Cancer Mortality in Type 2 Diabetes: A Population-Based Cohort Study Quantifying Relationships with Body Mass Index

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Introduction

Type 2 diabetes (T2D) is associated with increased cancer mortality. However, the associations by obesity related versus non-obesity related cancer mortalities, and relationships with body mass index (BMI) at T2D diagnosis, have not been evaluated.

Aims To assess whether T2D is associated with increased cancer-related mortality, stratified by obesity- and non-obesity related cancers (Box. 1);

In patients with T2D, to assess whether BMI is associated with increased cancer mortality, stratified by obesity and non-obesity related cancers.

BOX 1: OBESITY RELATED CANCERS (ORC)

- Oesophageal adenocarcinoma
- Liver
- Pancreas
- Gallbladder
- Ovary
- Kidney
- Endometrial
- Colorectal
- Gastric cardia
- Post-menopausal breast
- Thyroid
- Meningioma
- Multiple myeloma

Method

We used the Clinical Practice Research Datalink linked with hospital data and national mortality data (1998 to 2015)

- **cohort of patients with T2D (187,968)**
- Matched on gender, year of birth (+/- 2 years) and GP practice with a never diabetes control (1:5 ratio)
- Thirteen obesity-related cancers (ORC) as defined based on the IARC 2016 report

We used Cox proportional hazards models to evaluate all-cancer, ORC and non-ORC mortality in individuals with T2D compared with individuals without.

- **cohort of patients with T2D and BMI recorded (145,769)**

In individuals with T2D, we evaluated the association of BMI with all cancer, ORC and non-ORC mortality, using multiple imputation methods for missing BMI data.

Results

Table 1: Baseline characteristics for those with and without T2D

	T2D		Never Diabetes	
	Men	***Women***	***Men***	***Women***
No. of individuals	99,767	77,119	476,889	376,057
Mean age (SD), years	60.0 (12.4)	62.5 (12.9)	59.5 (12.4)	62.3 (13.0)
Current smoker (%)	25,701 (25.8)	18,131 (23.5)	131,204 (27.5)	92,640 (24.6)
Ex-smoker	44,916 (45.0)	25,759 (33.4)	158,958 (33.3)	109,778 (29.2)
Never smoker	27,835 (27.9)	32,069 (41.6)	152,125 (31.9)	161,156 (42.9)
Unknown	1,315 (1.3)	1,160 (1.5)	34,602 (7.3)	12,483 (3.3)
Mean BMI (SD), kg/m²	30.8 (5.8)	32.3 (7.3)	27.5 (4.8)	27.3 (5.9)

Table 2: HR (95% CI) of cancer-related mortalities; men and women <85 years; T2D vs. never diabetes

	All cancer deaths		ORC deaths		Non-ORC deaths	
	Men	***Women***	***Men***	***Women***	***Men***	***Women***
Never Diabetes						
No. of deaths/ no. of Individuals	21,829/ 476,889	16,021/ 376,057	4,484/ 476,889	7,188/ 376,057	17,345/ 476,889	8,833/ 376,057
Incidence (per 1000 py)	6.2	5.5	1.3	2.5	4.9	3.0
Type 2 Diabetes						
Incidence (per 1000 py)	11.2	9.8	3.3	4.8	7.9	5.0
No. of deaths/ no. of Individuals	5,667/ 99,767	3,934/ 77,119	1,667/ 99,767	1,925/ 77,119	4,000/ 99,767	2,009/ 77,119
HR (95% CI) **	1.22 (1.18-1.26)	1.31 (1.26-1.37)	**1.84 (1.72-1.96)**	**1.48 (1.39-1.56)**	1.05 (1.02-1.11)	1.18 (1.10-1.28)

**Adjusted for age, ethnicity, deprivation, calendar year, smoking

Table 3: Death from any cancer, ORC and non-ORC across BMI categories in men with T2D

	BMI kg/m² category					
	18.5 – 22.49	**22.5 – 24.9**	**25.9 – 29.9**	**30.0 – 34.9**	**35.0 – 39.9**	**40.0 – 59.9**
All Cancer deaths						
HR (95% CI) **	0.87 (0.76-0.99)	1.00	0.74 (0.66-0.84)	0.69 (0.60-0.78)	0.62 (0.52-0.74)	0.65 (0.53-0.81)
ORC death						
HR (95% CI) **	0.83 (0.64-1.07)	1.00	0.72 (0.57-0.91)	0.64 (0.50-0.83)	0.60 (0.43-0.84)	0.66 (0.45-0.95)
Non-ORC death						
HR (95% CI) **	0.88 (0.75-1.04)	1.00	0.75 (0.64-0.87)	0.70 (0.60-0.82)	0.63 (0.51-0.76)	0.65 (0.49-0.85)

** Adjusted for age, ethnicity, deprivation, calendar year, smoking

Conclusion

- This is the largest data to-date, which confirms the literature that T2D is associated with increased cancer mortality compared with individuals without T2D
- There were two unexpected findings:
  - (i) increased non-ORC mortality among individuals with T2D;
  - (ii) an inverse relationship between BMI and ORC deaths was seen in individuals with T2D.
- There are likely to be 'drivers' other than obesity contributing the observed increased cancer mortality.