Chronic Kidney Disease, Diabetes, and Risk of Mortality After Acute Myocardial Infarction: Insight From the FAST-MI Program

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Diabetes is associated with a substantially increased risk of all-cause death, mainly driven by cardiovascular (CV) mortality. Furthermore, diabetes is associated with poorer outcomes after acute myocardial infarction (AMI) (1). Impaired glomerular filtration rate (GFR) is also associated with an increased risk of CV mortality (2). However, whether diabetes still confers a higher risk of mortality in patients with impaired GFR remains unknown.

The aim of this study was to assess the long-term prognostic significance of both diabetes and renal impairment in two prospective nationwide cohorts of AMI patients: FAST-MI (French Registry of Acute ST-Elevation or non-ST-elevation Myocardial Infarction) 2005 (n = 3,670 [reg. no. NCT00673036, ClinicalTrials.gov]) and FAST-MI 2010 (n = 4,169 [NCT01237418]) (3). Both registries consecutively included patients with AMI admitted to cardiac intensive care units within 48 h of symptom onset during a specified 1-month period. AMI was defined by increased levels of cardiac biomarkers together with either compatible symptoms or electrocardiogram changes. Vital status at 5 years was available in >95%. We assessed all-cause mortality at 5 years according to estimated GFR (eGFR) (calculated with Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula and based on KDIGO [Kidney Disease: Improving Global Outcomes] GFR categories with eGFR <30 and <15 mL/min/1.73 m^2 pooled) and diabetes status at inclusion. Multivariable proportional hazards models (assumptions checked) were used with covariates chosen based on their potential prognostic relevance: year of inclusion; sex; age; BMI categories; hypertension; current smoking; prior AMI; peripheral artery disease; history of heart failure, stroke, cancer, and chronic obstructive pulmonary disease; type of myocardial infarction (MI) (STEMI or NSTEMI); GRACE risk score; percutaneous coronary intervention or coronary artery bypass during hospitalization; and left ventricular ejection fraction.

Among the 7,839 participants, 7,656 had creatinine values, assessed before percutaneous coronary intervention, at entry available. Mean ± SD age was 66.1 ± 14.2 years, 2,230 (29.1%) were female, and 2,090 (27.3%) had diabetes, with a duration of diabetes >10 years in 30.0% (missing data 35.6%). Mean ± SD HbA_{1c} at entry was 7.5 ± 1.5%, and eGFR was <30 mL/min/1.73 m^2 in 398 (5.2%), 30–45 in 688 (9.0%), 45–60 in 1,151 (15.0%), 60–90 in 3,328 (43.5%), and >90 in 2,091 (27.3%). Five-year mortality was 38% (n = 796) in patients with diabetes versus 19% (n = 1,058) in patients without diabetes (adjusted hazard ratio [HR] 1.47, 95% CI 1.33–1.62, P < 0.001). According to eGFR, among all participants, 5-year mortality rates were 8.1% (n = 170) for eGFR >90 mL/min/1.73 m^2, 17.7% (588) for eGFR 60–90, 36.4% (n = 419) for eGFR 45–60, 57.6% (n = 396) for eGFR 30–45, and 70.6% (n = 281) for eGFR <30. Multivariable analysis suggested a gradual increase in mortality with decreasing renal function: adjusted HR versus eGFR >90 mL/min/1.73 m^2 as reference 0.91 (95% CI 0.75–1.11, P = 0.36) for eGFR 60–90 mL/min/1.73 m^2; 1.19 (0.96–1.46, P = 0.11) for eGFR 45–60; 1.48 (1.19–1.85, P = 0.001) for eGFR 30–45, and 1.86 (1.48–2.35, P < 0.001) for eGFR <30.

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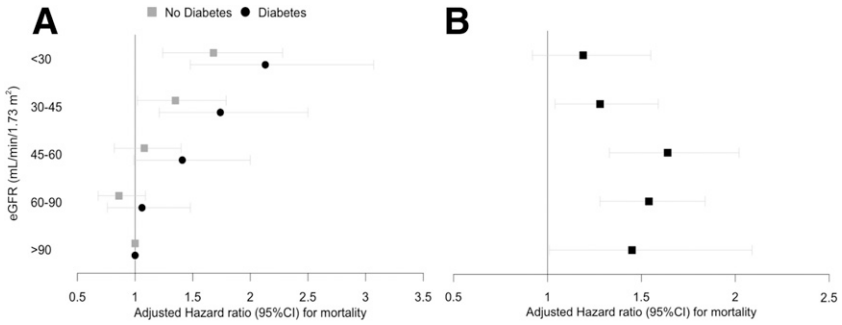

Figure 1—HR for 5-year mortality according to eGFR and diabetes. *A*: HR according to eGFR in participants without and participants with diabetes (reference eGFR >90 mL/min/1.73 m^2, with separate reference groups in the diabetes and no diabetes strata). *B*: HR for presence of diabetes compared with no diabetes within each renal function category.

Stratified analysis showed that increasing renal impairment was associated with an increased risk of death for participants with diabetes under a threshold of 60 mL/min/1.73 m^2 but only below a threshold of 45 mL/min/1.73 m^2 for participants without diabetes (Fig. 1*A*).

Compared with no diabetes, diabetes was associated with an increased risk of 5-year death throughout eGFR categories, except for eGFR <30 mL/min/1.73 m^2: HR 1.45 (95% CI 1.01–2.09) for eGFR >90, HR 1.54 (1.28–1.84, $P < 0.001$) for eGFR 60–90, HR 1.64 (1.33–2.02, $P < 0.001$) for eGFR 45–60, HR 1.28 (1.04–1.59, $P = 0.02$) for eGFR 30–45, and HR 1.19 (0.92–1.55, $P = 0.19$) for eGFR <30 (Fig. 1*B*).

The trend of a lower prognostic impact of diabetes in patients with the most severe chronic kidney disease was observed both in men and in women, with no interaction between eGFR categories and diabetes ($P = 0.52$); likewise, the interaction between eGFR <30 vs. ≥30 mL/min/1.73 m^2 and diabetes was not significant ($P = 0.17$).

The study is observational, with some missing data such as proteinuria in all patients and HbA_{1c} in some patients. Also, the group with the lowest eGFR was comparatively small. Finally, as we wished to describe long-term follow-up, we only included patients from the 2005 and 2010 cohorts. Since then, newer glucose-lowering medications have documented an impact on CV and renal outcomes, which might modify the relationship among diabetes, eGFR, and clinical outcomes.

Thus, the risk of 5-year all-cause mortality progressively increases with declining renal function in AMI patients; the eGFR threshold below which mortality increases, however, appears to be higher in patients with diabetes than in patients without diabetes (60 vs. 45 mL/min/1.73 m^2). Likewise, diabetes is associated with higher mortality, although the increased risk of mortality associated with diabetes is attenuated for patients with eGFR <45 mL/min/1.73 m^2 and no longer significant for those with eGFR <30 mL/min/1.73 m^2.

These results suggest that in post-MI patients, *1*) chronically impaired renal failure and diabetes are both associated with an increased risk of mortality, *2*) renal function requires specific attention in patients with diabetes as soon as it is mildly impaired (45–60 mL/min/1.73 m^2), and *3*) tight glycemic control, which is controversial in post-MI patients (4), may not be essential in patients with diabetes with eGFR <30 mL/min/1.73 m^2.

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