1177

Cardiovascular outcomes and mortality in type 2 diabetes with associated cardio-renal-metabolic comorbidities

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Background and aims: Cardio-renal-metabolic comorbidities (CRMCs) in patients with type 2 diabetes (T2D) are associated with high morbidity and mortality rates. We evaluated the incremental contribution of various CRMCs to the risk of myocardial infarction, stroke, or cardiovascular death (MACE), heart failure (HF) and all-cause mortality in patients with newly diagnosed T2D.
Materials and methods: Using International Classification of Diseases (ICD)-9 codes and Read codes, CRMCs (hypertension [HTN], hyperlipidaemia [HPLD] and chronic kidney disease [CKD]) were identified at the time of T2D diagnosis using databases in the UK (Clinical Practice Research Datalink [CPRD]) and the US (Humedica/Optum). The CPRD database includes longitudinal primary care data from 714 real-life clinical practices and covers approximately 8% of the UK population while the Humedica/Optum databases are US electronic medical records that are claim based and derived mainly from hospitals and outpatient clinics. Humedica databases include approximately 18.5 million patients from 38 States. Both the UK and US (Humedica/Optum) databases are broadly representative of the demographic and geographic breakdown of their respective populations. Patients were followed post-diagnosis of T2D for the occurrence of MACE, HF and mortality and evaluated for the increase in relative risk due to CRMCs.
Results: Between 1 Jan 2011 and 31 Mar 2015, we identified 59,362 patients in the UK and 180,722 patients in the US with incident T2D (mean age [SD]: 61.8 [13.6] and 62.4 [13.5] years; 55.9% and 52% men, respectively). There were no significant differences in the effects of CRMCs on outcomes between countries. The risk of MACE, HF and mortality increased with the number of CRMCs (Table). CKD was associated with the highest incremental risk, with an HR (95% CI) of 2.23 (2.17, 2.49) for mortality compared with T2D alone.
Conclusion: In patients with a new diagnosis of T2D, the risk of MACE, HF and death increased with the number of CRMCs, with CKD being the largest driver of mortality. These results may have implications for risk stratification of patients with T2D, and highlight the importance of identifying novel renoprotection strategies among T2D patients with various CRMCs.

Table. Combined analyses of US and UK databases: MACE, HF and mortality rates in patients with incident T2D and cardio-renal-metabolic diseases

Outcomes	CRMCs at the time of T2D diagnosis	N	Events/100 PY (95% CI)	Incremental % increase in event rate	Adjusted HR (95% CI)
MACE	T2D only	31881	4.34 (4.21, 4.47)	Reference	Reference
	T2D + HTN + HPLD	73448	5.71 (5.61, 5.81)	31.57	1.18 (1.14, 1.23)
	T2D + HTN + HPLD + CKD	21570	8.30 (8.06, 8.54)	43.36	1.56 (1.47, 1.65)
HF	T2D only	31881	4.01 (3.88, 4.14)	Reference	Reference
	T2D + HTN + HPLD	73448	4.84 (4.75, 4.93)	20.70	1.11 (1.07, 1.16)
	T2D + HTN + HPLD + CKD	21570	7.34 (7.12, 7.57)	51.65	1.79 (1.69, 1.90)
Mortality	T2D only	31881	2.14 (2.05, 2.23)	Reference	Reference
	T2D + HTN + HPLD	73448	2.66 (2.60, 2.73)	24.30	1.0 (1.0, 1.1)
	T2D + HTN + HPLD + CKD	21570	5.44 (5.27, 5.62)	104.51	2.23 (2.17, 2.49)

CRMC, cardio-renal-metabolic comorbidity; CKD, chronic kidney disease; HF, heart failure; HPLD, hyperlipidaemia; HTN, hypertension; MACE, myocardial infarction, stroke, or cardiovascular death; N, number of patients; PY, patient-years; T2D, type 2 diabetes

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