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Incidence of and risk factors for hospitalisations due to vascular complications: A population-based type 1 diabetes cohort (n = 1316) followed into early adulthood

Matthew N. Cooper [a], Martin I. de Bock [b], Kim W. Carter [a], Nicholas H. de Klerk [a,c], Timothy W. Jones [a,b,c], Elizabeth A. Davis [a,b,c,*]

[a] Telethon Kids Institute, The University of Western Australia, Perth, Australia
[b] Department of Endocrinology and Diabetes, Princess Margaret Hospital for Children, Perth, Western Australia, Australia
[c] The School of Paediatrics and Child Health, The University of Western Australia, Perth, Western Australia, Australia

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ABSTRACT

Aim: To determine the incidence of hospitalisations and risk factors for vascular complications experienced during early adulthood in patients with childhood onset type 1 diabetes.
Methods: A population-based childhood onset type 1 diabetes cohort was identified from a statewide register (1992–2012). Data linkage was used to identify a matched comparison cohort. Hospital admissions data were extracted to follow up both cohorts into early adulthood (1975–2012).
Results: The type 1 diabetes cohort (n = 1316) had a mean age of diagnosis of 9.5 years, 49.5% were women and mean age at the end of follow-up was 26.3 years (range 18–38). Within the type 1 diabetes cohort 32 (2.4%) were hospitalised with a vascular complication during early adulthood. Poor glycaemic control during paediatric management was associated with a significant increase in risk for ophthalmic complication with 19.4% (n = 12/62) of those with a mean HbA1c > 12% (108 mmol/mol) diagnosed compared to 0.72% (n = 5/696) of those with mean HbA1c < 9% (75 mmol/mol), adjusted hazard ratio 8.4 (95% CI 2.0, 34.7).
Conclusion: Severe vascular complications requiring hospital admission continue to be observed during early adulthood. Both women and those with poor glycaemic control are at increased risk of requiring a hospital admission for these complications during early adulthood.

1. Introduction

Complications from chronic microvascular and macrovascular complications remain a reality for those living with type 1 diabetes despite improvements in insulins, glucose self-monitoring devices, and insulin administration devices (American Diabetes Association, 2012). The DCCT was the first study to thoroughly characterise the impact of good glycaemic control on the subsequent risk of microvascular complications including progression of retinopathy, nephropathy, and neuropathy (The Diabetes Control and Complications Trial Research Group, 1993). The subsequent epidemiology of diabetes intervention and complications study demonstrated this effect for macrovascular complications including nonfatal myocardial infarction and stroke (Nathan et al., 2005). Further evidence for this relationship has since been demonstrated by numerous cohort studies including data from The Pittsburgh Epidemiology of Diabetes Complications (EDC) Study (Miller, Secrest, Ellis, Becker, & Orchard, 2013), data from the Swedish registries (Möllsten et al., 2010), and the EURODIAB IDDM Complications study (Stephenson & Fuller, 1994).

The subsequent adoption of intensive diabetes management has translated into improved glycaemic control in many diabetes cohorts (Bulsara, Holman, Davis, & Jones, 2004; Chase et al., 2001). More recently, technology advances such as insulin pump therapy, continuous glucose monitoring, and sensor augmented pump therapy have translated into further improvement in glycaemic control (Johnson, Cooper, Jones, & Davis, 2013; Weissberg-Benchell, Antisdel-Lomaglio, & Seshadri, 2003). However, despite landmark studies and improved average glycaemic control within type 1 diabetes populations, a significant proportion of those with type 1 continue to struggle to achieve tight glycaemic control, particular during childhood and adolescence (McKnight et al., 2014; Wood et al., 2013), and hence remain at increased risk of developing microvascular and macrovascular complications

Cohorts of patients treated with intensive management regimens since or soon after type 1 diabetes diagnosis are only now beginning to reach a duration by which these chronic complications typically begin (Pambianco et al., 2006). The aims of this study were to utilise statewide Western Australia (WA) data registries and linked data methodology to: (i) calculate the incidence rates of microvascular and macrovascular

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* Corresponding author at: Princess Margaret Hospital for Children, Department of Endocrinology and Diabetes, GPO Box D184, Perth WA 6840, Australia. Tel.: +61 8 9340 7023; fax: +61 8 9340 8605.
E-mail address: Elizabeth.Davis@health.wa.gov.au (E.A. Davis).

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complications requiring hospitalisation during early adulthood in those with childhood onset type 1 diabetes and compare these to the general population; and (ii) within the type 1 diabetes cohort, utilise comprehensive clinical records collected during paediatric management to profile those patients that went on to develop these complications during early adulthood.

2. Materials and methods

2.1. Data sources

The type 1 diabetes cohort was identified through the Western Australia Children's Diabetes Database (WACDD), described in detail previously (Cooper, O'Connell, Davis, & Jones, 2013; Haynes, Bower, Bulsara, Jones, & Davis, 2004). This is a population-based database (established 1987), which includes demographic and diabetes management data for all children under the age of 16 years in WA (2015 population 2.6 million) with diabetes (Australian Bureau of Statistics, 2015). Patients attend clinics, facilitated by a multidisciplinary team from Princess Margaret Hospital, approximately every 3 months where these data are collected. Consent for use of the data for research purposes is gained during the initial clinic visits; case ascertainment has been demonstrated as >99% (Haynes et al., 2004).

In WA, data pertaining to primary and secondary diagnoses, procedures performed, length of stay and other pertinent information, for all hospital admissions (capturing both inpatient hospitalisations and many same-day operative procedures) within both public and private hospitals, are stored in the Hospital Morbidity Data System. Electronic records date back to 1970; this was used as the source of hospitalisation data. The diagnosis and procedure variables are coded using the International Classification of Diseases, Ninth Revision (ICD-9) from January 1979 to December 1987, the ICD-9 Clinical Modification (ICD-9-CM) from 1988 to June 1999, and the ICD-10 Australian Modification (ICD-10-AM) from July 1999 through January 2012. The WA Mortality Register is a statutory collection containing cause of death data for all deaths in WA. Electronic records date back to 1969; this was used as the source of death information. The WA Birth Register contains details of all births in WA; registration into the Birth Register within 60 days of the birth is mandatory, with electronic records dating back to 1974.

2.2. Subjects

The type 1 diabetes cohort consisted of all patients from the WACDD with type 1 diabetes who had reached 18 years of age prior to 31 January 2012. A general population sample, matched 5:1 for sex and (exact) date of birth, was randomly selected from the Birth Register to form the comparison-cohort. The WA Department of Health Data Linkage Branch carried out the matching and identification of the comparison cohort, and the linkage of both cohorts to the Hospital Morbidity Data System and the Mortality Register. The study was approved by the Princess Margaret Hospital's Ethics Committee #1939/EP; consent for data linkage was approved by the Human Research Ethics Committee of the Western Australian Department of Health #2011/77.

2.3. Outcomes and risk factors

There were seven primary outcomes defined a priori based on commonly described complications; these are described in Table 1, with the specific ICD codes used to identify each outcome in Supplementary Table 1. The outcomes were two microvascular diagnoses (end-stage renal disease (ESRD) and ophthalmic complications), four macrovascular diagnoses (amputation, any vascular intervention (including stent insertion, angioplasty), myocardial infarction and stroke), and any microvascular or macrovascular diagnosis. Ophthalmic complication was defined as the diagnosis of either retinopathy requiring vitrectomy or diabetic cataract concurrent with a lens extraction (or similar) procedure. These are reported separately but were analysed together, both to align with previous studies of diabetes complications (DCCT/EDIC Research Group et al., 2015; Kohner, 2008) and due to the increased risk of retinopathy development or progression following surgical treatment for diabetic cataracts (Fong et al., 2004). Thus, the 'any vascular complication' variable is presented both including and excluding diabetic cataract concurrent with a lens extraction. Where an ICD code of interest was identified within the primary diagnosis or primary procedure field, all hospitalisation records pertaining to those subjects identified were extracted and examined in detail by two members of the study team. This was to reduce the risk of outcomes likely due to external causes being incorrectly included in the analysis (for example amputation due to injury in a car accident).

Table 1
Definitions used for outcome diagnosis.

Outcome	Definition [a]
End-stage renal disease (ESRD)	Diagnosis of diabetic nephropathy in addition to commencing haemodialysis or having undergone a kidney transplant.
Ophthalmic complications	Vitrectomy or cataract treatment — Diagnosis of diabetic retinopathy or cataract in addition to undergoing a surgical procedure (vitrectomy) or similar (lens extraction) based ophthalmic repair.
Retinopathy requiring vitrectomy	Diagnosis of diabetic retinopathy in addition to undergoing a surgical procedure (vitrectomy).
Amputation	Limb amputation surgery with no sign of acute trauma present, diabetes specified as the primary cause with a documented history of diabetic neuropathy.
Myocardial Infarction	Primary diagnosis and cause for hospitalisation were an acute myocardial infarction with no sign of acute trauma present
Stroke	Primary diagnosis and cause for hospitalisation were an acute stroke with no sign of acute trauma present.
Vascular Intervention	Hospital admission for artery bypass procedure, angioplasty or insertion of a stent or similar procedure to prevent or rectify blockage of an artery.
Any vascular complication	Any of the above
Any vascular complication (excluding cataract)	Any of the above, excluding cataract diagnoses and lens extraction procedures

[a] IC8/ICD9/ICD9CM/ICD10AM codes used to identify records pertaining to outcomes are available in Supplementary Table 1.

2.4. Clinical data

Within the type 1 diabetes cohort, clinical predictors of interest included age of type 1 diabetes diagnosis, sex, glycaemic control, severe hypoglycaemia episodes and socio-economic status. These variables were available from diagnosis, or first attendance at the WA clinic for those patients who migrated to WA, through to either age 18 years or the last clinic appointment prior to transition to adult care. The term paediatric management is used to define this period.

HbA1c level was determined at each clinic visit via agglutination inhibition immunoassay (non-diabetic reference <44.3 mmol/mol (6.2%); Siemens DCA Vantage; Siemens Healthcare Diagnostics, Erlangen, Germany). HbA1c was analysed in two forms, firstly, using the mean HbA1c across all clinic visits as a measure of glycaemic control and then categorised as <9%, 9%–10%, 10%–11%, 11%–12% and ≥12%. Severe hypoglycaemia was defined in line with previous publications (Cooper et al., 2013), as a hypoglycaemic event leading to loss of consciousness or seizure. This was analysed in two forms, firstly, as a dichotomous variable for having ever had an episode of severe hypoglycaemia, and secondly, as a rate per 100 patient-years (grouped into categories 0, 1–9, 10–19 and ≥20 per 100 patient-years) to adjust for duration of diabetes. Socio-economic status (SES) was assessed using the Australia Bureau of Statistics' index of relative socio-economic disadvantage measure

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