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Prompt myocardial reperfusion is the therapeutic goal for patients presenting with ST-segment elevation acute myocardial infarction (AMI). However, there remains a paucity of clinical data from single centers solely dedicated to a catheter-based reperfusion strategy. Therefore, we sought to identify significant predictors of in-hospital mortality, to determine the changing profile of patient demographics and to identify the mortality trend over time. Consecutive patients who underwent percutaneous coronary intervention (PCI) for an AMI between January of 1982 and December of 1999 were included in this analysis. AMI was defined as an evolving myocardial infarction within the preceding 24 hours. The primary endpoint for this analysis was in-hospital mortality. There were 2,745 patients identified in this study. The significant multivariate predictors of in-hospital mortality included creatinine > 1.5 mg/dL (Point Estimate 5.7, 95% Confidence Limits 4.0-8.1), Ejection Fraction < 40% (Point Estimate 6.6, 95% Confidence Limits 4.3-10.0), multivessel disease (Point Estimate 2.8, 95% Confidence Limits 1.9-4.2) female gender (Point Estimate 2.3, 95% Confidence Limits 1.6-3.1) and age > 70 years (Point Estimate 1.6, 95%, Confidence Limits 1.1-2.2). The incidence of patients with these high-risk characteristics increased in recent years, thus, the unadjusted slope of the mortality trend over 20 years was not significant. However, following adjustment for the temporal shift in high-risk variables, there was a significant reduction in the adjusted in-hospital mortality rate (Point Estimate 0.89, 95% Confidence Limits 0.8-0.98), p = 0.017. Despite the changing risk-profile, the short-term mortality continues to improve for patients undergoing AMI PCI.