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Prevalence, management and prognostic impact on long-term mortality of familial hypercholesterolemia in patients with acute or stable coronary artery disease

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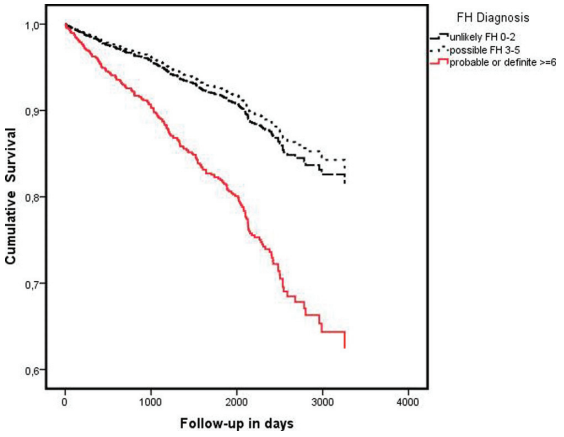
Background: Patients suffering from familial hypercholesterolemia (FH) are at increased risk for premature and subsequent cardiovascular disease. However, data on long-term adverse outcome in patients with FH after coronary stenting is scarce.
Purpose: We aimed to assess the prevalence, the rate of optimal lipid-lowering therapy at discharge (by means of high-intensity statins) and long-term adverse outcome of clinical diagnosed FH among patients undergoing coronary stenting presenting with stable coronary artery disease (SCAD) or acute coronary syndromes (ACS).
Methods: We analysed 1584 patients of a single-centre registry undergoing coronary stenting between 2007 and 2012, of whom 746 patients had SCAD while 838 patients presented with ACS. Patients were stratified into "unlikely FH" (0–2 points), "possible FH" (3–5 points) and "probable or definite FH" (≥6 points) based to the Dutch Lipid Clinic Network criteria. As primary endpoint, we assessed the prevalence and management of FH in this cohort. As secondary endpoint, we compared long-term all-cause mortality between these groups in Cox proportional hazards analysis adjusting for ACS/SCAD, age, gender, body mass index, kidney function, admission with shock, atrial fibrillation, heart failure, hypertension, smoking status, diabetes mellitus, malignancy, femoral or radial access site, number of affected vessels and discharge with high-intensity statins.
Results: Among our cohort, 68 (4.3%) patients had probable or definite FH, 334 (21.1%) had possible FH and 1182 (74.6%) were unlikely to suffer from FH. Fourty-eight (75.0%) patients with probable or definite FH, 244 (77.0%) patients with possible FH and 675 (63.4%) of the patients with unlikely FH were discharged with high-intensity statins. After adjusting for multiple confounders, patients with probable or definite FH (HR 2.305 [95% CI 1.042–5.098], p=0.039), but not patients with possible FH (HR 0.884, p=0.611), had an approximately 2-fold increased relative risk of all-cause death after a mean follow-up of 7.9 years (Figure).



Adjusted KM-curves for MACE based on FH

Conclusion: Clinical diagnosis of FH is not uncommon in patients presenting with coronary artery disease. Patients with probable or possible FH face a >2-fold increased risk of long-term all-cause mortality compared to patients without FH despite the widespread use of high-intensity statins.
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Impact of non-cardiovascular multimorbidity after acute coronary syndrome

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Background: Patients with multiple chronic conditions may be at particular risk of mortality after acute coronary syndrome (ACS) because they are usually older, fragile and polymedicated. The impact of non-cardiovascular (CV) multimorbidity on risk of recurrence after ACS remains unknown.
Purpose: To evaluate the impact of non-CV multimorbidity on the incidence of CV events after ACS.
Methods: We studied 5,635 men and women from a prospective cohort of patients hospitalized with ACS in Switzerland between 2009 and 2014. We defined non-CV multimorbidity as having 2 or more disorders including history of: severe renal disease (dialysis or clearance<30 mL/min), cancer, chronic obstructive pulmonary disease, gastrointestinal bleeding, inflammatory systemic disease (lupus erythematosus, polymyosite, mixed connective tissue disease, polymyalgia rheumatica, rheumatoid arthritis, or psoriasis) and liver disease (hepatic cirrhosis or chronic hepatitis).
We used multivariable adjusted Cox proportional models to assess risk of first major CV event (defined as CV death, myocardial infarction, or ischemic stroke), and risk of coronary event (defined as fatal and non-fatal myocardial infarction). Adjustment was done for: age, gender, body mass index, tobacco consumption, hypertension, diabetes, pre-existing CV disease, use of high statin dose and use of cardiac rehabilitation program.
Results: Over the year after ACS, 350 (6.2%) patients had a CV event, 275 (4.9%) had a coronary event, and a total of 209 (3.7%) died. A total of 147 patients (2.6%) had non-CV multimorbidity at baseline. The risk of CV event and coronary event after ACS was higher in patients with non-CV multimorbidity, as compared with patients without non-CV multimorbidity, with age and gender adjusted hazard ratios (HR) of 2.58 (95% CI 1.75–3.78, p<0.001) and 2.55 (95% CI 1.66–3.93, p<0.001), respectively. Further adjustment did not change the results, with fully adjusted HR of 2.59 (95% CI 1.70–3.94, p<0.001) and 2.63 (95% CI 1.62–4.26, p<0.001), respectively.
Conclusions: Patients with ACS suffering from non-CV multimorbidity have more than a two-fold higher risk of recurrence of CV and coronary events within the first year after discharge than patients without non-CV multimorbidity, independently of traditional CV risk factors. Intensive preventive management should be tested in patients with non-CV multimorbidity after ACS.
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Significance of renal function in progression of coronary artery calcification in general population

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Background: The presence of chronic kidney disease (CKD) is considered as a coronary artery disease equivalent, with more advanced coronary artery calcification (CAC) and subsequent high incidence of adverse cardiac outcome. Conversely, prior studies have shown that CAC progression was strongly associated with renal function, but exclusively in patients with CKD. Yet, it is unclear whether the progression of CAC is dependent on the degree of renal function in general population.
Purpose: We investigated the association between CAC progression and renal function in general population.
Methods: A total of 2,505 apparently-healthy individuals who performed serial CAC scoring for a routine health examination with at least one year interval were retrospectively reviewed. The estimated glomerular filtration rate (eGFR) was calculated using the 2009 CKD Epidemiology Collaboration (CKD-EPI) creatinine equation, and the distribution of eGFR was categorized as ≥90, 60–89, 30–59, <30 ml/min/1.73m^2. CAC progression was defined by absolute change in CAC scores by per-year and the binary classification by categories grouped according to change in CAC (0: any increase, 1–99: >10, ≥100: ≥10% of baseline).
Results: During a median follow up period of 39 months (interquartile range, 25 to 55 months), CAC progression was observed in 1,009 subjects (40.3%, mean CAC scores 81.5±242.2 at baseline to 163.5±411.8 at follow-up). The mean eGFR was significantly lower in CAC progressors (74.2±12.3 vs. 76.3±12.2 ml/min/1.73m^2, p<0.001). Further, the prevalence of CAC progressors is increasing in accordance with decreasing eGFR categories (37.0 vs. 43.9 vs. 49.3 vs. 100%; p=0.010). In univariate analysis, CAC progression showed strong association with eGFR, age, gender, and established cardiovascular risk factors including smoking, hypertension and diabetes mellitus. Particularly, decreasing eGFR was an independent determinant of CAC progression even after adjusting confounding factors in general population (adjusted OR 1.34, 95% CI 1.13–1.60, p=0.001).
Conclusions: The eGFR showed significant inverse relationship with CAC progression in general population. When a subject had the lower renal function despite not CKD, the more intensive cardiovascular risk factor management and close monitoring should be emphasized.