Dementia and its Associated Non-psychotic and Psychiatric Comorbidities

Demencia y sus comorbilidades no psicóticas y psiquiátricas asociadas:

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RESUMEN

La demencia es una enfermedad en la que la función cognitiva se deteriora y interfiere con las tareas diarias. La disfunción cognitiva en la demencia incluye deterioro en las siguientes facultades: memoria, función ejecutiva, lenguaje, capacidad visuoespacial, personalidad y comportamiento. Esta revisión sistemática tiene como objetivo examinar las comorbilidades de la demencia en base a artículos que involucren diagnósticos tanto psiquiátricos como no psiquiátricos. Los artículos se publicaron entre 2017 y 2022 y cumplen con el criterio de edad de la población de 50 años o más. Los artículos se buscaron, seleccionaron y aceptaron utilizando las bases de datos PubMed, DOAJ y EBSCO. Se logró el objetivo a través del descubrimiento de las comorbilidades asociadas a la demencia basadas en los 9 artículos, que son: hipoglucemia, disfagia orofaríngea, diabetes mellitus tipo 2, cáncer, tromboembolismo venoso, trastornos convulsivos, depresión y ansiedad.

Palabras Clave: Alzheimer, comorbilidad, demencia,cuerpos de Lewy

ABSTRACT

Dementia is a disease in which cognitive function deteriorates and interferes with daily tasks. Cognitive dysfunction in dementia includes deterioration in the following faculties: memory, executive function, language, visuospatial ability, personality, and behavior. This systematic review aims to examine the comorbidities of dementia based on articles involving non-psychiatric and psychiatric diagnoses. The articles are published between 2017 and 2022 in a population age criterion ranging from 50 years old and older. Articles were searched, selected, extracted, and accepted using the databases: PubMed, DOAJ, and EBSCO. The objective was fulfilled through the discovery of the comorbidities associated with dementia based on the 9 articles which are: hypoglycemia, oropharyngeal dysphagia, type 2 diabetes mellitus, cancer, venous thromboembolism, seizure disorders, depression, and anxiety.

Key Words: Alzheimer, dementia, comorbidity, dementia,Lewy's bodies

According to the Alzheimer's Association (AA), dementia is characterized by impaired cognition and function (AA, 2022). This disorder has a significant impact on individuals, families and the healthcare system due to its impact on behavior and ability to function independently (AA, 2022). Memory, executive function, language, visuospatial ability, personality, and behavior are the five primary domains of cognitive deficits fundamental to dementia diagnosis (Cunningham et al., 2015). As dementia progresses, cognitive deficits will widen, affecting more areas and deepen, resulting in increasing functional impairments (Cunningham et al., 2015). The most common causes of dementia are Alzheimer's disease, vascular dementia, and dementia with Lewy bodies, accounting for over 90% of cases (Sheehan, 2015). The prevalence of dementia is increasing as the world's population ages, and this trend is expected to continue (Sheehan, 2015). Assessment scales for dementia require criteria such as face validity, concurrent validity, inter-rater reliability, and test-retest reliability (Sheehan, 2015).

Comorbidity refers to any diseases or conditions that coexist with the primary disease of the patient (Yetman, 2022). It can be defined by the nature of the condition, the significance of the coexisting conditions, and the order in which the conditions are presented (Valederas et al., 2009). Studies have linked Alzheimer's dementia to comorbidities such as diabetes, cardiovascular illness, depression, and inflammatory bowel disease (Santiago & Potashkin, 2021). Hyperglycemia may contribute to the link between Alzheimer's dementia and type 2 diabetes (Macauley et al., 2015, as cited in Santiago & Potashkin, 2021). Additionally, amyloidosis has been discovered to be a possible common pathogenic characteristic linking Alzheimer's dementia with type 2 diabetes (Cooper et al.,1987, as cited in Santiago & Potashkin, 2021).

The objective of this paper is to investigate dementia and associated comorbidities. The systematic review focuses on analyzing that include a population aged 50 years and older, with a particular emphasis on both non-psychiatric and psychiatric medical comorbidities. The review covers the period between 2017 and 2022.

Method

A systematic review was conducted using the databases: PubMed, DOAJ, and EBSCO using the keywords 'dementia' and 'comorbidity' to search for articles and reviews related to the subject. In PubMed, 60 results were generated by filtering for research published in the last five years using the keywords and article types were filtered to clinical trials and randomized controlled trials, one of which was selected. The second search was conducted again in PubMed using the keywords: 'dementia risk in comorbid', which generated 25 results filtered by the category clinical trial, in which one result was selected. The third search was conducted through the keywords "patients with psychiatric comorbidities" which generated 10 results, one of which was selected. The fourth search was carried out using the keywords 'anxiety in dementia' which generated 109 results, two of which were selected. The final search on PubMed was conducted through the keywords 'dementia and comorbid depression' which generated seven results, none of which was selected. In total, five articles were selected from PubMed.

In DOAJ, the search results were generated using the keywords 'dementia and comorbidity' in addition to being filtered by the following years: 2017 (18 results, one was selected), 2018 (25 results, one was selected) 2019 (30 results, three were selected), 2020 (43 results, one was selected), 2021 (60 results, none were selected), and 2022 (17 results, one was selected). The search was repeated in DOAJ again, using the keywords: 'comorbidity and dementia cohort' filtered by the following years: 2017 (four results, none selected), 2018 (seven results, none selected), 2020 (9 results, none selected), 2021 (15 results, none selected), and 2022 (43 results, none selected). The final search in DOAJ was

conducted using the keywords 'dementia and depression' which generated 93 results, filtered by title, and four results were selected. In total, 10 articles were selected from DOAJ. In EBSCO, 898 results were generated through the keywords: 'dementia cohort, comorbidity' filtered by the publication Journal of Alzheimer's disease in which four articles were selected. This systematic review is composed of articles that were published between 2017 and 2021.

The inclusion criteria comprise the following:

- Dementia and the risk of comorbidities are the common themes.
- Study population age range above 50 years old.
- Publication type must be empirical articles namely clinical trials, journal articles, and cohort studies.
- Articles published in and after 2017.
- Articles must be available in English.

Exclusion criteria include:

- Articles such as systematic reviews, editorials, and non-peered reviews.
- Titles are irrelevant to the topic.
- Absence of comorbidities.
- Dementia is regarded as a comorbid condition.
- Population age below 50 years old and younger.
- Articles published before 2017.

Among the 19 selected articles, 9 were accepted. A PRISMA statement was assembled to illustrate the data searching and extraction process (Figure 1).

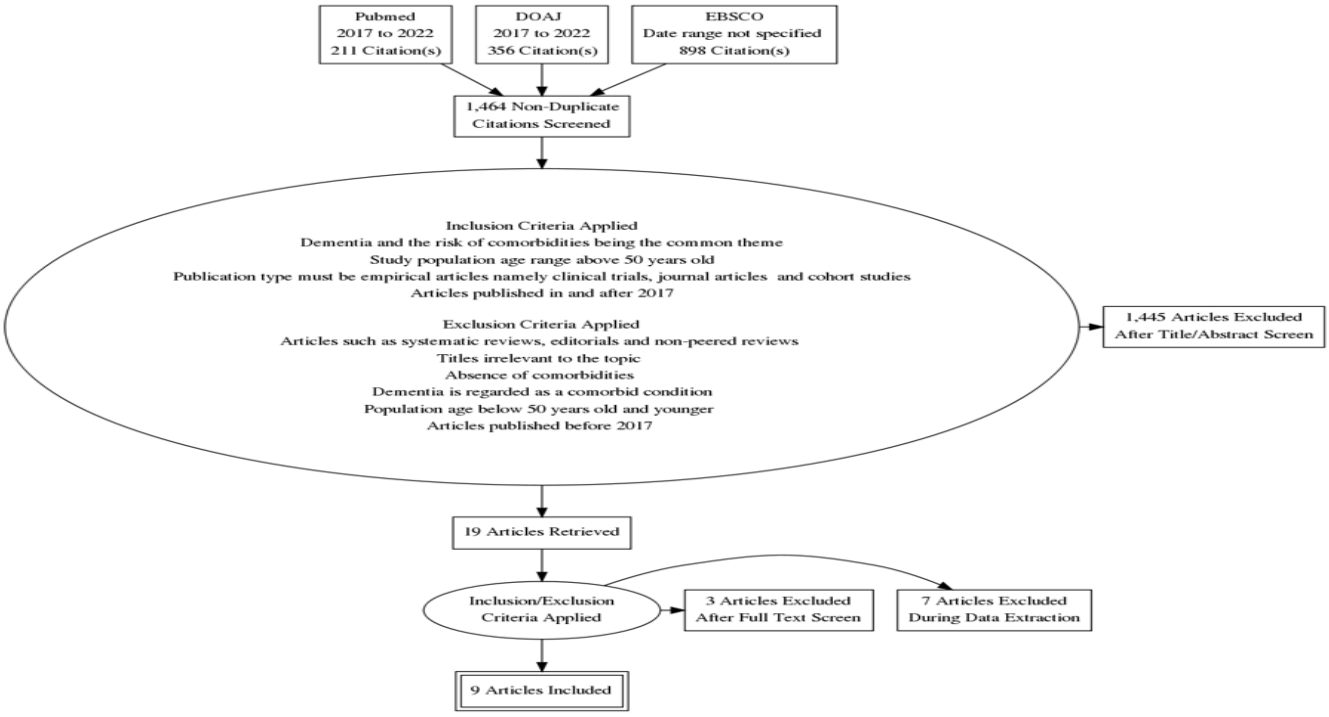

Figura 1
PRISMA Statement

Table 1.

Articles selected for the systematic review

Study	Authors	Country and year	Aim/Objective	Sample
Diabetes in a Large Dementia Cohort: Clinical Characteristics and Treatment From the Swedish Dementia Registry	Secnik et al.	Sweden 2017	The purpose of this study is to examine the changes in clinical characteristics and pharmacological treatment linked with diabetes in a large cohort of dementia patients.	Total amount patients = 29,(
Dementia, Subtype of Seizures, and the Risk of New Onset Seizures: A Cohort Study	Habeych et al.	United States 2021	The objective is to compare the frequency and risk of different seizure subtypes (focal and generalized) in patients with and without dementia.	Estimated total of patients 2,885,336
Venous Thromboembolism and Risk of Cancer in Patients with Dementia: A Danish Population-Based Cohort Study	Fuglsang et al.	Denmark 2021	Compare the risk of cancer in dementia patients to the risk in the general population after a venous thromboembolism.	Total of patien with dementia and venous th boembolism (= 3,552
The Risk Factors of Severe Hypoglycemia in Older Patients with Dementia and Type 2 Diabetes Mellitus	Chen et al.	Taiwan 2022	Analyze the status of glycemic control and determine the risk of hypoglycemia in older patients with dementia and type 2 diabetes mellitus.	Total of patien with Type 2 di tes mellitus (T and dementia = 3,877
Depression in dementia with Lewy bodies: A comparison with Alzheimer's disease	Chiu et al.	Taiwan 2017	The frequency, severity, and symptoms of depression in dementia with Lewy bodies (DLB) and Alzheimer's disease will be compared in this study (AD).	Total of patien 312 Pat with Alzheime Dementia (AD 241 P tients with De- mentia with Le bodies (DLB)
Prevalence, Risk Factors, and Complications of Oropharyngeal Dysphagia in Older Patients with Dementia	Espinosa-Val et al.	Spain 2020	Examine the prevalence, risk factors, and long-term nutritional and respiratory issues of oropharyngeal dysphagia in older dementia patients.	Total of patien with dementia 255

e	Tests/Scales used	Results
of 630	Data was extracted and combined from the Swedish Dementia Registry and Prescribed Drug Register for the diabetes diagnosis. After adjusting for confounders, logistic regression was used to confirm if the variables were linked to diabetes.	Diabetes was linked to a lower age at dementia diagnosis, male sex, vascular dementia, and mixed dementia in the fully adjusted model.
=	Data from the Optum Insight informatics-data Mart database was used. ICD-9 diagnoses were used to identify frequency of generalized or focal seizure disorders. The continuity-adjusted chi-square was used to analyze differences between dementia and non-dementia groups.	A dementia diagnosis was found in 79,561 patient records, with 56.38% of them being females. Patients with dementia showed a higher risk of seizure disorders than those without dementia.
nts (AD) hrom- VTE)	Comorbidity using the Charlson Comorbidity Index (CCI). Data extracted from the Danish National Patient Registry (DNPR) to identify patients 50 years and older with a first time VTE diagnosis and a previous or a current dementia diagnosis.	Dementia patients had a 90% increased risk of cancer within the first year after VTE.
nts abe- T2DM) (AD)	Dementia (AD) diagnosis was based on International Class of Disease, Ninth Revision, Clinical Modification codes (ICD-9-CM codes). The diagnosis of T2DM was based on ICD-9) codes 250.X. Based on the ICD-9 codes 251.0, 251.1, 251.2, and 250.8x, hypoglycemia was described. Comorbidity was evaluated using the Charlson Comorbidity Index (CCI).	T2DM with more than two comorbidities were found in older patients with concurrent AD, putting them at risk for severe hypoglycemia and major side effects.
nts = tients r's) = Pa- - ewy = 71	Hamilton Depression Rating Scale. The Cornell Scale for Depression in Dementia. The depression subscale in Neuropsychiatric Inventory	Major depression was found to be substantially more common in DLB (19.7%) than in AD (p = 0.017).
nts =	Oropharyngeal dysphagia (OD) was assessed with the Volume-Viscosity Swallowing Test in addition to a geriatric evaluation.	After 18 months of follow-up, OD patients were older, had worse functioning, nutritional condition, and dementia severity than those without OD, and had increased rates of respiratory illnesses and mortality.

Table 1.

Articles selected for the systematic review (cont.)

Study	Authors	Country and year	Aim/Objective	Sampl
Depression and Dementia in Old-Old Population: History of Depression May Be Associated with Dementia Onset. The Tome Project	Liu et al.	Japan 2017	In a community-based old cohort, the objective is to arrive at the connection between a history of depression, depressed episodes, and dementia.	Total of partic = 181
Anxiety and Depression as Risk Factors in Frontotemporal Dementia and Alzheimer's Disease: The HUNT Study	Rasmussen et al.	Norway 2018	Anxiety and depression will be investigated as separate risk factors for FTD and AD.	Total of partic = 757
Brain Networks Involved in Depression in Patients with Frontotemporal Dementia and Parkinson's Disease: An Exploratory Resting-State Functional Connectivity MRI Study	Alfano et al.	Italy 2022	This study compared patients with FTD and Parkinson's disease PD to healthy controls (HC) to see which brain networks are involved in depression.	Total of partic = 50

Note VTE: venous thromboembolism; T2DM: Type 2 diabetes mellitus; D: Dementia; WD: without dementia; DLB; Dementia with Lewy bodies; AD: A
Depressed patients with frontotemporal dementia: depressed patients with Parkinson's disease; NFTD: Non-depressed patients with frontotempo

Results

Sociodemographic Data

Among the selected articles, there is one cross-sectional registry-based study (Secnik et al., 2017), four articles are cohort studies (Habeych et al., 2021; Fuglsang et al., 2021; Chen et al., 2022; Liu et al., 2017), one is clinical study (Chiu et al., 2017), two articles are longitudinal studies (Espinosa-Val et al., 2020; Rasmussen et al., 2018) and finally, there are two MRI case studies (Alfano et al., 2022; Liu et al., 2017). **Table 1** explores the details of each of the 9 selected papers.

The selected articles incorporate sociodemographic variables such as gender, age, and clinical characteristics in differing population ranges. To discuss the socio-demographic data, the articles will be categorized based on population size, ranging from the smallest to the largest sample size. Among the selected articles, the smallest sample size is 255 in Espinosa-Val et al. (2020) and the largest is 2,885,336 in Habeych et al. (2021).

The articles with the smallest samples are Alfano et al. (2022) with 50 participants, Espinosa-Val et al. (2020) with 255 participants, Chiu et al. (2017) with 312 participants, Liu et al. (2017) with 181

le	Tests/Scales used	Results
cipants	Mini–Mental State Examination (MMSE). Geriatric Depression Scale. The Clinical Dementia Rating (CDR). MRI scans and MTA scans	Depression was associated with poorer Mini–Mental State Examination scores, higher CDR scores, and medial temporal lobe atrophy.
cipants	Hospital Anxiety and Depression Scale (HADS)	Anxiety and FTD were found to have significant relationships, as did depression and AD.
cipants	Beck depression inventory (BDI-II). Mini-mental state examination (MMSE), Unified Parkinson's disease rating scale (UPDRS), and magnetic resonance imaging (MRI).	The research suggests a consistent channel for depression in both FTD and PD patients

Alzheimer's dementia: oropharyngeal dysphagia; WOD: without oropharyngeal dysphagia; NP: normal participants; CH; cognitively healthy; DFTD: oral dementia; NPD: non-depressed patients with Parkinson's disease; HC: healthy controls; MCI: mild cognitive impairment.

participants and Rasmussen et al. (2018) with 757 participants. The articles with medium sample sizes are Fuglsang et al. (2021) with 3,552 participants and Chen et al. (2022) with 3,877 participants. Finally, the articles with the largest population sizes are Secnik et al. (2017) with 29,630 participants, and Habeych et al. (2021) with 2,885,336 patients.

Chiu et al. (2017), and Fuglsang et al. (2021) are the only studies that included information about both female and male participants. For instance, Chiu et al. (2017) divided the patients into two categories: female (n = 33) and male participants (n = 38) in the group with dementia with Lewy bodies (DLB), and the female (n = 157) and male participants (n = 84) in the AD group. In addition, Fuglsang et al. (2021) specified that 64% of participants are female (n = 2,274) and 36% of participants (n = 1,278) are male. Another study with gender total specificity is Chen et al. (2022) in which 37.5% of participants (n = 1,454) are male and 62.5% of participants (n = 2,423) are female.

According to Secnik et al. (2017), the average age of patients with diabetes is 78.8 and the average age of patients without diabetes is 79.5.

Chiu et al. (2017) stated that the average age of participants in the group with Lewy's bodies is 79.7 and the average age of participants in the group with AD is 77.1. Based on the 79,561 dementia patient records in Habeych et al. (2021), the population range was between 60 to 80 years old. However, the average age was divided into two groups: the group with dementia and the group without dementia. In the group with dementia, 24.51% are between the ages of 60 and 69, and 55.84% are between the ages of 70 and 79. Furthermore, 17.42% are between the ages of 60 to 69, and 29.58% are between the ages of 70 to 79 in the group without dementia.

Fuglsang et al. (2021) stated that the median age of dementia patients diagnosed with venous thromboembolism (VTE) is 82.0 years old. Chen et al. (2022) concluded that the median age of patients with dementia and type 2 diabetes mellitus (T2DM) is 77.5 years old. Espinosa-Val et al. (2020) revealed that the average age of the overall sample is 83.4 years, however, the average age of dementia patients with oropharyngeal dysphagia (OD) is 84.0 and the average age of dementia patients without OD is 80.16 years.

Liu et al. (2017) based the average age of the sample on three categorized groups: normal (M = 80.9), mild cognitive impairment (M = 84), and dementia (M = 84). Furthermore, the mean age in Rasmussen et al. (2018) was based on three groups: the group with FTD (M = 67.7), the group with AD (M = 71.8), and the control CH group (M = 61.2). The average age in Alfano et al. (2022) is divided into five groups: depressed patients with FTD (M = 63.2), depressed patients with Parkinson's disease (PD) (M = 65.5), non-depressed patients with FTD (M = 70.1), non-depressed patients with PD (M = 64.2), and healthy controls (M = 57.7).

Secnik et al. (2017) described that the clinical characteristics include registration at memory clinics, presence of AD, mixed diagnosis, hypertension, obesity, dyslipidemia, and diabetes complications. Chiu et al. (2017) included visual hallucinations (VHS), Parkinsonism, REM sleep behavior disorder (RBD), and neuroleptic sensitivity. Habeych et al. (2021) required the existence of medical comorbidities by organ system excluding infections, hepatic, and immunological issues. Fuglsang et al. (2021) categorized clinical characteristics based on types of VTE which included deep vein thrombosis, pulmonary embolism, and a dementia diagnosis. Chen et al. (2022) studied patients with T2DM, dementia, and frequent follow-up visits for more than two years. Espinosa-Val et al. (2020) included AD, mixed dementia, Lewy's bodies, mild cognitive impairment, vascular dementia, and Parkinson's disease-associated dementia. Liu et al. (2017) did indicate clinical characteristics for categorization purposes such as the presence of depressive episodes, and dementia. The clinical characteristics of Rasmussen et al. (2018) included heart disease, hypertension, metabolic disease, smoking, obesity, anxiety, and depression. Alfano et al. (2022), included depression and PD. Table 2 demonstrates the demographic data of the nine selected articles.

Assessment Tools

The majority of the articles used a variety of scales and assessment tools based on their objectives. However, three studies have used the Charlson Comorbidity Index to assess the presence of comorbidities in dementia patients (Fuglsang et al., 2021; Chen et al., 2022; Espinosa-Val et al., 2020). Four studies have used the International Classification of Disease codes (ICD) for dementia diagnosis and comorbid diagnoses (Secnik et al., 2017; Habeych et al., 2021; Fuglsang et al., 2021; Chen et al., 2022).

ICD-9-CM codes were applied in three studies (Secnik et al., 2017; Habeych et al., 2021). Based on the Swedish Patient Register, Secnik et al. (2017) used it to identify the presence of diabetes, hypertension, obesity, and dyslipidemia, while Habeych et al. (2021) used it to define the risk of seizure disorders in dementia patients. It was employed by Chen et al. (2022) to identify

the presence of AD and T2DM. Two studies used the ICD-10-CM codes (Fuglsang et al., 2021; Chen et al., 2022). Fuglsang et al. (2021) used it to identify patients with a first-time VTE diagnosis and Chen et al. (2022) used it to confirm the presence of hypoglycemia. Table 3 demonstrates the variety of tools used in each article.

Table 2

Sociodemographic data

Study	Dementia	Dementia + comorbidity	Control group	Total sample size	Gender	Average age	Median age
Secnik et al.	x	Dementia with diabetes = 4,881	Dementia without diabetes = 24,749	29,630	F = 29,630.	D = 78.8	x
Habeych et al.	79561 p	Patients without dementia = 2,805,775	x	2,885,336	F= 44,857 M = 34,704	x	x
Fuglsang et al.	x	Dementia with VTE = 3,552	x	3,552	F = 2,274 M = 1,278	x	82
Chen et al.	x	Dementia with T2DM = 3,877	x	3,877	F = 2,423 M = 1,454	x	77.5
Chiu et al.	DLB = 71p AD = 241p	x	x	312	F = 190 M = 122	DLB = 79.7 AD= 77.1	x
Espinosa-Val et al.	255 p	x	x	255	F = 157 M = 98	OD = 84.0 WOD= 80.16	x
Liu et al.	27 p	x	NP = 66 Participants with MCI = 88	181	F = 53% M = 47%	NP = 79.2. MCI = 80.9 D = 84	x
Rasmussen et al.	AD = 556p FTD = 84p	x	CH = 117	757	x		x
Alfano et al.	x	DFTD = 9 DPD=8 NFTD = 8 NPD =9	HC = 16	50	F = 21 M = 29	FTD = 67.7 AD=71.8 CH=61.2	x

Table 3

Scales and assessment tools used in each article

Study	Dementia	Comorbidity	Additional tools
Secnik et al.	ICD-10	X	The ICD-code E10-E3 , ICD-10 codes I10, E66, and E78
Habeych et al.	ICD-9-CM code	X	
Fuglsang et al.	ICD-10	Charlson Comorbidity Index (CCI)	The Union for International Cancer Control's Tumor, Nodes, and Metastases (TNM)
Chen et al.	ICD-9-CM codes	Charlson Comorbidity Index (CCI)	The ICD-9 codes 251.0, 251.1, 251.2, and 250.8. (ICD-9) codes 250.x
Chiu et al.	The Clinical Dementia Rating (CDR)	X	The Chinese version of the Cognitive Abilities Screening Instrument (CASI C-2.0) The 7-Item HDRS, the CSDD, and the NPI depression subscale Mini-International Neuropsychiatric Interview (MINI) 5.0.0 edition
Espinosa-Val et al.	Global Deterioration Scale (GDS) Functional Assessment Staging Test (FAST)	Charlson Comorbidity Index (CCI)	The Barthel Index and V-VST
Liu et al.	The Clinical Dementia Rating (CDR)	X	Mini–Mental State Examination (MMSE) Geriatric Depression Scale MRI scans and MTA scans
Rasmussen et al.	X	X	Hospital Anxiety and Depression Scale (HADS)
Alfano et al.	X	X	Mini-mental state examination (MMSE) Unified Parkinson's disease rating scale (UPDRS) Magnetic resonance imaging (MRI)

Note: ICD: International Classification of Diseases

Comorbidity Analysis

A total of five studies focused on non-psychiatric comorbidities (Chen et al., 2022; Secnik et al., 2017; Habeych et al., 2021; Espinosa-Val et al., 2020). A total of four studies focused on psychiatric comorbidities (Chiu et al., 2017; Liu et al., 2017; Rasmussen et al., 2018; Alfano et al., 2022).

Two studies centered particularly on diabetes as comorbidity, one of which included diabetes mellitus in Chen et al. (2022), and the other focused on unspecified diabetes (Secnik et al., 2017). There are three studies involving non-psychiatric comorbidities (excluding diabetes) which include Habeych et al. (2021) on focal or generalized seizure risk in dementia patients, Fuglsang et al. (2021) which investigated cancer risk in dementia patients after a year of VTE diagnosis, and Chen et al. (2022) on hypoglycemia in dementia patients with T2DM. Another study involving non-psychiatric comorbidity is Espinosa-Val et al. (2020) which centered on the presence of OD in older dementia patients.

The findings of Chen et al. (2022) concluded that 12.7% of older patients with comorbid AD had more than two T2DM comorbidities and are at risk for severe hypoglycemia and major side effects. Espinosa-Val et al. (2020) evidenced that 85.6 % of dementia patients showed indications of OD according to the V-VST results. Older patients with OD have lower functional capacity on admission and have a higher severity of dementia than non-dysphagic patients.

Secnik et al. (2017) concluded that when compared to individuals without diabetes, dementia patients with diabetes were substantially younger and had a lower MMSE score at the time of diagnosis. Mixed dementia exhibited the strongest link to diabetes when compared to Alzheimer's disease. DLB and PDD, however, were negatively associated with diabetes.

Fuglsang et al. (2021) confirmed that patients with dementia have an increased cancer risk after the first year of a VTE diagnosis. Within the first year after a VTE diagnosis, 97 cancers were discovered which confirmed the risk of cancer to be 2.8% for the first year. Lung, colon, prostate, kidney, and urinary bladder cancers, as well as metastases and unidentified cancer in lymph nodes, were the most prevalent tumors recorded during the first year of follow-up.

Following a ten-year follow-up period that saw an increase in the prevalence of new-onset seizures (NOS), Habeych et al. (2021) found that in patients with dementia the incidence rate of NOS was 12.34% per year, compared to 2.21% in the non-dementia sample.

A total of four studies focused on the presence of depression in patients with dementia (Chiu et al., 2017; Liu et al., 2017; Rasmussen et al., 2018; Alfano et al., 2022). Despite having depression as a common theme, the statistical methodology and outcomes of these articles differ.

Chiu et al. (2017) evidenced that patients with Lewy bodies have a higher probability of comorbid severe depression than patients with AD. Compared to the AD group, the DLB group displayed higher rates of fluctuation, parkinsonism, RBD (REM Sleep Behavior Disorder), and significant neuroleptic sensitivity.

Rasmussen et al. (2018) revealed that in a comparison analysis between individuals with AD and CH, anxiety and depression are risk factors for AD more than CH. The AD and FTD were more likely than the CH group to have heart disease, diabetes, metabolic disease, obesity, anxiety, and depression. FTD patients were also more likely to suffer from hypertension, metabolic illness, and, anxiety.In Liu et al. (2017) patients with higher CDR scores have a history of depressive symptoms, according to the nonparametric comparative analysis among the three groups. The depressive group included 22.2% of dementia patients. Depressive symptoms were associated with lower MMSE scores, worse clinical dementia, a smaller hippocampus and shrinkage in medial temporal lobe. Alfano et al. (2022) confirmed, through a network-to-network analysis, consistent depression pathway in both FTD and PD patients, implying that large-scale brain networks are involved as a shared neurological substrate for these conditions.

Causal factors

Three studies provided a causal component (Rasmussen et al., 2018; Chen et al., 2022; Espinosa-Val et al., 2020).

Rasmussen et al. (2018) confirmed that anxiety and depression are risk factors for both FTD and AD, as anxiety was more commonly reported in people with FTD than people with AD. This may be due to a connection between apolipoprotein E, anxiety, and dementia, and the use of drugs like benzodiazepines.

Chen et al. (2022) found that drug regimens, particularly insulin and sulfonylurea, were linked to an elevated risk of hypoglycemia in older individuals with AD and T2DM. The number of comorbidities is large and connected with hypoglycemia episodes. Hypoglycemia is due to the frequent use of glucose-lowering medicines. Sulfonylureas and glinides, in contrast to metformin, were linked to an increased hypoglycemia incidence.

Espinosa-Val et al. (2020) found that older age, functional reliance, and dementia severity are all risk factors for OD in dementia patients. Poor dental health and respiratory infections are also common in these patients. However, adherence to high viscosity fluids and texture-modified foods is as poor as their clinical outcomes.

Discussion

The objective to investigate dementia and its associated non-psychiatric and psychiatric medical comorbidities was accomplished. Regarding the non-psychiatric diagnosis, for instance, older dementia patients are at risk of severe hypoglycemia (Chen et al., 2022). Dementia severity is higher in patients with OD than in dementia patients without OD (Espinosa-Val et al., 2020) and patients with mixed dementia have the strongest link to diabetes compared to patients with AD (Secnik et al., 2017). Furthermore, dementia patients have an increased risk of cancer after the first year of a VTE diagnosis (Fuglsang et al., 2021). Lastly, dementia patients have a higher risk of seizure disorders than patients without dementia (Habeych et al., 2021).

Among the psychiatric diagnoses, patients with Lewy bodies have a higher depression risk than patients with AD in addition to other complications (Chiu et al., 2017). Patients with FTD and patients with AD have a higher anxiety and depression risk than the healthy control groups (Rasmussen et al., 2018). Lifetime depressive episodes and dementia are unlikely to be caused by smaller hippocampus or white matter abnormalities (Liu et al., 2017). Evidence supports a strong link between thalamic activity and both depressive symptoms and treatment-resistant depression in the FTD and PD groups, (Alfano et al., 2022).

In contrast to prior studies in which Santiago and Potashkin (2021) revealed cardiovascular disorders, inflammatory bowel disease, and amyloidosis are comorbidities associated with dementia, yet none of the three illnesses were detected in the 9 accepted publications. However, one article did incorporate hypoglycemia (Chen et al., 2022) and four articles included depression (Chiu et al., 2017; Liu et al., 2017; Rasmussen et al., 2018; Alfano et al., 2022).

There were a variety of limitations that did not fulfill extensive causal details regarding comorbidities associated with dementia. For instance, a total of six studies have not provided the causal component (Secnik et al., 2017; Habeych et al., 2021; Fuglsang et al., 2022; Liu et al., 2017; Chiu et al.,2017; Alfano et al., 2022).

Secnik et al. (2017) acknowledged that one of the study's drawbacks is that it is observational, which limits the ability to verify causal correlations. Even though type 2 diabetes is the most common, other forms of diabetes were not identified. Habeych et al. (2021) did not find any causal links between seizure types and dementia. Although a very feasible causal explanation for the seizures could be the dementia patients' psychotropic medications. For instance, olanzapine, quetiapine, donepezil, and ginkgo biloba are the most used medications in dementia patients.

Fuglsang et al. (2021) addressed the lack of causal relations in their findings. Cancer risk is not enhanced in patients with dementia with a first-time VTE, according to one interpretation.

Another possibility is that there is a surveillance or survival bias. Liu et al. (2017) discovered that white matter hyper-intensities (WMHs) are unlikely to be the common causes of lifetime depression episodes and dementia.

Since the study by Chiu et al. (2017) is based exclusively on clinical criteria, the causal reasons for depressive symptoms in patients with DLB and AD are not identified despite confirmed dopamine deficit related to differing depressive symptoms between DLB and AD. The results in Alfano et al. (2022) suggest a positive relationship between thalamic activity and both depression symptoms and treatment-resistant depression in FTD and PD patients. However, causal correlations between brain networks and depression were not discovered due to the lack of a fourth group of the depressed healthy control group.

It's strongly recommended to delve further into the causal relations between associated comorbidities with dementia, especially with larger sample sizes with both even-numbered gender groups which is not the case in (Secnik et al., 2017) and (Rasmussen et al., 2018). For instance, the MRI study by Alfano et al. (2022) only has 50 participants and the absence of a depressed healthy controls group.

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