The interaction effect between myocardial infarction and comorbidity: nationwide cohort study

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Topic(s):
Coronary Artery Disease – Epidemiology, Prognosis, Outcome

Citation:

Funding Acknowledgements:
Department of Clinical Epidemiology’s Research Foundation; Program for Clinical Research Infrastructure (PROCRIN)

Background: Comorbid diseases may influence the prognosis of acute myocardial infarction (MI) directly by increasing the mortality hazard and indirectly by modifying treatment intensity.

Purpose: To examine whether comorbid diseases and MI interact to increase mortality beyond the sum of their independent effects.

Methods: Using Danish medical databases, we conducted a nationwide cohort study of patients diagnosed with MI between 1995 and 2016 (n = 179,515) and a comparison cohort of persons without MI (n=880,347) matched on age, sex, and comorbidities in the Charlson Comorbidity Index. The study outcome was time-to-death and the cohorts were followed from the MI/index date until death, emigration, five years of follow-up, or 31 December 2016, whichever came first. Standardized mortality rates with 95% confidence intervals (CIs) were computed using age and sex weights based on the inception MI cohort. The interaction was examined on the additive scale by calculating the interaction contrasts (the difference in rate differences), which measure the combined mortality effect of MI and comorbidity that cannot be explained by summing their individual effects. The follow-up period was stratified by the first 30 days, 31–365 days, and 1–5 years after the index date. Analyses were repeated within strata of comorbidity levels (1, 2–3, 4+).

Results: 62% of patients were male. The median age was 70 (interquartile range: 60, 80) years. Among individuals without comorbidity, the mortality rate per 1000 person-years during 30-day follow-up was 1,851 (95% confidence interval: 1,818 to 1,884) for myocardial infarction patients and 22 (21 to 24) for comparison cohort members, yielding a rate difference of 1,829. For individuals with low comorbidity, corresponding baseline mortality rates per 1,000 person-years were 2,498 (2,436 to 2,560) in the myocardial infarction and 54 (50 to 57) in the comparison cohort (rate difference=2,444). The interaction contrast was 616, indicating that the interaction accounted for 25% (616/2,498) of the total mortality rate in MI patients with low comorbidity. The percentage of the 30-day mortality rate explained by interaction increased further for moderate (35%) and severe (45%) comorbidity levels. Absolute and relative interaction effects were largest within the first 30 days, but similar dose-response patterns were observed during 31–365 days and 1–5 years of follow-up (all p-values for trends<0.002). Conclusions: Comorbidities interact with myocardial infarction to increase short- and long-term mortality beyond that explained by the additive effect of myocardial infarction and comorbid diseases acting alone.
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Conclusions:
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