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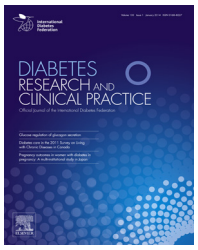

High rate of hypoglycemia in 6770 type 2 diabetes patients with comorbid dementia: A multicenter cohort study on 215,932 patients from the German/Austrian diabetes registry

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ABSTRACT

Aims: Dementia and type 2 diabetes (T2D) are two major phenomena in older people. To compare anti-hyperglycemic therapy and diabetes-related comorbidities between elderly T2D patients with or without comorbid dementia.

Methods: 215,932 type 2 diabetes patients aged ≥40 years (median [Q_1;Q_3]: 70.4 [61.2;77.7] years) from the standardized, multicenter German/Austrian diabetes patient registry, DPV, were studied. To identify patients with comorbid dementia, the registry was searched by ICD-10 codes, DSM-IV/-5 codes, respective search terms and/or disease-specific medication. For group comparisons, multiple hierarchic regression modeling with adjustments for age, sex, and duration of diabetes was applied.

Results: 3.1% ($n = 6770$; 57% females) of the eligible T2D patients had clinically recognized comorbid dementia. After adjustment for demographics, severe hypoglycemia (insulin group: 14.8 ± 0.6 vs. 10.4 ± 0.2 events per 100 patient-years, $p < 0.001$), hypoglycemia with coma (insulin group: 7.6 ± 0.4 vs. 3.9 ± 0.1 events per 100 patient-years, $p < 0.001$),

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depression (9.9 vs. 4.7%, $p < 0.001$), hypertension (74.7 vs. 72.2%, $p < 0.001$), stroke (25.3 vs. 6.5%, $p < 0.001$), diabetic foot syndrome (6.0 vs. 5.2%, $p = 0.004$), and microalbuminuria (34.7 vs. 32.2%, $p < 0.001$) were more common in dementia patients compared to T2D without dementia. Moreover, patients with dementia received insulin therapy more frequently (59.3 vs. 54.7%, $p < 0.001$), but metabolic control (7.7 ± 0.1 vs. 7.7 ± 0.1%) was comparable to T2D without dementia.

Conclusions: In T2D with dementia, higher rates of hypoglycemia and other diabetes-related comorbidities were observed. Hence, the risks of a glucocentric and intense diabetes management with insulin and a focus on tight glycemic control without considering other factors may outweigh the benefits in elderly T2D patients with comorbid dementia.

1. Introduction

One major public health problem in older people is the occurrence of neurocognitive disorders such as dementia. The prevalence of dementia has increased over the last years, especially in people 85 years and older [1]. It is estimated that globally 35.6 million people live with dementia [2]. The most common type of dementia is Alzheimer's disease [3]. It accounts for 60% to 80% of cases [3]. Other forms of dementia are: (i) vascular dementia, (ii) mixed forms of dementia, (iii) Lewy body dementia, (iv) frontotemporal dementia, and (v) dementia caused by other degenerative conditions (e.g., Creutzfeldt-Jakob disease, Parkinson's disease, normal pressure hydrocephalus) [3]. A review concluded that type 2 diabetes (T2D) is related to a 1.5–2.5-fold higher risk of dementia [4]. The etiology of dementia in T2D is suspected to be multifactorial [4]. Mechanisms linking T2D with dementia might be: acute hyperglycemia, recurrent hypoglycemia, hyperinsulinemia, insulin resistance, functional brain insulin deficiency, and hypothalamic–pituitary–adrenal axis dysregulation [5,6]. Moreover, genetic predisposition, cerebral microvascular diseases, hypertension, dyslipidemia, macrovascular diseases, amyloid-β deposition, oxidative stress, and inflammatory mediators are discussed [5,6]. Physical inactivity and obesity contribute to hypertension, insulin resistance and low-level inflammation, and thereby may also increase dementia risk [6]. Mayeda and colleagues reported that in the US the risk of dementia in T2D varies between ethnicities even after adjustment for sociodemographic and diabetes-related characteristics [7]. It is lowest in Asians and increased by 40–60% in Native or African Americans, and 19–30% in Latinos, or non-Hispanic whites [7]. Besides genetic factors, behavioral, or environmental factors are discussed, although more research is needed [7].

Dementia and its symptoms can influence the course of diabetes, namely diabetes therapy and diabetes-related complications [8–10]. The main objective of this research was to compare a large number of German/Austrian T2D patients with or without clinically recognized comorbid dementia with regard to diabetes therapy and outcome. Questions to be answered:

(1) Do sex distribution and BMI differ between T2D with and without dementia?
(2) Is insulin treatment more frequent in T2D with dementia?
(3) Is metabolic control worse in T2D with dementia?
(4) Are acute diabetes-related complications (e.g., hypoglycemia) or chronic comorbidities (e.g., hypertension, stroke, depression, and microalbuminuria) more common in T2D with dementia?
(5) Is hospital admission more frequent and duration of hospital stay longer in T2D with dementia?

2. Subjects, materials and methods

2.1. *Subjects and diabetes patient registry*

Subjects for the present study were retrieved from the multicenter, prospective diabetes patient registry, DPV (Diabetes-Patienten-Verlaufsdokumentation). The registry data is collected by a standardized electronic health record system. For nearly 20 years, more than 400 specialized German/Austrian diabetes care centers enter demographics and clinical data on a regular basis. Every half year, the locally documented data are anonymized and transmitted to the University of Ulm, Germany. Inconsistent data are reported back to the centers for correction. The establishment and analysis of the database have been approved by the ethics committee of the University of Ulm, Germany. The local review board of each participating center has approved the anonymized data collection.

By March 2014, the registry comprised data on 338,981 patients with any type of diabetes. For the present study, 215,932 T2D patients aged ≥40 years from 161 German and 7 Austrian centers were considered (Fig. 1). To identify patients with clinically recognized comorbid dementia in the database, ICD-10 codes, DSM-IV, and DSM-5 codes, specific search terms for a diagnosis of dementia and/or drugs specific for dementia treatment were used. Data entries were made by physicians and health care professionals at each site based on clinically available data from routine care. Dementia was either already diagnosed in patients, or diabetologists made the diagnosis jointly with neurologists. If a positive result in a mental status test used to screen for dementia (e.g., mini mental state examination, and clock-drawing test) was documented, patients were also assigned to the dementia group. A mental status test was defined positive by using generally accepted cut-offs. As an abnormal mental status test is solely an indicator for cognitive impairment, on the