

RISK FACTORS FOR VASCULAR DEMENTIA

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Dementia is a devastating disorder that commonly affects people over the age of 65. Alzheimer's disease and vascular dementia are the most common forms of dementias. A number of studies have implicated cardiovascular risks as important factors in the development of dementia. These risks include high-risk behaviors such as smoking and risks related at least partially to health behaviors such as diet and exercise. This study examines a group of cardiovascular risk factors, as defined by the Framingham study, to ascertain if they are predictors of dementia. A retrospective chart review of 481 consecutive patients seen in a geriatric medicine clinic produced a sample of 177 individuals diagnosed with dementia and 304 individuals without a dementia diagnosis. Relative risk ratio (RRR) results indicate that a history of hypertension (RRR= 1.80, $p = .009$) and a history of hypercholesterolemia (RRR = 1.85, $p = .016$) are significant predictors of Alzheimer's disease. A history of tobacco use (RRR = 2.18, $p = .01$) is a significant predictor of vascular dementia. Stepwise regression analyses indicate that hypercholesterolemia is an independent predictor of dementia ($\beta = -.113$, $p = .009$) and hypercholesterolemia ($\beta = -.104$, $p = .018$) and hypertension ($\beta = -.094$, $p = .031$) clustered together have an additive risk factor effect. These results are discussed in terms of the importance of specific health behaviors in the development and possible prevention of dementia.

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INTRODUCTION

Vascular dementia is the second most common form of dementia following Alzheimer's disease, and commonly affects elderly people over the age of 65 (Roman, and Royall, 2004; Roman, 2000; Kalaria, 2002; and Schmidtke, and Hull, 2002). Vascular dementia is caused by decreased or interrupted blood flow to parts of the brain, which is predominantly caused by cerebrovascular accident or stroke (Schmidt, Schmidt, and Fazekas, 2000; Watari, and Gatz, 2002; Schmidtke and Hull, 2002; Rockwood, 2002; and Alva, and Potkin, 2003). Both cardiovascular disorders, such as myocardial infarction, stroke, and coronary artery disease and vascular dementia are caused by either small or large arterial damage and/or blockage. Research indicates there is a common pathology between Alzheimer's disease and vascular dementia (Sadowski et al., 2004) in that risk factors such as hypertension, Type 2 diabetes, and high cholesterol have been shown to increase the risk of vascular dementia as well as Alzheimer's disease.

Among the cardiovascular risk factors related to vascular dementia are hypertension, atherosclerosis, coronary artery disease, diabetes mellitus, and smoking (Kalaria, 2002; and Schmidt, Schmidt, and Fazekas, 2000). Additionally factors such as advancing age, low level of education, blue-collar employment, exposure to environmental pollutants, and stress have been related to vascular dementia (Watari, and Gatz, 2002). The Framingham model of cardiovascular risk factors identified several physiological and behavioral factors that are predictors of cardiovascular disease, which include hypertension, diabetes mellitus, and smoking. It is apparent that the risk factors for these two vascular diseases are similar.

The Framingham Study was instrumental in identifying the risk factors for cardiovascular disease, stroke, and other vascular diseases (Kannel, Dawber, Kagan, Revotskie, and Stokes, 1961; and Mehta, and Khan, 2002). This initial study spanning from 1948 to 1961 was the first to

include women in a cardiovascular risk study. The Framingham Study's longitudinal design was instrumental in identifying risk factors, provide information for managing risk factors, identifying the etiology of cardiovascular diseases, and identifying the complications of cardiovascular disease. The Framingham Study showed that hypertension, smoking, and hypercholesterolemia are major risk factors for cardiovascular disease (Mehta, and Khan, 2002).

Recent research on vascular dementia has identified risk factors for vascular dementia including arterial hypertension, atrial fibrillation, myocardial infarction, coronary heart disease, diabetes, generalized atherosclerosis, lipid abnormalities, and smoking (Erkinjuntti, 1999; Kalaria, 2002; and Leys, and Pasquier, 1998).

Hypertension is common in the older population. In fact, the incidence of hypertension increases with advancing age (Vasan, Larson, Leip, Kannel, and Levy, 2001). High blood pressure is identified as being a major risk factor for cardiovascular disease, stroke, and vascular dementia (Bornebroek, and Breteler, 2004; Vasan et al., 2001; Guo, Viitanen, Fratiglioni, and Winblad, 1997; Kannel, 2000; Launer, Ross, Petrovich, Masaki, Foley, White, and Havlik, 2000; Roman, 2002; and Schmidt, Schmidt, and Fazekas, 2000). Long-term, uncontrolled hypertension, especially elevated systolic blood pressure (Kannel, 2000), causes structural changes in arterial resistance (Guo et al., 1997). This resistance is caused by the constant accommodation of the vessels to the ever-elevated blood pressure, causing atherosclerosis, wall thickening, luminal narrowing, and other vessel damage (Guo et al., 1997). Due to these effects, the auto-regulation of blood flow to the brain is changed (Launer, 2000). This change further adds to vessel resistance, causing more increases in blood pressure, sustaining elevated pressure and producing a vicious cycle that can lead to stroke, cardiovascular disease, and dementia (Guo et al., 1997). In fact, approximately 70% of stroke patients have a history of hypertension. It is

believed that the change in blood pressure following a stroke is a major contributor to vascular dementia (Guo et al., 1997).

In the Honolulu-Asia aging study, researchers found that persons who had hypertension at mid-life, were at an increased risk for dementia late in life (Launer et al., 2000; and Bornebroek, and Breteler, 2004). Hypertension is associated with brain atrophy, large and small artery infarction, and white matter lesion progression due to altered auto-regulation of blood flow to the brain (Launer et al., 2000). Small artery disease causes periventricular white matter ischemia and lacunar strokes that manifests as vascular dementia (Roman, 2002).

Risk factors for stroke do not independently contribute to dementia (Schmidt, Schmidt, and Fazekas, 2000) but commonly occur in clusters of risk factors. For example, when a person has hypertension, they usually also have one or more of the following co-risk factors: obesity, dyslipidemia, glucose intolerance, and left ventricular hypertrophy (Kannell, 2000). In fact, Kannell (2000) found that 80% of persons with hypertension also have high triglyceride and LDL cholesterol levels, lowered HDL levels, glucose intolerance, hyperinsulinemia, obesity, and left ventricular hypertrophy. Hypercholesterolemia is a major risk factor for cardiovascular disease and cerebrovascular disease (Bray, and Clark, 1984). High cholesterol and hypertension can promote atherosclerosis, which reduces blood flow. This decreased blood flow increases the risk of vascular dementia (Frye-Pierson, and Toole, 1987; and Kivipelto, Helkala, Laakso, Hanninen, Hallikainen, Alhainen, Soininen, Tuomilehto, and Nissien, 2001).

Type-2 diabetes mellitus is another common progressive and disabling disease in persons over the age of 65 (Allen, Frier, and Strachan, 2004). In fact, 10% of persons over 65 develop diabetes and more than 50% develop diabetes over the age of 85 (Allen, Frier, and Strachan, 2004). Cognitive decline and dementia have been associated with diabetes (Allen et al., 2004). As stated earlier, vascular risk factors commonly cluster together in groups of risk factors

(Schmidt, Schmidt, and Fazekas, 2000; and Allen et al., 2004). The longer a person has diabetes, the more at risk they are for significant cognitive decline (Bruce, Harrington, Davis, and Davis, 2001). Elderly diabetic persons are approximately twice as likely to develop dementia as the normal population (Bruce et al., 2001). Many older adults may have had diabetes for several years before they actually receive a diagnosis and therefore may have unknowingly been at a higher risk for dementia (Allen et al., 2004). Since diabetes is often not diagnosed, it often does not appear as a significant risk for the development of cognitive disorders (MacKnight, Rockwood, Awalt, and McDowell, 2002). The prevalence of hypertension and dyslipidemia in diabetic persons may explain this increased risk (Bruce et al., 2001), thus the clustering effect of risk factors.

Diabetes and hypertension have been found to be independent risk factors for cerebrovascular disease and cardiovascular disease (Game, and Jones, 2001; and Kannel, 2000). Persons who have mild dementia are more likely to have heart disease and diabetes than persons without these factors (Coker, and Shumaker, 2003) suggesting that diabetes may be a risk factor for vascular dementia (Coker, and Shumaker, 2003).

In order for cortical neurons to be able to maintain normal functioning, the brain has to maintain a consistent supply of glucose (Launer, 2002). Diabetes interrupts this consistent supply of glucose thus causing cortical insufficiency (Coker, and Shumaker, 2003) and ultimately neuronal death (Bornebroek, and Breteler, 2004). Another negative effect of diabetes is that hyperglycemia alters the metabolism of glucose, which in turn reduces the production of acetylcholine neurotransmitter, which decreases memory (Launer, 2002). Hypoglycemia affects the brain's efficiency in that it causes a deprivation of nutrients (glucose) to the brain and increases glutamate, which becomes toxic in large amounts (Launer, 2002). Diabetes also contributes to microvascular changes in the brain, which in turn contribute to stroke and also

cognitive dysfunction (Coker, and Shumaker, 2003). These vascular changes may cause a decrease in the cerebral blood flow, thus contributing to vascular dementia (Bornebroek, and Breteler, 2004).

Smoking is one of the most well known risk factors for cardiovascular disease and cerebrovascular diseases and increases the risk of vascular dementia in this population (Ott, Slioter, Hofman, van Harskamp, Witteman, van Broekhoven, van Duijn, and Breteler, 1998; and Tyas, White, Petrovich, Ross, Foley, Heimovitz, and Launer, 2003; and Bornebroek, and Breteler, 2004). In one study, researchers found that the number of packs of cigarettes per year (pack-years) predicted the risk of dementia with increased risk with more pack-years (Tyas et al., 2003). According to the American Heart Association and American Stroke Association, tobacco smoke, even second hand smoke, places people at a 30%+ risk of cardiovascular disease (American Heart Association, 2002).

Smoking causes the blood vessels to spasm and to constrict producing increased resistance, and impairing blood flow (Frye-Pierson, and Toole, 1987). This decreased blood flow to the brain increases the risk of stroke, and increases the risk of other micro and macro vascular diseases, which ultimately lead to dementia. Smoking also increases blood pressure due to this increased vascular resistance. Due to the increased blood pressure over time, the vascular walls deteriorate and harden, which promotes arteriosclerosis (hardening of the arteries) and atherosclerosis (build up of plaques on artery walls) (Bray, and Clark, 1984).

Risk factors for cardiovascular and cerebrovascular disorders do not occur in a vacuum; they often occur in clusters and have an additive effect. The risk factors that have been discussed represent risk factors that have a behavioral component. The ability for persons at risk and those who treat them, to know and understand how behavior affects physiological and psychological health is paramount for the prevention of devastating vascular disorders and dementia. The

purpose of the current study is to explore and identify risk factors for dementia. This information may aid in the future diagnosis, management, and treatment of persons at risk for or diagnosed with vascular dementia. The hypothesis of this study is that hypertension, diabetes, smoking, and hypercholesterolemia are risk factors for dementia.

METHODS

A sample of 481 participants were recruited from a list of all patients assessed or admitted to the Geriatric Assessment Program (GAP) clinic at the University of North Texas-Health Science Center (UNT-HSC) from January 1998 through April 2003. The sample consisted of 111 male and 370 female participants ranging in age from 55 years old to 98 years old with a mean age of 77.39. All included participants received a complete initial medical evaluation in the GAP clinic. A review of patient charts was conducted to gather all data. The institutional review board at UNT-HSC approved the retrospective chart review and did not require informed consent. All information gathered is kept in a locked file cabinet with limited access to ensure confidentiality of all subject information and the data collected.

The data collection sheet that was used in the current study included many variables that were used in the Framingham study (Wilson et al., 1998), see (Appendix). Categories of these variables included demographic information, behavioral risk factors, medication history, diagnosis of dementia, and past medical history.

Demographic information included each participant's gender, age, race, and date of initial evaluation. Behavioral risk factors included participant's tobacco use, alcohol use, and illicit drug use. The participant's currently prescribed medications were included in the medication history. Individuals who received a diagnosis of dementia either from a physician or by a psychologist or both were identified with a diagnosis of dementia. If a participant did not receive a diagnosis, this section was left blank, indicating no diagnosis. The final category of variables included a medical history. The variables included cardiovascular risk factors, cardiopulmonary risk factors, and cerebrovascular risk factors.

One set of statistical analyses used included stepwise linear regression, multinomial logistic regression and proportional hazards regression (relative risk ratio analysis) using a

polynomial independent variable. Regression analyses provided information on the relationship between the individual cardiovascular risk factors used, as defined by the Framingham study (Wilson et al., 1998) associated with the study subjects (Dupont, 2002). The second set of statistical analyses included logistic regression and odds ratio using a binomial independent variable. The reason for the different statistical analyses was to obtain the information needed to compare relative risk of cardiovascular risk factors for categorical dementia diagnoses (Alzheimer's disease, vascular dementia, other dementia diagnosis, and no dementia diagnosis) to a general dementia diagnosis (dementia diagnosis and no dementia diagnosis). A correlation analysis was conducted to explore the relationship between the risk factors used in this study.

In the original Framingham study a Cox regression was used. A Cox regression analysis needs to have continuous variables in order to elicit meaningful data. This type of analysis was not possible in the current study as the variables used included categorical variables. Multinomial logistic regression was used instead of the Cox regression in order to explore logistical odds of the independent variables to the dependent variable (Dupont, 2002). This type of statistic is similar to proportional hazard analyses (relative risk ratio). Proportional hazard analyses were used to identify the relative risk of each cardiovascular risk factor to the diagnosis of Alzheimer's dementia, vascular dementia, and other dementias (Dupont, 2002).

RESULTS

Participants range in age from 55 to 98 and a mean age of 77, $SD = 8.13$. The sample consisted of 481 participants, 111 male and 370 female. This gender difference is indicative of a 3:1 gender ratio that is consistent with elderly adults. The sample consisted of 116 persons with a diagnosis of Alzheimer's disease, 61 with vascular dementia, and 304 with no diagnosis of dementia. The participants with no diagnosis of dementia were further separated into three subcategories (medical concern, memory concern, or no specific concern) depending on why they were referred to the Geriatric Assessment Program (GAP) clinic

Analyses using Polynomial Independent Variable for Demented Participants

Relative risk ratio analyses indicate that a history of hypertension ($RRR = 1.80, p = .009$) and a history of hypercholesterolemia ($RRR = 1.85, p = .016$) are robustly significant risk factors for Alzheimer's disease (See Table 1). The significance of hypertension and hypercholesterolemia (Bray, and Clark, 1984), high cholesterol, and hypertension (Frye-Pierson, and Toole, 1987; and Kivipelto, Helkala, Laakso, Hanninen, Hallikainen, Alhainen, Soininen, Tuomilehto, and Nissien, 2001) are consistent with prior research.

A history of tobacco use ($RRR = 2.18, p = .01$) is a robust significant risk factor for vascular dementia (See Table 1). This significance is consistent with prior research indicating that tobacco use, especially smoking, increases the risk of dementia (Frye-Pierson, and Toole, 1987). The fact that the other risk factors (hypercholesterolemia, hypertension, and diabetes) were not statistically significant risk factors contradicts prior research. This discrepancy may be due to the presence of other risk factors not assessed in this study.

Multinomial logistic regression analyses produced similar results as the relative risk ratio analyses. This analysis indicates that a history of hypertension ($\beta = .59, p = .009$) and a history

of hypercholesterolemia ($\beta = .61, p = .016$) are strong indicators for placing individuals at a higher risk for Alzheimer's disease. It also indicates that tobacco use ($\beta = .78, p = .01$) is a strong indicator for placing individuals at a higher risk for vascular dementia (See Table 2).

Stepwise regression analyses were used to see how the variables in the study are a quantitative measure of the diagnosis of dementia. Results indicate that hypercholesterolemia is an independent risk factor for dementia ($\beta = -.113, p = .009$). The analysis of hypercholesterolemia ($\beta = -.104, p = .018$) and hypertension ($\beta = -.094, p = .031$) together indicate a cluster risk factor effect. When the other variables are factored in, analyses indicate that they are not significant risk factors for dementia. These results may be due to the presence of other risk factors not assessed in this study (See Table 3).

Analyses using Binomial Independent Variable for Demented Participants

Odds ratio analyses indicate that none of the individual variables included in this study is a significant risk factor for a diagnosis of dementia (history of high cholesterol, OR = 1.304, $p = .157$; history of diabetes, OR = 1.177, $p = .488$; history of hypertension, OR = 1.292, $p = .154$, and history of tobacco use, OR = 1.282, $p = .159$) (See Table 4)

Logistic regression analyses produced similar results as the Odds Ratio analyses. This analysis indicates that the variables included in this analysis are not independent indicators of a dementia diagnosis (history of high cholesterol, $\beta = .31, p = .092$, history of diabetes, $\beta = .254, p = .268$; history of hypertension, $\beta = .296, p = .092$; and history of tobacco use, $\beta = .234, p = .180$) (See Table 5).

Analyses using Polynomial Independent Variable for Not Demented Participants

Relative risk ratio analyses indicated that participants who were not diagnosed as having either Alzheimer's disease or vascular dementia and who presented for referral for a medical concern or a memory concern were not statistically at a greater risk for developing these

detrimental cognitive disorders. However, surprisingly those participants who presented with no specific medical or memory concern were found to be statistically at a greater risk of developing dementia if they had a history of tobacco use (RRR = .543, $p = .036$) and a history of hypercholesterolemia (RRR = .474, $p = .012$) (See Table 6). These findings may be due to the presence of other risk factors not assessed in this study. It is often the case that individuals present with similar risk factors but do not manifest similar physiological outcomes. These different outcomes are beyond the scope of this study.

Correlation Analysis of Risk Factors

A correlation analysis of the risk factors used in this study indicated that a history of hypertension is correlated with a history of hypercholesterolemia ($r = .104$, $p = .018$) and with a history of diabetes ($r = .166$, $p < .01$). Hypercholesterolemia is correlated with a history of diabetes ($r = .157$, $p < .01$) (See Table 7). Although we found statistical significance, the correlation does not account for a significant amount of the variance; therefore, the risk factors were treated as independent factors in the current study. The significance is a product of the relatively large sample used.

DISCUSSION

Present treatment for dementia includes reducing the symptoms of dementia, slowing the progression of the disorder, and treatments of secondary, psychological disorders that often occur with dementia (Erkinjuntti, 1999). Therefore, treatment only targets symptomology and does not address the etiology of the disorder. In order to fully treat a disorder such as dementia, the etiology is paramount. The purpose of this study was to explore some of the cardiovascular risk factors that are also believed to be risk factors for dementia. This information, along with future research on risk factors for dementia, may aid in the prevention of dementia. It will also be helpful in the treatment and maintenance of the damaging effects that dementia has on those afflicted with this disease.

Cognitive disorders in the past have been treated in a reactive manner. Once a person exhibits symptoms of a cognitive disorder, they are diagnosed and treated for the symptoms. With this type of treatment, there is minimal prevention and maximal need for reactive intervention. The findings of this study provide some insight into the etiology of vascular dementia and Alzheimer's disease and thus provide information to help in the prevention of these cognitive disorders. With this, a more proactive method can be used to treat these disorders. Prevention of these diseases can have great positive implications on quality of life for the affected and their caregivers. It can also decrease medical intervention thus decreasing medical costs.

Taken together, the findings of this research provide a valuable glimpse into the etiology of dementia. The impact of such findings can be beneficial in the prevention, treatment, and maintenance of this devastating disease. The more we know about this elusive disease, the more we can work toward preventing it altogether.

The results of this study have provided some insight into the etiology of dementia. They indicate that cardiovascular risk factors, such as hypercholesterolemia, hypertension, diabetes, and smoking need to be considered for the etiology for the diagnosis of dementia. Thus, the findings of this study indicate that some factors that are common between cardiovascular disease and dementia do exist. In fact, this study found that some cardiovascular risk factors are not independent risk factors for dementia, but the combination or cluster of the included risk factors viewed together become significant risk factors. For this reason, further research needs to examine other cardiovascular risk factors, identified by the Framingham study, that are possible risk factors for dementia.

Not all of the variables examined in this study indicated statistically significant risk for developing dementia. This may be an artifact of the relatively small sample size used.

Some factors that may be risk factors for dementia that were not discussed in this study include advancing age, diabetes differential mortality rates, exercise, and diet. Research has looked at advancing age as a risk factor for dementia (Perls, 2004; Fleischman, Wilson, Gabrieli, Bienias, and Bennett, 2004). Although there is some evidence that advancing age places individuals at a greater risk for developing chronic diseases such as dementia, (Fleischman et al., 2004) many do not suffer from these chronic, debilitating diseases (Perls, 2004). In the present study, age was not controlled for due to the limited range of participants.

In this study, the presence of diabetes was explored as a risk factor for dementia but was found not to be a statistically significant factor contrary to past research (Nutrition Action Healthletter, 2005). What this study did not explore was the differential mortality rates of diabetes and how control of blood glucose levels may affect and possibly place individuals at greater risk for dementia. These aspects of diabetes are thought to be potentially significant risk factors of dementia.

Finally, exercise and diet may also be potential risk factors for dementia. Many studies report the cognitive benefit of exercise and diet. Exercise can take many different forms such as walking (Cortlandt Forum, 2004) and even working in a garden (Brawley, 2004) and have beneficial effects. Diet and nutrition greatly affect physical and mental health (McKevith, 2004) in many ways. Individuals who overeat and do not exercise are reportedly at greater risk for contracting cardiovascular disease and dementia (McKevith, 2004). Therefore, these factors should be considered when exploring risk factors for dementia.

The present study is cross sectional, which limits its generalizability. It is limited in that the data collected is only a snapshot of individual factors. In order to more completely study the risk factors for dementia, longitudinal studies should be considered. Longitudinal studies provide more in depth information over a significant length of time. Being able to study the progression of factors over time may allow researchers to monitor the up and down trends that potentially lead to greater risk of developing dementia. Also, future research should examine the variables used in this study along with other factors in order to provide more clues into the etiology of dementia. This information would be valuable for the prevention and maintenance of dementia. Future studies should also consider using a larger, more diverse sample.

Table 1

Relative Risk Ratio Analyses of Dementia by Category

Category	Variable	RRR	<i>p</i>	95% Conf. Interval
Alzheimer's	History of Tobacco Use	1.04	.856	.67 to 1.61
	History of Hypertension	1.80	.009**	1.16 to 2.80
	History of Diabetes	1.14	.674	.61 to 2.13
	History of Hypercholesterolemia	1.85	.016*	1.12 to 3.04
Vascular	History of Tobacco Use	2.18	.01**	1.20 to 3.96
	History of Hypertension	.78	.41	.44 to 1.41
	History of Diabetes	1.26	.55	.59 to 2.70
	History of Hypercholesterolemia	1.12	.70	.62 to 2.02

* indicates statistical significance at the .05 level

** indicates statistical significance at the .01 level

Table 2

Multinomial Logistic Regression Analyses of Dementia by Category

Category	Variable	β Coefficient	<i>p</i>	95% Confidence Interval
Alzheimer's	History of Tobacco Use	.04	.86	-.40 to .48
	History of Hypertension	.59	.009**	.14 to 1.03
	History of Diabetes	.13	.67	-.49 to .75
	History of Hypercholesterolemia	.61	.016*	.12 to 1.11
Vascular	History of Tobacco Use	.78	.01**	.18 to 1.38
	History of Hypertension	-.24	.41	-.83 to .34
	History of Diabetes	.23	.55	-.53 to .99
	History of Hypercholesterolemia	.11	.70	-.48 to .70

* indicates statistical significance at the .05 level

** indicates statistical significance at the .01 level

Table 3

Step-wise Linear Regression of Dementia by Category

Variable	β Coefficient	p
History of Hypercholesterolemia	-.113	.009**
History of Hypercholesterolemia	-.104	.018*
History of Hypertension	-.094	.031*
History of Diabetes	-.036	.418
History of Hypertension	-.094	.031*
History of Tobacco Use	-.036	.413
History of Diabetes	-.22	.627
History of Tobacco Use	-.040	.352

* indicates statistical significance at the .05 level

** indicates statistical significance at the .01 level

Table 4

Odds Ratio of Diagnosis of Dementia

Variable	Odds Ratio	<i>p</i>	95% Confidence Interval
History of Tobacco Use	1.28	.159	.91 to 1.81
History of Hypertension	1.29	.154	.91 to 1.84
History of Diabetes	1.18	.488	.74 to 1.87
History of Hypercholesterolemia	1.30	.157	.91 to 1.88

Table 5

Logistic Regression of Diagnosis of Dementia

Variable	β Coefficient	<i>p</i>	95% Confidence Interval
History of Tobacco Use	.23	.18	-.11 to .58
History of Hypertension	.30	.09	-.05 to .64
History of Diabetes	.25	.27	-.19 to .70
History of Hypercholesterolemia	.31	.09	-.05 to .67

Table 6

Relative Risk Ratio Analysis for Non-Demented by Category

Category	Variable	RRR	<i>p</i>	95% Conf. Interval
Medical Concern	History of Tobacco Use	1.11	.62	.73 to 1.67
	History of Hypertension	.81	.35	.52 to 1.26
	History of Diabetes	.84	.51	.49 to 1.43
	History of Hypercholesterolemia	.69	.07	.45 to 1.04
Memory Concern	History of Tobacco Use	.78	.38	.45 to 1.36
	History of Hypertension	1.15	.66	.62 to 2.13
	History of Diabetes	.64	.22	.32 to 1.29
	History of Hypercholesterolemia	.95	.86	.54 to 1.67
No Specific Concern	History of Tobacco Use	.54	.04*	.31 to .96
	History of Hypertension	.47	.01**	.26 to .85
	History of Diabetes	1.92	.15	.79 to 4.66
	History of Hypercholesterolemia	.75	.33	.42 to 1.33

* indicates statistical significance at the .05 level

** indicates statistical significance at the .01 level

Table 7

Correlation Analysis for Risk Factors

	Tobacco	History of hypertension	History of hypercholesterolemia	History of diabetes
History of Tobacco		$r = -.048$ $p = .274$	$r = .018$ $p = .683$	$r = -.030$ $p = .486$
History of hypertension	$r = -.048$ $p = .274$		$r = .104^*$ $p = .018$	$r = .166^{**}$ $p = .000$
History of hypercholesterolemia	$r = .018$ $p = .683$	$r = .104^*$ $p = .018$		$r = .157^{**}$ $p = .000$
History of diabetes	$r = -.030$ $p = .486$	$r = .166^{**}$ $p = .000$	$r = .157^{**}$ $p = .000$	

* Statistically significant relationship between the variables at the .05 level.

** Statistically significant relationship between the variables at the .01 level.

APPENDIX
PROTOCOL FORM

Initial Assessment: (date ____/____/____)

Ethnicity: Caucasian Af-Am Asian-Am Latino-Am Other Gender: M F

DOB: ____/____/____ Age:____ Height: _____ Weight : _____

BP: ____/____ Marital Status: M S D W # prior surgeries:____
most recent ____/____/____

Occupation: _____ ECG: Normal Abnormal

Caffeine Use: Y N Tobacco: Y N EtOH: Y N

Hx of EtOH Abuse: Y N Hx of Drug Abuse: Y N MRI/CT Infarcts: Y N

GDS Score (from LCSW): ____/15 GDS Score (from PhD): ____/30

MMSE (from LCSW): ____/30 MMSE (from PhD): ____/30

Lab Values: (use date closest to initial assessment)

HDL: _____	B12: _____
LDL: _____	Folate: _____
Total Cholesterol: _____	Creatinine: _____ (blood or urine)
Triglycerides: _____	if diabetic, HbA1C: _____
Ratio: _____	

Medications (*current*):

HTN	Y	N	if Y, length of Tx: _____	Y	N	length: _____
Diabetes	Y	N		Y	N	
Anti-depressants	Y	N		Y	N	
AChE Inhibitors	Y	N		Y	N	
HRT	Y	N	if Y, length of Tx: _____	Y	N	length: _____
Synthroid	Y	N	if Y, length of Tx: _____	Y	N	length: _____
Cholesterol	Y	N	if Y, length of Tx: _____	Y	N	length: _____
Dementia	Y	N	if Y, length of Tx: _____	Y	N	length: _____

History of:

Dementia: Date of Dx: ____/____/____

MD/DO/LCSW: Alzheimer's Vascular Cognitive Disorder NOS
Other (_____) None

PhD: Alzheimer's Vascular Cognitive Disorder NOS
Other (_____) None Not Seen

History of:

Hypercholesterolemia	Y	N	Bronchitis	Y	N
CVD	Y	N	HTN	Y	N
PVD	Y	N	Stroke	Y	N
Diabetes	Y	N	TIAs	Y	N
Cancer (_____)	Y	N	COPD	Y	N
MI	Y	N	Asthma	Y	N
Thyroid	Y	N	Emphysema	Y	N

BIBLIOGRAPHY

- Allen, K., Frier, B., and Strachan, M. (2004). The relationship between type 2 diabetes and cognitive dysfunction: Longitudinal studies and their methodological limitations. *European Journal of Pharmacology*, 490, 169-175.
- American Heart Association (2002). *Heart disease and stroke statistics – 2003 update*. Dallas, TX: American Heart Association.
- Bornebroek, M. and Breteler, M. (2004). Epidemiology of non-AD dementias. *Clinical Neuroscience Research*, 3, 349-361.
- Brawley, E., (2004). Gardens of memories. *Alzheimer's Care Quarterly*, 5, 154 – 164.
- Bray, G. and Clark, G. (1984). Stroke, its causes and consequences. *A stroke family guide and resource*. Clark, G. and Muller-Rohland, J. (Eds.) Springfield, Illinois: Charles C. Thomas.
- Bruce, D., Casey, G., Grange, V., Clarnette, R., Almeida, O., Foster, J., Ives, F., and Davis, T. (2003). Cognitive impairment, physical disability and depressive symptoms in older diabetic patients: The Fremantle Cognition in Diabetes study. *Diabetes Research and Clinical Practice*, 61, 59-67.
- Bruce, D., Harrington, N., Davis, W., and Davis, T. (2001). Dementia and its associations in type 2 diabetes mellitus: The Fremantle Diabetes study. *Diabetes Research and Clinical Practice*, 53, 165-172.
- Coker, L. and Shumaker, S. (2003). Type 2 diabetes mellitus and cognition: An understudied issue in women's health. *Journal of Psychosomatic Research*, 54, 129-139.
- Cortlandt Forum. (2004). Walking wards off dementia. *Cortlandt Forum*, 17, 22 – 23

- De la Torre, J. (2002). Alzheimer's disease: How does it start? *Journal of Alzheimer's Disease*, 4, 497-512.
- Desmond, D. (2004). Vascular dementia. *Clinical Neuroscience Research*, 3, 437-448.
- Erkinjuntti, T. (1999). Cerebrovascular dementia: Pathophysiology, diagnosis and treatment. *CNS Drugs*, 12, 35-48.
- Fleischman, D., Wilson, R., Gabrieli, J., Bienias, J., and Bennett, D. (2004). A longitudinal study of implicit and explicit memory in old persons. *Psychology and Aging*, 4, 617 – 625.
- Frye-Patterson, J. and Toole, J. (1987). *Stroke: A guide for patient and family*. New York, New York: Raven Press.
- Game, F. and Jones, A. (2000). Coronary heart disease risk assessment in diabetes mellitus-a comparison of PROCAM and Framingham risk assessment functions. *Diabetic Medicine*, 18, 355-359.
- Guo, Z., Viitanen, M., Fratiglioni, L., and Winblad, B. (1997). Blood pressure and dementia in the elderly: Epidemiologic perspectives. *Biomedicine & Pharmacotherapy*, 51, 68-73.
- Hauw, J. and Duyckaerts, C. (2002). Dementia, the fate of brain? Neuropathological point of view. *C.R. Biologies*, 325, 655-664.
- Kalaria, R. (2002). Similarities between Alzheimer's disease and vascular dementia. *Journal of the Neurological Sciences*, 203-204, 29-34.
- Kannel, W. (2000). Risk stratification in hypertension: New insights from the Framingham study. *American Journal of Hypertension*, 13, 3S-10S.

- Kannel, W., Dawber, T., Kagan, A., Revotskie, N., and Stokes, J. (1961). Factors of risk in the development of coronary heart disease-six-year follow-up experience: The Framingham study. *Annals of Internal Medicine*, 55, 33-50.
- Kivipelto, M., Helkala, E., Laakso, M., Hanninen, T., Hallikainen, M., Alhainen, K., Soininen, H., Tuomilehto, J., and Nissien, A. (2001). Midlife vascular risk factors and Alzheimer's disease in later life: Longitudinal, population based study. *BMJ*, 322, 1447-1451.
- Launer, L. (2002). Demonstrating the case that AD is a vascular disease: Epidemiologic evidence. *Ageing Research Reviews*, 1, 61-77.
- Launer, L., Ross, G., Petrovitch, H., Masaki, K., Foley, D., White, L., and Havlik, R. (2000). Midlife blood pressure and dementia: The Honolulu-Asia Aging study. *Neurobiology of Aging*, 21, 49-55.
- Letenneur, L, Larrieu, S., and Barberger-Gateau, P. (2004). Alcohol and tobacco consumption as risk factors of dementia: A review of epidemiological studies. *Biomedicine & Pharmacotherapy*, 58, 95-99.
- Leys, D. and Pasquier, F. (1998). Subcortical vascular dementia: Epidemiology and risk factors. *Arch. Gerontol. Geriatr. Suppl.*, 6, 281-294.
- Liebman, B. (2005). Fading memories: The heart-weight connection. *Nutrition Action Healthletter*, Jan/Feb, 3 – 6.
- MacKnight, C., Rockwood, K., Awalt, E., and McDowell, I. (2002). Diabetes mellitus and the risk of dementia, Alzheimer's disease and vascular cognitive impairment in the Canadian study of health and aging. *Dementia and Geriatric Cognitive Disorders*, 14, 77 – 83.
- McKevith, B., (2004). Nutrition, cognition, and Alzheimer's. *British Nutrition Foundation Nutrition Bulletin*, 29, 359 – 361.

- Mehta, N., and Khan, I. (2002). Cardiology's 10 greatest discoveries of the 20th century. *Texas Heart Institute Journal*, 29, 164-171.
- Ott, A., Slioter, A., Hofman, A., van Harskamp, F., Wittteman, J., van Broeckhoven, C., van Duijn, C., and Breteler, M. (1998). Smoking and risk of dementia and Alzheimer's disease in a population-based cohort study: The Rotterdam study. *The Lancet*, 351, 1840-1843.
- Perls, T. (2004). The oldest old. *Scientific American*, 14, 6 – 13.
- Rockwood, K. (2002). Vascular cognitive impairment and vascular dementia. *Journal of Neurological Sciences*, 203-204, 23-27.
- Roman, G. (2002). Vascular dementia may be the most common form of dementia in the elderly. *Journal of the Neurological Sciences*, 203-204, 7-10.
- Roman, G. (2002). Defining dementia: Clinical criteria for the diagnosis of vascular dementia. *Acta Neurologica Scandinavica*, 106, 6-9.
- Roman, G. and Royall, D. (2004). A diagnostic dilemma: Is "Alzheimer's dementia" Alzheimer's disease, vascular dementia, or both? *The Lancet Neurology*, 3.
- Sadowski, M., Pankiewicz, J., Scholtzova, H., Yong-sheng, L., Quartermain, D., Duff, K., and Wisniewski, T. (2004). Links between the pathology of Alzheimer's disease and vascular dementia. *Neurochemical Research*, 29, 1257 – 1266.
- Schmidt, R., Schmidt, H., and Fazekas, F. (2000). Vascular risk factors in dementia. *Journal of Neurology*, 247, 81-87.
- Schmidtke, K. and Hull, M. (2002). Neuropsychological differentiation of small vessel disease, Alzheimer's disease and mixed dementia. *Journal of the Neurological Sciences*, 203-204, 17-22.

- Thomas, A., Kalaria, R., and O'Brien, J. (2004). Depression and vascular disease: What is the relationship? *Journal of Affective Disorders*, 79, 81-95.
- Tyas, S., White, L., Petrovitch, H., Ross, G., Foley, D., Heimovitz, H., and Launer, L. (2003). Mid-life smoking and late-life dementia: The Honolulu-Asia Aging study. *Neurobiology of Aging*, 24, 589-596.
- Vasan, R., Larson, M., Leip, E., Kannel, W., and Levy, D. (2001). Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart study: A cohort study. *The Lancet*, 358, 1682-1686.
- Watari, K. and Gatz, M. (2002). Dementia: A cross-cultural perspective on risk factors. *Generations. Diabetic Medicine*, 18, 355-359.
- Wilson, P., D'Agostino, R., Levy, D., Belanger, A., Silbershatz, H., and Kannel, W. (1998). Prediction of coronary heart disease using risk factor categories. *Circulation*, 97, 1837-1847.
- Zekry, D., Hauw, J., and Gold, G. (2002). Mixed dementia: Epidemiology, diagnosis, and treatment. *Journal of the American Geriatric Society*, 50, 1431-143