Heart Failure, Metabolic Risk Factors and Dementia in South-Central United States

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Abstract

Objective: Heart failure (HF) is a frequent co morbid condition in the geriatric population and is the most common cause for hospitalizations and readmission in the elderly. The objective of this study was to attempt to define the impact of HF and its common co-morbid conditions on development of dementia.

Research Design & Methods: This was a retrospective study of elderly patients attending the out-patient geriatric clinic at the University of Arkansas for Medical Sciences. We analyzed the electronic health records of 252 HF patients with a mean age of 83 years for co-morbid conditions of hypertension, hyperlipidemia, diabetes mellitus and dementia. The relationship of BMI with these conditions was also determined.

Results: The most common co-morbid condition associated with HF was hypertension (97.2%), followed by hyperlipidemia (73.4%), diabetes (35.3%), and dementia (38.8%). Patients on average had 2 -3 co-morbid conditions in addition to HF. In the group with two co-morbid condition in addition to HF, the most common were hypertension and hyperlipidemia (72.6%), followed by hypertension and dementia (15.8%). In HF plus three co-morbid conditions, a combination of hypertension, hyperlipidemia, diabetes were the most common at 52.2%, followed a combination of hypertension, hyperlipidemia, dementia (42.2%).

Conclusion: Dementia appears to be a common co-morbid condition associated with HF and if the co-morbid conditions are well-managed, the progression of dementia could be reduced or modified. Primary healthcare providers as well as cardiologists should evaluate all HF patients for dementia through quick screening procedures.

Keywords: Heart failure, Metabolic syndrome, Dementia

Introduction

Heart failure (HF) is a frequent co morbid condition in the elderly and is the most common cause for hospitalizations and hospital re-admission in the elderly [1-5]. The estimated direct and indirect cost of HF in the Unites States for 2012 was $30.7 billion [6]. In the USA approximately 1.5-2% of the total population and over 10% of the elderly suffer from HF [7,8]. Additionally, the prevalence of HF increases dramatically with age. From about age 55 years onward, it doubles every 10 years in men and every 7 years in women [1,2,7,8]

Advancing age is the top risk factor for cardiovascular diseases and for dementia [1-8], although life-style & nutritional choices also have an effect [9-16]. The rapidly changing demographics estimates that by 2040, people over 65 will comprise approximately 21%, of the US population [1]. This growth will result in a significant increase in the incidence and prevalence of age-associated diseases, including HF, cardiometabolic diseases and dementias [1, 17-19].

Many of the common co-morbid conditions associated with HF such as hypertension (HTN), hyperlipidemia (HLD), obesity, and diabetes (DM) also predispose to cognitive decline [17-19]. However, dementia has not been as well studied in the context of HF [20-25]. Older individuals with a history of midlife or current HTN are nearly twice as likely to develop dementia as those who have never had HTN [26]. This may be due to long term HTN leading to more severe vascular disease and impacting cerebral blood perfusion. However, HTN treatment may lower the dementia risk; directly through lowering high blood pressure, and indirectly through a neuroprotective effect

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[27,28]. While HLD has been associated with increased HF risk, there is some evidence that it might be associated with increased dementia risk and β-amyloid, Alzhemier's-like pathology both in animal models and humans [15,29-34]. Chuang et al. found that risk of dementia may decrease with statin use [33]. There is mounting evidence that dementia may have a similar relationship to body mass index (BMI) to that of cardiovascular disease. Additionally, the data indicate that individuals who have low BMI in midlife are nearly twice as those with normal BMI to develop dementia [35,36]. However, there is some conflicting evidence as to whether obesity increases, decreases, or has no effect on dementia risk [35-37]. In the study of metabolic diseases there is considerable literature to support a strong relationship between DM and increased risk of dementia [13,14,38-41].

In as much as there is an ongoing rapid increase of the aging population, we conducted a retrospective review of community dwelling elderly to assess the associations between HF and the common co-morbid conditions of hypertension, diabetes, hyperlipidemia and dementia.

Methods

Study Population

A Dataware house search for elderly patients with HF at the University of Arkansas for Medical Sciences (UAMS) was performed and a total of 252 records of subjects with a documented diagnosis of HF who had attended the geriatric out-patient clinic from 2011 to 2016 were randomly selected for review. Data were collected from the most recent visit recorded in the electronic medical records (EMR). Data included subject demographics, physiologic, metabolic, biochemical and medication information. This study was reviewed and approved by the UAMS Institutional Review Board.

Criteria and definition

The inclusion criteria used for this analysis were: age ≥ 65 years, both genders, all ethnic groups, with a clinically documented diagnosis of any subtype of HF, including, diastolic, systolic, combined heart failure or heart failure with preserved ejection fraction (HFPEF). Data on co-morbidities included diagnoses of HTN, HLD, DM and dementia from the problem list. In addition, the medication list was reviewed in case the problem list was not comprehensive. In the event that the medication list indicated the presence of one of the listed diagnoses, the condition was added to our analysis as if it were on the problem list. Patients were grouped according to the number of comorbid conditions they were diagnosed with in addition to HF. HTN was defined as a need for anti-hypertensive medications or systolic ≥140 mmHg or diastolic ≥90 mmHg. HLD was defined as a need for hypolipidemic medications or a total plasma cholesterol level over 200mg or LDL over 130 or treatment with lipid-lowering agents. DM was defined as FPG ≥126 mg/dL (7.0 mmol/L), HbA1C ≥6.5% or treatment with insulin or oral hypoglycemic medications. Dementia was defined as clinical diagnosis of any subtype of dementia (vascular, Alzheimer, Lewy Body, post-traumatic, Parkinsonian or documentation of cognitive impairment due to other causes) of any degree requiring treatment with dementia drugs.

BMI was divided up into the categories of underweight (BMI ≤24), normal (BMI 25-29), overweight (BMI 30-34), and obese (BMI ≥35).

Results

The mean age of the study population was 84±7.6 years. There were 65.5% White and 35.5% African Americans (Table 1 and Figure 1). The percentage of individual comorbid conditions with HF in the study were HTN (97.2%), HLD (73.4%), dementia (38.8%) and DM (35.3%) (Figure 2). However, more frequently patients had 2 or 3 coexisting health conditions in addition to HF
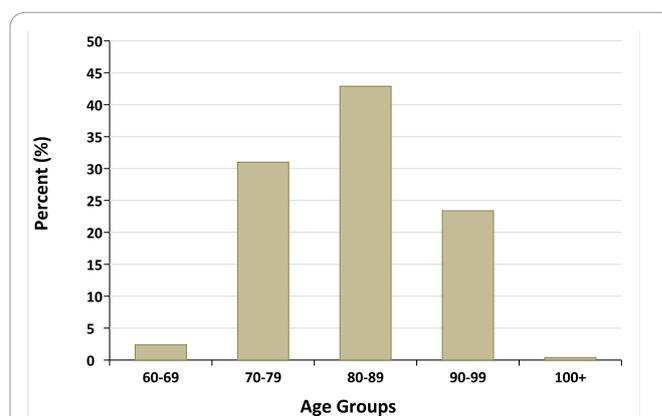

Figure 1: Age distribution of patients in the study. Mean age of the patients was 84 ± 7.6

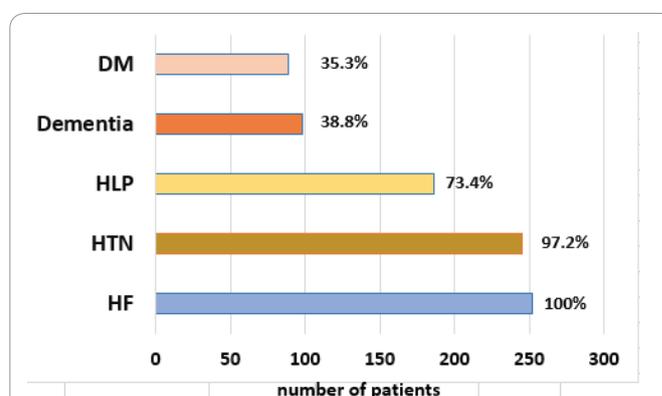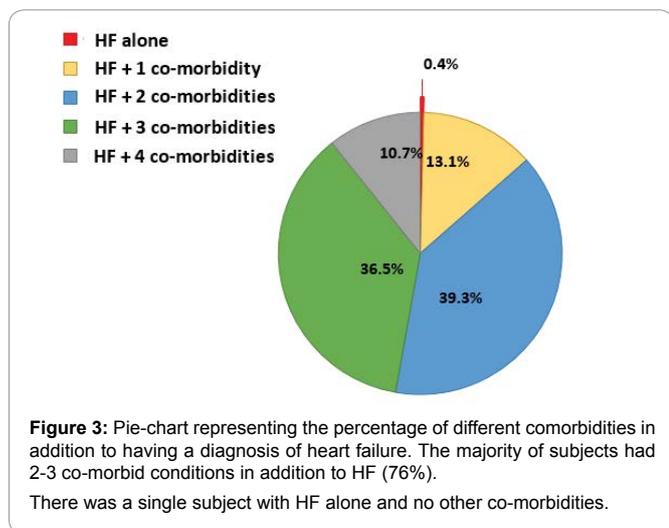| Demographics	N	Percent (%)
Race/Ethnicity		
African American	87	34.5
White	165	65.5
Gender		
Female	192	76.2
Male	60	23.8
N=252 patient charts, analyzed at their most recent encounter. Mean age = 84±7.6		

Table 1: Population demographics

Figure 2: The number and percentage of subjects with comorbid conditions of heart failure (HF), hypertension (HTN), hyperlipidemia (HLP), dementia or diabetes mellitus (DM) in the study.

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Figure 3: Pie-chart representing the percentage of different comorbidities in addition to having a diagnosis of heart failure. The majority of subjects had 2-3 co-morbid conditions in addition to HF (76%).

There was a single subject with HF alone and no other co-morbidities.
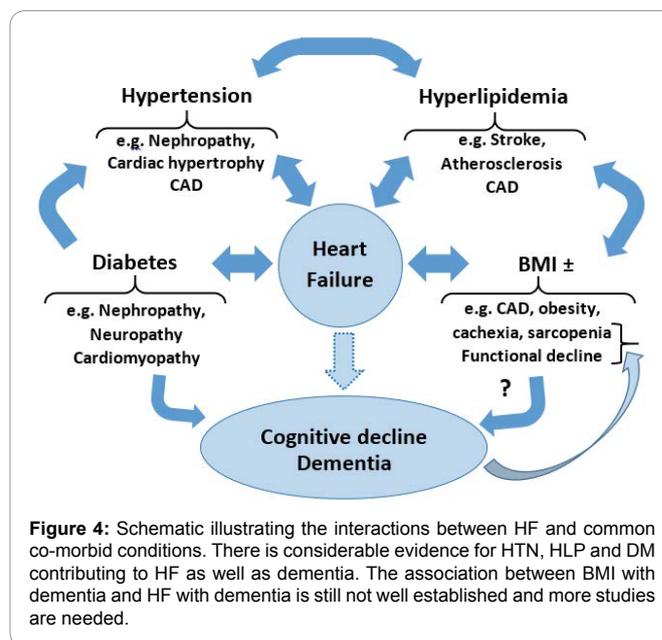
(Figure 3). In the group of patients who had 2 comorbidities in addition to HF, the greatest number had HTN plus HLD (72.6%), followed by HTN plus dementia (15.8%). In the group of patients who had 3 comorbidities in addition to HF, HTN, HLD, DM were the most common (52.2%), followed by a combination of HTN, HLD, dementia (42.2%). A maximum of four co-morbidities with HF were present in only 10.7% patients (Figure 3).

We also categorized patients according to BMI levels as ≤ 25 (underweight), 25-29 (normal weight), 30-34 (over-weight), and over 34 (obese). Data on BMI was available on 241 patients. The underweight group was the largest at 34% followed by the normal weight at 29.1%, over-weight at 22.4% and obese at 14.5% of patients. Since BMI can be affected by anti-psychotics, we reviewed the records and found 161 patients with complete medication documentation. In the subset of patients with recorded medications, only 14 patients (8.7%) were on antipsychotics. Additionally, we did a separate analysis of the subset of patients who had a diagnosis of dementia and found that 91.8% of demented patients had HTN, 69.3% had HLP and 33.6% had DM. In the same group of demented patients, 35.7% were underweight, 20.4% were overweight and 9.1% were obese. Only about one-third of the demented patients had BMIs within the normal range.

Discussion

There are several interesting findings from this retrospective study: 1) Most patients had at least two comorbidities in addition to HF; 2) If a patient with HF had HTN, they were more likely to have HLD or dementia; 3) In the presence of 3 comorbid conditions, HF appeared to have a slightly greater association with dementia than DM.

Our report is among only a few studies, particularly those regarding metabolic syndrome, that have included such a high percentage of octagenarians and nonagenarians [16,21]. Additionally, all of these patients had HF, allowing us to explore the interactions between HF, and the various comorbidities that comprise the metabolic syndrome plus the association with dementia. These complex interactions are discussed below and are also outlined in the schematic in Figure 4.

Figure 4: Schematic illustrating the interactions between HF and common co-morbid conditions. There is considerable evidence for HTN, HLP and DM contributing to HF as well as dementia. The association between BMI with dementia and HF with dementia is still not well established and more studies are needed.

Hypertension

HTN is prevalent in more than 75% of adults over 75, and is associated with HF and many other health conditions [6]. It is therefore not surprising that HTN was the most common comorbidity of HF in our study and although we used a criteria of 140/90 as a cut-off for HTN diagnosis in this study, there is recent evidence to support that in elderly ≥ 75 years, a systolic BP of 120 mm Hg resulted in significantly lower rates of fatal and nonfatal major cardiovascular events and death from any cause [42]. Hypertension is also associated with dementia, as those with a history of HTN have nearly twice the risk of developing dementia compared to those who do not have hypertension [26,28]. However, very few studies have investigated whether anti-hypertensive agents affect either the risk of developing dementia, or exacerbate existing dementia. Conversely, few studies have been performed on cerebral blood perfusion although there is evidence to suggest that a U-shaped relationship exists between pulse pressure and dementia [43]. This will need further investigation controlling for age-groups, gender, BMI and other co-morbidities. In our study, approximately nine out ten patients with dementia also had HTN. However, it is not clear whether in a population without HF, there will be a close association of HTN with dementia.

Hyperlipidemia

While HLD has been implicated in the development of various cardiovascular issues, the literature is unclear as to whether it may increase dementia risk [41,44]. One study reported that HLD occurred in 3-4% of those with dementia, and another study found that it increased dementia risk slightly in those with DM [45,46]. Additionally, atherosclerosis, cerebrovascular disease, and ischemic heart disease, conditions for which HLD is a risk factor, were found in approximately 3%, 6%, and up to 7% of those with dementia, respectively [45]. Contrary to the low prevalence of HLP in patients with dementia in some studies, approximately one-third of the demented patients in our study had HLP. This difference could reflect a lower screening for HLD in other studies as well as a lower prevalence of HLP in other

populations compared to our patient population from south central United States. Apart from ischemic heart disease, HLD is also a risk factor for stroke, which is present in approximately 20% of demented patients [47]. Additionally, increased LDL and decreased HDL have been shown to be associated with greater amyloid-β (Aβ) deposits [34,48]. Aβ degradation appears to be less efficient in a hyperlipidemia microenviroment, increasing the overall burden of amyloid deposits and consequently dementia [48]. Although statins are considered beneficial in dementia associated with cardiovascular disease and hyperlipidemia, there are a few small reports that suggest a higher risk of cognitive impairment with the use of statins, [21,33,44].

Suboptimal BMI

In our study, approximately one-third of the patients with dementia and heart failure were underweight and about nine percent were in the obese range. Since we did not have data on body composition, this obesity could have reflected the poorly controlled HF and fluid-overload in some patients.

Interestingly, people with low BMI are 1.9 times more likely and obese individuals 1.6 times more likely vs those with normal BMI to develop dementia in late life. This U-shaped relationship that exists between increased risk of developing dementia and BMI in midlife that seems to disappear in late life [35]. Sarcopenic obesity is independently associated with increased risk of cardiovascular mortality [49]. A higher BMI might also contribute to the risk of dementia risk through decreased insulin sensitivity and development of DM [50,51]. However, some investigators have found that high BMI may not have any association, or even a reverse association, with dementia risk [36,37]. With the increasing number of studies providing ever more evidence between suboptimal BMI and increased risk of dementia, finding ways to promote and maintain optimal BMI might be key in reducing the prevalence of dementia as well as the associated co-morbid cardiovascular risk factors (Table 2).

Diabetes

DM is associated with high morbidity and mortality in the

BMI Demographics				
	African American		White	
	Male	Female	Male	Female
N	16	68	42	115
Average Age	80	83	84	84
BMI Groups				
Under 25	31.25	26.471	38.095	37.39
25-29	6.25	29.412	28.571	32.17
30-34	31.25	30.882	21.429	16.52
Over 34	18.75	10.294	19.048	14.78
BMI data available in 241 patients.				

Table 2: Distribution of BMI in the study population.

elderly and has recently been linked to dementia [38-40,50,51]. Patients with DM are 1.5-2.5 times more likely to develop dementia vs non-diabetics [38-40,51-55]. In our subset of patients with HF and Dementia, approximately one-third also had Type 2 DM. It is known that DM increases the dementia risk through multiple mechanisms including, increased systemic inflammation, micro- and macrovascular disease, hyperglycemia and hypoglycemic episodes, and insulin dysfunction that directly and indirectly influences the brain health [39-41,56-63]. Cerebral infarcts also occur with greater frequency in DM patients vs non-diabetics [40,52,55]. The majority of the patients in our study (≈80%) had been managed only on oral hypoglycemic agents, with metformin being the most commonly used agent. Cheng et al. and Kuan et al. found a reduction in increased dementia risk in diabetics treated with oral anti-diabetic medications and in hypertensive diabetics treated with anti-hypertensive medications [58,59].

Dementia

Advancing age is the top risk factor for cardiovascular diseases and dementia and a number of studies have suggested a strong association between the two [1,60,64-66]. A literature review of co-morbid conditions in the geriatric population during the last quarter of a century demonstrated less than 100 primary studies [47]. Data from a number of studies show that only 12% of patients with dementia had no reported comorbidities [45]. In spite of the high prevalence of HF in the elderly, relatively few studies have investigated the association of HF with dementia, especially with Alzheimer disease [9,11,21,60,65]. However, this is an area of increasing interest in basic science and currently many models of heart failure with different common co-morbid conditions are being explored to enhance our understanding of the complex connections between the heart and the brain and the possible therapeutic options that will benefit both organs [58,63,67].

Study limitations and strengths

There were several limitations to this study. First, the retrospective nature of this study dictated the interval at which patient data was recorded, which was sometimes irregular or incomplete. Additionally, the small sample size from rural Arkansas might not be representative for the whole country. The diet in the southern part of the country is different from that in the north and could have influenced the metabolic profile of the subjects. Because of small study sample, we did not stratify HF or dementia by sub-types. Nevertheless, there were also few strengths which included a large percentage of African Americans in our study population compared to the national mean (34 % vs 12%). We have one of the largest geriatric out-patient clinics in the country and it is possible that there was greater screening for dementia by geriatricians than what ordinarily occurs in other primary care settings.

Conclusions

HF is a classic example of a common geriatric condition that is associated with multiple co-morbid conditions that require careful evaluation. Similar to HF, dementia might also have potential modifiable cardiometabolic risk factors that should be reviewed. The diagnosis of dementia is often made in a primary care or neurology clinic. However, many geriatric patients with chronic diseases visit specialty clinics focused on non-

cognitive issues, hence the diagnosis of dementia is often missed. Conversely, the primary care physician might not fully appreciate the effect of HF on cognition. Healthcare providers should keep the cognitive health of the patient in mind while diagnosing HF and prescribing treatment. Adequate management of HF and associated co-morbid conditions could potentially prevent further cognitive decline and preserve functional independence of older adults.

Conflict of Interest

The authors have no conflicts of interest to declare.

Author contributions

All authors contributed to the manuscript.

Acknowledgments

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