shown in Figure 2 (HR 1.84; 95% CI 1.16-2.93; p = 0.010 by the Cox model). In the multivariate analysis, PR+ correlated independently with a higher risk of long-term mortality (adjusted HR=1.83; 95% CI 1.08 to 3.11; p=0.024).

**CONCLUSIONS** In AMI patients, the presence of angiographic aspect suggestive of PR+ at the culprit coronary artery was independently associated with decreased long-term survival.

## Introduction

Cardiovascular diseases (CVDs) constitute the leading cause of global mortality (1) and the majority of these deaths are attributable to ischemic heart disease (IHD) or cerebrovascular disease (2). Most importantly, acute myocardial infarction (AMI) is the main cause of death among IHD (3).

Atherosclerotic plaque rupture leading to coronary thrombosis (7) is the most common pathophysiologic mechanism in the development of acute coronary syndromes (ACS) (8), with erosion being the second more common mechanism, with approximately 20% of the cases. (9). Both of these phenomena trigger a thrombotic process that is highly unpredictable. Thrombosis and thrombolysis tend to occur simultaneously causing intermittent coronary blood flow (10) and turbulent flow obstruction (9).

The diagnosis of coronary plaque rupture by angiography were correlated with the presence of thrombi and with the degree of residual obstruction of the culprit coronary artery (CCA)(11). Using optical coherence tomography (OCT), previous reports found that patients with ACS and intact fibrous cap in comparison with patients with PR+ had fewer major adverse cardiac events (14% vs. 39%,  $P=0.001$ ) (9), and higher event-free survival when compared with PR+ or massive thrombus precluding plaque visualization(10).

Despite the prognostic importance of the culprit plaque characteristics in AMI, very little is known about the prognostic role of PR+ diagnosed by coronary angiography, main objective of the present study.

## **Patients and Methods**

### **Study population**

We analysed 500 consecutive patients admitted to the Coronary Care Unit of the Heart Institute (InCor/HCFMUSP) of the University of São Paulo Medical School, from February 1998 to February 2001, with diagnosis of AMI, within 1 week of evolution. The survival status of the population was obtained through phone contacts for up to 17 years (mean  $10.3\pm 5.3$  years). Phone contacts with patients and/or relatives were developed annually by medical students trained specifically to apply a questionnaire on survival status. A patient was considered lost to follow-up after at least three consecutive failed attempts to obtain any information, including vital status. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Because the databank and telephone calls were used primarily for administrative purposes, informed consent form was waived according to local laws.

### **Inclusion criteria**

The study inclusion criteria have been previously reported (11). Briefly, all patients hospitalized with AMI diagnose and referred for coronary angiography in our institution, were considered for inclusion.

### **Exclusion criteria**

The exclusion criteria were the presence of an occluded infarct-related artery and impossibility to identify the CCA.

## **Acute myocardial infarction definition**

AMI was diagnosed when at least two of the following criteria were present: (1) ischemic thoracic pain lasting >20 min (2) ST-segment elevation  $\geq 1$ mm in at least two contiguous leads and (3) peak CK–MB activity elevation of at least twice its normal value (>20 UI/l).

## **Angiography**

Angiographic aspects of plaque rupture in patients with AMI and its correlation with clinical variables were published by our group previously (11). Coronary angiography was indicated for all patients, preferentially, between 48 and 96 h. and performed in 91% of the population. The analysis of the exam was done visually by a single observer with a large experience, who was blinded to any other information about the patient, except the AMI location (when available). Plaque rupture at the angiography was defined as the presence of irregular borders at the culprit lesion. Thus, plaques with symmetrical or non-symmetrical smooth-edged stenosis (“watch-glass” type), described as type I lesion by Levin and Fallon (21) were considered to have absence of rupture. Identification of the CCA considered the infarct location (when available), in association with angiographic details of coronary anatomy, as the presence of “lack of stuffing” (thrombi), contrast retention, and severity of artery stenoses. Besides the presence of PR+, other angiographic characteristics were analyzed, such as: degree of antegrade flow according to the Thrombolysis in Myocardial Infarction (TIMI) angiographic criteria (22); degree of coronary collateral flow according to the proposition of Schwartz et al (23); number of coronaries obstructed >50%. Considering the presence of atherosclerosis in the left anterior descending, circumflex or right coronary artery systems, patients were categorized as with one-vessel or multi-vessel disease.

## Treatment regimen

Patients were treated according to Brazilian and North-American Guidelines in force at the time of the index event (February 1998–2001). Final decision about invasive treatments (percutaneous coronary intervention or surgical coronary revascularization) was done by the patient's attending physician.

## Statistical analysis

Categorical variables were expressed as absolute numbers. The baseline characteristics of PR+ and PR- groups were compared with the chi-square Pearson test or the Fisher exact test, when indicated.

In the long-run, the Kaplan-Meier method was used to estimate rates of all-cause death and is depicted graphically. Patients were censored at the time of last contact. Log-rank test was used to assess the differences between the incidence rates among the two groups. Adjusted model analyzing possible independent predictors to all-cause mortality was developed using the stepwise Cox regression analysis test, with a  $p$ -value = 0.05 threshold to enter the model and  $p$  = 0.10 threshold to exit the model. All-cause mortality was included as the independent variable in the model, and the following variables were included as independent ones, besides PR+: age; sex; history of hypertension, diabetes, previous MI, heart failure (HF), hypercholesterolemia; previous smoker; ST-segment elevation MI (STEMI); multi-vessel disease; degree of residual stenosis at culprit artery; left ventricular ejection fraction <40%. Schoenfeld residuals were assessed to confirm the proportional hazards assumption. A  $P$ -value <0.05 was considered statistically significant (two-tailed). Only patients with valid information were included in the adjusted models and no imputation was done for missing data. No adjustments for multiplicity were done. Data were analysed using IBM SPSS Statistics 26.0 (Microsoft, Chicago, IL, USA) and Stata™ version 15.1 (Statacorp, College Station, TX, USA).

## Results

### Study population

From the initial population of 500 patients, we excluded those without available coronary angiography, either because the patient refused to, died before the test could be done, or had contra-indication for the exam (45 patients, 9%); patients that were referred from another hospital (13 patients, 2.6%); patients for whom identification of the CCA could not be properly ascertained at the coronary angiogram (11 patients, 2.2%); and patients with pre-procedural TIMI flow grade 0, for the impossibility to access the culprit plaque characteristics (195 patients, 39%). At the end, 236 patients (47.2 % of the total population) fulfilled the inclusion/exclusion criteria and were included in the study. In the long-term follow-up (up to 17 years), six patients were lost follow-up (2.5 %) (Figure 1).

The clinical characteristics of the population are depicted in Table 1. As can be seen, 123 patients had angiographic aspect of PR+ and 113 had angiographic aspect of PR-. Patients with PR+ were older and had higher prevalence of previous MI. Regarding angiographic characteristics, patients with PR+ were more frequently submitted to primary and non-primary percutaneous coronary intervention (PCI) during hospitalization. In addition, they presented more often coronary artery disease in 3 vessels, and a higher number of vessels with obstruction >70%, worse CCA's TIMI flow grades and higher levels of collateral circulation (Table 2).

### Clinical outcomes

During follow-up, there were 50 deaths and 28 deaths, respectively, in the PR+ and PR- group, with total estimated all-cause mortality at the end of follow-up of 41.6% vs. 25.4% respectively. The mortality rate at 15 years, estimated by Kaplan

Meier method, was higher in the PR+ cohort ( 49.6% vs. 28.0%, respectively;  $p = 0.0085$  by long-rank), as shown in Figure 2 (HR 1.84; 95% CI 1.16-2.93;  $p = 0.010$  by the Cox model).

Table 3 shows the multivariate analysis results. After adjustment for confounders, the presence of angiographic aspects suggestive of plaque rupture was associated with higher risk of death, with an adjusted HR of 1.83 (95% CI 1.08 to 3.11;  $p = 0.024$ ). Other variables that correlated significantly and independently with all-cause mortality were Ventricular dysfunction defined as Left ventricular ejection fraction  $< 40\%$  with an adjusted HR of 2.24 (95% CI 1.07 to 4.66;  $p = 0.031$ ); Age (risk increase for every 10 years) with an adjusted HR of 2.64 (95% CI 2.07 to 3.37;  $p < 0.001$ ); History of heart failure with an adjusted HR of 5.41 (95% CI 1.69 to 17.28;  $p = 0.004$ ) and History of diabetes with an adjusted HR of 2.12 (95% CI 1.27 to 3.51;  $p = 0.004$ ).

## **Discussion**

To the best of our knowledge, this is the first study analysing the impact of plaque rupture detected by coronary angiography, in the long-term mortality of patients with AMI. In a mean follow-up time of 10 years, we demonstrated that plaque rupture correlated significantly and independently with all-cause mortality.

### **Comparison with prior studies:**

Previous studies analysing plaque characteristic by OCT showed a good correlation between plaque rupture and MACE up to 3 years of follow-up, but not with all-cause mortality isolated (9-10). The present study analysed the presence or not of plaque rupture by coronary angiography and showed higher mortality rates in the PR+ in a follow-up of up to 17 years.

**Other independent predictors of long-term mortality:**

Low left ventricle ejection fraction and heart failure are well known risk factors for worse outcomes, including all-cause mortality in the short- and long-term follow-up post AMI (14-15). The present study confirm the previous findings, with hazard-ratios of 2.24 for ejection fraction <40% and 5.41 for history of heart failure. For every 10 years of age at the time of the index event we found a 3-fold increase in the long-term all-cause mortality, with is in accordance with previous studies (24). We found that diabetes increased the risk of death almost 2-fold, not much different from the numbers found by Nauta at al. in a 20-years follow-up study (25).

**Study strengths and limitations:**

First, in the present analysis plaque characteristics was assessed by coronary angiography, which is subject to observer bias and interobserver variability. However, we understand that the demonstration of a significant correlation between plaque rupture diagnosed by this “accessible” method with long-term mortality is externally relevant. In an era of highly precise coronary intravascular imaging, such as IVUS and OCT, our results reinforce the prognostic value of coronary angiography findings. Despite much lower accuracy to evaluate plaque characteristics comparing to IVUS and OCT, angiography is a widely available method and with a much lower cost than the intravascular imaging.

Second, as with all non-randomized studies we cannot ascertain an actual causal-effect relationship between plaque rupture and increased mortality, since unmeasured confounders could have driven our results. Nevertheless, we applied statistical methods to adjust for potential confounding factors, all of them showing consistent results and therefore strengthening our conclusions.

Third, our patients were included more than two decades ago, when pharmacological treatment for secondary prevention did not commonly include high-



intensity lipid-lowering therapy and long-term DAPT. However, this allowed us to report the role of plaque rupture in the longest follow-up ever (> 10 years). Moreover, the Kaplan-Meier curves suggest that the impact of PR+ is continuous along the follow-up, when many patients certainly were taking statin and other proven therapies.

## Conclusion

In AMI patients, the presence of culprit plaque rupture analysed by coronary angiography was independently associated with decreased long-term survival compared to the absence of plaque rupture. Those results reinforce the prognostic role of baseline coronary angiography and the atherosclerotic plaque characteristics in the long-run after AMI.

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**Table 1. Clinical characteristics of the population**

<b>Variables</b>	<b>PR + (n= 123)</b>	<b>PR - (n= 113)</b>	<b>p value</b>
Age (Years)	62.2 ± 12.32	57.9 ± 13.42	0.024
Male sex (%)	53.9	46.1	0.328
White ethnic (%)	54.8	45.2	0.005
Black ethnic (%)	12.5	87.5	0.030
Previous MI (%)	78.1	21.9	0.002
History of Hypertension (%)	56.7	43.3	0.084
Diabetes (%)	61.5	38.5	0.124
Prior PCI (%)	72.2	27.8	0.076
Prior CABG (%)	71.4	28.6	0.136
Chest pain at admission (%)	51.9	48.1	0.866
Length of hospital stay (days)	15 ± 14.7	13.2 ± 8.5	0.866

Data expressed as mean ± standard deviation; % = percentage of patients; \* Confidence Interval for Odds Ratio; \*\* Confidence interval for differences in means. PR+ = presence of plaque rupture; PR- = absence of plaque rupture; MI = Myocardial Infarction; PCI = Percutaneous Coronary Intervention; CABG = Coronary Artery Bypass Graft.

**Table 2. Angiographic characteristics of the population**

<b>Variables</b>	<b>PR + (n= 123)</b>	<b>PR - (n= 113)</b>	<b>p value</b>
One vessel disease (%)	41.77	58.22	0.01
Two vessels disease (%)	60	40	0.148
Three vessel disease (%)	63.63	36.37	0.05
Primary PCI	77.78	22.22	0.023
Non primary PCI	62.89	37.11	0.006
Time from pain beginning to coronary angiography (hours)	90.46 ± 104	84.53±54.25	0.584
Residual stenosis at the culprit artery (%)	90.50 ± 10.64	71.87 ± 29.52	<0.001
Anterograde flow by TIMI criteria	2.61 ± 0.66	2.83 ± 0.44	0.002
Collateral circulation	0.20 ± 0.61	0.03 ± 0.23	0.009
Number of vessels > 70% (mean)	2.04 + 1.01	1.56 + 1.29	0.001
LVEF (%)	61.66 ± 15.27	65.68 ± 14.53	0.035

Data expressed as mean ± standard deviation; % = percentage of patients; \* Confidence Interval for Odds Ratio; \*\* Confidence interval for differences in means. PCI= percutaneous coronary intervention; LVEF= left ventricular ejection fraction

**Table 3. Multivariable Cox regression: variables independently correlated with long-term all-cause mortality**

	<b>Adj Hazard Ratio</b>	<b>95% CI</b>	<b>p value</b>
Plaque rupture at the CCA	1.83	1.08-3.11	0.024
Ventricular dysfunction*	2.24	1.07-4.66	0.031
Age (risk increase for every 10 years)	2.64	2.07-3.37	<0.001
History of previous myocardial infarction	0.47	0.23-0.96	<0.001
History of heart failure	5.41	1.69-17.28	0.004
History of diabetes	2.12	1.27-3.51	0.004

\*Ventricular dysfunction: Left ventricular ejection fraction < 40%

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