

Comorbidity Profile of Dementia Patients in Primary Care: Are They Sicker?

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OBJECTIVES: To compare the medical comorbidity of older patients with and without dementia in primary care.

DESIGN: Cross-sectional study.

SETTING: Wishard Health Services, which includes a university-affiliated, urban public hospital and seven community-based primary care practice centers in Indianapolis.

PARTICIPANTS: Three thousand thirteen patients aged 65 and older attending seven primary care centers in Indianapolis, Indiana.

MEASUREMENTS: An expert panel diagnosed dementia using *International Classification of Diseases, 10th Revision*, criteria. Comorbidity was assessed using 10 physician-diagnosed chronic comorbid conditions and the Chronic Disease Score (CDS).

RESULTS: Patients with dementia attending primary care have on average 2.4 chronic conditions and receive 5.1 medications. Approximately 50% of dementia patients in this setting are exposed to at least one anticholinergic medication, and 20% are prescribed at least one psychotropic medication. After adjusting for patients' age, race, and sex, patients with and without dementia have a similar level of comorbidity (mean number of chronic medical conditions, 2.4 vs 2.3, $P = .66$; average CDS, 5.8 vs 6.2, $P = .83$).

CONCLUSION: Multiple medical comorbid conditions are common in older adults with and without dementia in primary care. Despite their cholinergic deficit, a substantial proportion of patients with dementia are exposed to anticholinergic medications. Models of care that incorporate this medical complexity are needed to improve the treatment of dementia in primary care. *J Am Geriatr Soc* 54:104–109, 2006.

Key words: dementia; comorbidity; Alzheimer's disease

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In 2000, 35 million Americans were aged 65 and older, representing 12.4% of the U.S. population; 65% of these older Americans suffer from two or more chronic diseases, such as hypertension, diabetes mellitus, osteoarthritis, and coronary artery disease.¹ Medically managing older patients with multiple chronic conditions is challenging. When these patients also suffer from dementia, clinical decision-making and patient self-management become even more difficult.

It is estimated that 3% to 11% of older Americans have dementia.² Dementia leads to a substantial individual, family, and societal burden.² One study found that demented patients reported fewer symptoms during outpatient visits than those without dementia, in spite of having similar degrees of medical comorbidity.³ Even more alarming, in a group of elderly outpatients undergoing evaluation for cognitive impairment, another study discovered a previously undiagnosed but treatable medical disease in almost half of the patients.⁴ Moreover, the interface between dementia and medical comorbidity extends to the hospital care setting. In comparison with hospitalized older adults admitted with an acute myocardial infarction and no history of dementia, those with dementia were less likely to receive optimal management of their myocardial infarction at the time of hospital discharge.⁵

Just as dementia complicates diagnosis and management of medical diseases, comorbidity can also make treating dementia problematic. For example, urinary incontinence, dizziness, and pain are common complaints in older people. Some medications used to treat these symptoms, such as meclizine, amitriptyline, and oxybutynin, have anticholinergic activity. If a cholinesterase inhibitor is being used to treat dementia in a patient who is also taking a drug with anticholinergic activity, pharmacological antagonism can result. This may render the dementia treatment ineffective.⁶ Ultimately, the interaction between dementia and other medical comorbidity presents unique challenges to an already stressed healthcare system and to primary care providers.^{7,8}

Most older adults with dementia, including those with various chronic medical conditions, receive their health care in a primary care setting.⁹ Most primary care practices do not have the resources to provide the appropriate diagnosis, evaluation, education, and complex management required for patients with dementia.^{10,11} Few studies have considered the complexity of providing medical care for patients with multiple comorbid conditions and dementia. As a step in efforts to enhance the primary care setting to accommodate the needs of patients with dementia, the medical comorbidity profile of primary care older adult patients with dementia is described, and their comorbidity is compared with that of patients without dementia. This study sought to shed light on the clinical complexity faced by generalists in a primary care setting when providing care to older adults with dementia.

METHODS

Subjects

The Indiana University—Purdue University Indianapolis institutional review board approved this study, which was conducted at Wishard Health Services (WHS). WHS includes a 450-bed, university-affiliated, urban public hospital and seven community-based primary care practice centers in Indianapolis. Thirty-five general internists on the faculty of Indiana University School of Medicine and 118 internal medicine residents staff these centers. WHS serves an older population consisting of 69% women, 63% African Americans, and 44% with 8 years or less of education.¹⁰ Eligible patients aged 65 and older who were receiving their primary health care within WHS from January 2002 through October 2003 were screened for dementia using the six-item screener instrument¹² and an abbreviated version of the Community Screening Instrument for Dementia.¹³ Prisoners, nursing home patients, patients unable to speak English, those not having access to telephone, and patients not having been seen by a WHS primary care physician within 2 years were excluded. Patients with a positive screening result underwent a subsequent formal neuropsychological assessment and a consensus diagnosis using *International Classification of Diseases, 10th Revision* (ICD-10), criteria. Patients who screened positive and were found to have dementia on further diagnostic confirmation served as a case group, whereas those who screened negative served as controls.

Dementia Diagnosis

The diagnostic examination of patients with a positive screen for dementia on the six-item screener and the Community Screening Instrument for Dementia included a neuropsychological evaluation using the Consortium to Establish a Registry for Alzheimer's Disease battery,¹⁴ a structured interview with an informal caregiver (a spouse, child, or other relative),¹⁵ and review of laboratory tests or brain imaging. The previous examination data were presented to a panel of experts in dementia diagnosis composed of a psychologist, neuropsychologist (FU), geriatrician (MB), and geriatric psychiatrist (HCH). The panel used the ICD-10 criteria¹⁶ to diagnose dementia. Most of the patients with dementia in this study had mild to mod-

erate levels of dementia, as evidenced by their mean Mini-Mental State Examination score \pm standard deviation of 17.7 ± 5.3 . A more-detailed description of the study enrollment and diagnostic methods has been published elsewhere.¹⁰

Assessing Comorbidity

All clinical data were obtained from the Regenstrief Medical Record System, a comprehensive electronic medical record that maintains detailed coded information on all inpatient and outpatient encounters within WHS, including diagnostic studies (e.g., chemistry, hematology, pathology, radiology, echocardiograms), physician orders, and clinical encounter information, including the full text of all dictated reports. Patients' comorbidity was determined using the following methods.

- (1) Common chronic conditions: The sample was evaluated for the presence of 10 common chronic diseases detected by physician-coded ICD-9 diagnoses in the year before enrollment: arthritis, congestive heart failure, coronary artery disease, cancer, chronic obstructive pulmonary disease, diabetes mellitus, stroke, hypertension, kidney disease, and liver disease. These conditions were chosen based on their high prevalence in this older-adult population.⁹
- (2) Chronic Disease Score (CDS): The CDS, a comorbidity measure that assesses the severity of comorbidity based on a participant's medication profile, was applied to each participant's prescription data in the year before enrollment.^{17,18} The CDS excludes medications used for treatment of acute problems (e.g., antibiotics) or common symptoms (e.g., nasal congestion). Individual medications are assigned to pharmacy classes, which are then mapped to the chronic diseases that that class of medication would treat. The original developers assigned each CDS class a weight based on expert judgment. These weights are used to calculate the patient's total CDS (range 0–24). The CDS has been validated as an indicator of comorbidity, and its scores are correlated with future resource utilization. Higher scores indicate greater chronic disease burden and utilization.¹⁹
- (3) Medication use: Prescription records for each patient were also searched to evaluate for the use of medications with central anticholinergic activities and psychotropic medications, such as antidepressants, anxiolytics, and antipsychotics. The anticholinergic activities of each drug were categorized into definite or possible anticholinergic activities based on data from four separate studies.^{20–23} These studies used the in vitro affinity of certain compounds for any muscarinic receptor, the opinion of clinical experts, and the serum anticholinergic activities of each compound. Table 1 provides a list of such anticholinergic medications.

Analysis

Chi-square tests and two-sample *t* tests were used to compare the differences in dichotomous and continuous measures of demographics and comorbidity between the two groups. Furthermore, multivariate logistic regression and analysis of covariance were used to compare comorbidity

Table 1. Medications with a Central Anticholinergic Activity

Definite Central Anticholinergics	Possible Central Anticholinergics
Amitriptyline	Alprazolam
Amoxapine	Brompheniramine maleate
Benzotropine	Bupropion hydrochloride
Chlorpromazine	Captopril
Chlorpheniramine	Chlorthalidone
Clozapine	Cimetidine
Desmethylinipramine	Clorazepate
Diphenhydramine	Codeine
Doxepin	Colchicine
Hydroxyzine	Coumadin
Hyoscyamine	Diazepam
Imipramine	Digoxin
Ipratropium bromide inhaler	Dipyridamole
Loxapine	Disopyramide phosphate
Mecizine	Furosemide
Meperidine	Haloperidol
Nortriptyline	Hydralazine
Oxybutynin	Hydrocortisone
Paroxetine	Isosorbide
Perphenazine	Nifedipine
Promazine	Olanzapine
Promethazine	Prednisone
Quetiapine	Quinidine
Thioridazine	Ranitidine
Trifluoperazine	Theophylline
	Triamterene

profiles between the two groups after adjusting for potential confounders (variables that are associated with both dementia and comorbidity and that are not distributed equally between the two comparison groups), including patients' age, sex, and race.

RESULTS

Three thousand thirteen patients were included in the study. Their mean age was 73.4, 66.6% were female, and 64.5% were African Americans. Patients with a confirmed dementia diagnosis ($n = 107$) were older and were more likely to be male and African American than those who screened negative for dementia ($n = 2,906$) (Table 2).

What is the medical comorbidity profile of dementia patients in primary care? Comorbidity was prevalent in patients with dementia attending primary care clinics. On average, these patients had 2.4 chronic medical conditions, were prescribed 5.1 medications, and had a moderate to severe comorbidity score, as indicated by a mean CDS of 5.8 points. Vascular conditions were common; 82% had hypertension, 39% had diabetes mellitus, 21% had coronary artery disease, 14% had chronic heart failure, and 10% had stroke. A significant proportion of these patients were exposed to medication with anticholinergic properties. Specifically, 22% were prescribed at least one medication with a definite central anticholinergic activity (Table 1), 40% were given at least one medication with a possible

Table 2. Demographic Characteristics of the Study Cohort

Variable	No Dementia (n = 2,906)	Dementia (n = 107)	P-value
Age, mean \pm standard deviation	71.1 \pm 5.6	75.6 \pm 6.2	<.001*
Female, %	70.6	62.6	.09 [†]
African American, %	59.7	69.2	.06 [†]

* Based on *t* test.

[†] Based on chi-square test.

central anticholinergic activity, and 50% were given at least one medication with definite or possible anticholinergic activity. In addition to medical comorbidity, 20% of older adults with dementia attending primary care were receiving at least one psychotropic medication such as an antidepressant (11%), an anxiolytic (7%), or an antipsychotic (4%).

Using various indicators of comorbidity, and after adjusting for patients' age, sex, and race, no differences were found in comorbidity profile between the two groups. The two groups had similar mean numbers of chronic comorbid conditions (2.3 vs 2.4, $P > .65$) and prescribed medications (6.1 vs 5.1, $P > .23$) and similar scores on the CDS (6.2 vs 5.8, $P > .82$) (Table 3). Moreover, the two groups had similar psychotropic (25% vs 20%, $P > .73$) and anticholinergic (55% vs 50%, $P > .36$) medication profiles.

DISCUSSION

This cohort of older adults with dementia cared for in primary care practices suffered from a high level of medical comorbidity and received complex medication regimens, including medications with significant anticholinergic activities. The magnitude of comorbidity in patients with dementia is similar to that in those without dementia, presenting primary care physicians with complicated diagnostic and management decisions for dementia patients who may have difficulty communicating symptoms and following treatment plans. Medical comorbidity, functional status, and cognition in patients with dementia are strongly associated.²⁴ Higher comorbidity in older adults with dementia is associated with lower Mini-Mental State Examination scores, poorer self-care ability, worse mobility, and more problems with incontinence.²⁴ Self-management is one of the cornerstones of effective chronic illness care,²⁵ and even without dementia, older adults struggle with self-management tasks.²⁶

Although this study found no differences in overall comorbidity between patients with and without dementia, the magnitude of comorbidity in patients with dementia is controversial. One study described a sample of patients in an outpatient geriatric program and concluded that patients with Alzheimer's disease were physically healthier than those who did not,²⁷ although another examined hospital discharge data on patients with dementia and found that, although controls matched for age and sex averaged 6.99 comorbid conditions, patients with dementia had a mean of 8.05 comorbidities. In their study, only 0.01% of the patients with dementia had no other chronic disease.²⁸ The data reported in the current study support the latter finding

Table 3. Comorbidity Profile of Older Adults with and without Dementia Attending Primary Care Clinics

Variable	No Dementia	Dementia	<i>P</i> -value	Adjusted <i>P</i> -value [§]
Chronic comorbid conditions, mean ± SD*	2.3 ± 1.4	2.4 ± 1.4	.37 [†]	.66
Hypertension, %	73.5	82.2	.04 [‡]	.06
Diabetes mellitus, %	34.9	39.3	.36 [‡]	.19
Coronary artery disease, %	20.5	20.6	1.00 [‡]	.97
Stroke, %	9.4	10.3	.74 [‡]	.89
Heart failure, %	14.6	14.0	1.00 [‡]	.47
Chronic obstructive pulmonary disease, %	16.7	12.2	.24 [‡]	.33
Cancer, %	12.0	8.4	.36 [‡]	.17
Osteoarthritis, %	36.5	41.1	.36 [‡]	.65
Liver failure, %	0.8	0.0	1.00 [‡]	.98
Renal failure, %	8.3	11.2	.28 [‡]	.77
Medication-based comorbidity				
Chronic disease score, mean ± SD	6.2 ± 4.7	5.8 ± 4.0	.39 [†]	.83
Number of medications, mean ± SD	6.1 ± 5.0	5.1 ± 3.8	.05 [†]	.24
Receiving definite ACH, %	25.7	21.5	.37 [‡]	.68
Receiving possible ACH, %	46.5	40.2	.24 [‡]	.27
Receiving any ACH, %	55.4	49.5	.24 [‡]	.37
Receiving anxiolytics, %	7.2	6.5	1.00 [‡]	.82
Receiving antidepressants, %	19.7	11.2	.03 [‡]	.17
Receiving antipsychotics, %	2.3	3.7	.31 [‡]	.26
Receiving any psychotropic, %	24.9	19.6	.25 [‡]	.73

* Based on International Classification of Diseases, Ninth Revision.

[†] Based on *t* test

[‡] Based on chi-square test.

[§] Based on a logistic regression model and analysis of covariance that adjusted for patients' age, sex, and race.

SD = standard deviation; ACH = medication with anticholinergic activities.

and show chronic disease comorbidity to be a similar burden for older people with and without dementia, although the lack of comorbidity differences between the two groups may be due to the underreporting of symptoms by the dementia patients³ and the underdiagnosing of medical problems by the primary care physicians.⁴ Nevertheless, this study is the first to describe and compare the magnitude of comorbidity in an entire population of primary care patients.

Medications with anticholinergic activities are considered to be a common source of central or peripheral adverse effects (AEs). Peripheral AEs include falls, dry mouth, constipation, urinary retention, blurred vision, increased heart rate, and decreased sweating.^{29,30} Central AEs vary from decreased concentration, memory problems, cognitive impairment, and mild confusion to a frank delirium.^{20,21,23,29} Both types of these AEs negatively affect the functional status and quality of life of older adults and increase their healthcare utilization. For example, in older adults undergoing elective major surgery, delirium increased the probability of major complications (15% in delirious patients vs 2%), death (4% vs 0%), length of stay (15 vs 7 days), and institutionalization (36% vs 11%).³¹ Approximately half of this study population received at least one medication with definite or possible anticholinergic properties. Depending on the measurement method, the clinical setting, and the population studied, the prevalence rate of anticholinergic medication use in this study falls in the range of 13% to 90% reported by other studies.^{21,32,33} In a random sample of 201 community-

dwelling older adults, 51% of participants were taking at least one anticholinergic medication,²¹ and in another study of 5,902 older patients published in 1983, 23% of individuals attending an ambulatory clinic and 60% of those residing in nursing homes received drugs with anticholinergic properties over 1 year.³³

Although patients with and without dementia had similar anticholinergic profiles, the already-depleted cholinergic state of patients with dementia puts them at higher risk for anticholinergic AEs. The high number of older adults with dementia who were prescribed anticholinergic medication (50%) is troubling. Patients with dementia who are receiving anticholinergics are more vulnerable to the development of delirium, falls, and worsening cognitive deficits.³⁴ Furthermore, they are less likely to benefit from the use of cholinesterase inhibitors, which are considered the current standard of therapy for patients with dementia of the Alzheimer type.² Improvement in prescribing patterns for dementia patients may influence cognitive and medical impairments and lead to better health outcomes.

The primary care provider faces significant complexity when approaching a patient with dementia. The patient may not be able to adequately recall recent symptoms, and language deficits may impair the reporting of ongoing symptoms or drug side effects. Given the significant comorbidity in outpatients found in this study, primary care providers must be vigilant for underlying medical conditions and must take detailed medication histories. Challenges exist when medications with anticholinergic side effects are necessary to treat medical conditions. Whether

mortality, excess disability, or time to institutionalization can be prevented or delayed with maximal medical management of comorbidity is unknown. Answers to such questions can only be obtained through research that addresses the management of dementia in the context of the patients' other comorbid conditions and their treatments.

Although patients with dementia have higher reported rates of behavioral and psychological symptoms associated with dementia (BPSDs) than those with no dementia,³⁵ the current study found no differences in the use of psychotropic medications between the two groups. This lack of drug treatment for prevalent symptoms does not indicate that these symptoms were less prevalent in patients with dementia attending primary care clinics. On the contrary, the similarity in psychotropic use between the two groups may be due to the underreporting of BPSDs by the patients with dementia³ and the low dementia recognition rates by the primary care system.² However, lack of differences in the use of psychotropic medications may also indicate that the severity of BPSDs did not trigger the need for pharmacological interventions by the physicians.

This study had some limitations. Patients who screened negative were not sampled to assess for the false-negative rate of the screening program. Therefore, the control group may have included some cases of mild dementia. The effect of these possible false negatives on the study aim is not known. Data were not collected on the reason for anticholinergic or psychotropic medication use, and thus a judgment cannot be made about the appropriateness of using such medications in the study population. Finally, the comorbidity measures were based on physician documentation of chronic medical condition and were not confirmed by objective tests.

In summary, patients with dementia in primary care have a high level of medical comorbidity and are prescribed complex medication regimens. Currently, guidelines for the care of older adults with dementia offer little direction on balancing the competing demands or AEs of treatments for comorbid conditions. Yet patients with multiple comorbid conditions are not the exception, but rather the rule, among older patients with dementia in primary care. Models of care that incorporate this medical complexity are needed to improve the care of dementia in primary care.

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