Long-Term Survival After an Admission for Syncope

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REVIEW OF THE LITERATURE

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A. The Syndrome of Syncope

Definition

Syncope is defined as a transient loss of consciousness that resolves spontaneously without requiring chemical or electrical intervention. It is a common medical syndrome that accounts for 3% of all ER visits and 1-6% of all hospital admissions[1-2], with a yearly incidence in the general population ranging from 2-8% (depending on the age group studied). The causes of a syncopal episode vary greatly, but in general have been classified as cardiovascular, non-cardiovascular and unexplained. The specific etiologies in the cardiovascular category include ventricular and supraventricular tachycardias, bradyarrhythmias, heart block, valvular disease and outflow obstruction. Some of the more common non-cardiovascular causes are situational syncope, vasovagal, orthostatic hypotension, carotid sinus syncope, seizures and psychogenic syncope.

Limitations of Previously Published Data

The difficulties in the evaluation of syncope lie in the complexity and variety of the underlying pathophysiologic mechanisms, its intermittent nature, the frequent absence of abnormalities after the index event and the lack of effective and accurate tests to re-induce symptoms. Wayne elegantly addressed these issues in a classic review article[3], stating that it is "apparent that a great deal is involved in the investigation of loss of consciousness; it requires not only an orderly classification, but also an understanding of basic mechanisms." Studies of syncope have been limited by factors inherent to the syndrome, but many have also had methodological weaknesses. The initial population-

based studies were limited by small numbers of patients; the largest series published included 204 patients in the initial evaluation[4], and 433 patients in a study of recurrence[5]. These studies were also limited by imperfect follow up, single institution experiences, and variable reporting of data on the process of care. More recently published data on syncope have also been hampered by small numbers of patients and single center experiences. They have almost exclusively studied referral populations, and have tended to focus on only one aspect of diagnostic testing. Despite these inadequacies, there has been a large amount of data published on the matter, which has guided clinicians in the management of syncope for the last two decades.

Mortality and Prognosis

The best outcome data on this heterogeneous subject was provided by population-based studies[4, 6-14] of syncope in various patient groups: hospitalized patients, ICU patients, emergency room patients and the institutionalized elderly. In some of these studies, patients were identified prospectively through emergency rooms or by monitoring the hospital admissions and clinic visits at a given site. Other studies used retrospective record analyses, identifying patients who had an admission or discharge diagnosis of syncope. Cardiovascular syncope accounted for 4-9% of the emergency room patients, and 20-36% of patients admitted to the hospital. Of the patients with cardiovascular syncope, two thirds were over 60 years of age, and there was 18-33% mortality over one year. This was in contrast to lower (0-12%) mortality with non-cardiovascular and unexplained syncope. The only long-term data[15] on the subject suggested that the increased risk associated with cardiovascular syncope persisted for several years.

Approximately 20% of the patients with syncope in these studies had had syncopal events prior to the index period. The recurrence rate of syncope was 31% over 30 months, but individuals with recurrences were not at risk for increased mortality[5]. The frequency of re-hospitalization has not been described.

Diagnostic Evaluation

The evaluation of syncope classically included tests that evaluate neurologic and cardiac function, as well as a complete history and physical examination. Studies[4, 6-14] from the 1980's documented a wide variety of diagnostic testing and relatively infrequent diagnoses being established. The cardiac screening tests that were widely used in the 1980's population studies included the 12 lead EKG, telemetry monitoring, exercise stress testing and 24-48 hour Holter monitor. None of these tests was very successful in determining the etiology of the event. Prolonged EKG monitoring seemed to perform better than the other tests, but not as good as a complete history and physical examination. Only rare patients in the early studies underwent more complex cardiac testing, including angiograms, echocardiograms and electrophysiology (EPS) testing. The use of head CT, EEG, lumbar puncture, exercise testing and angiography was also documented.

The costs generated by these evaluations were substantial, and several studies suggested that much of the diagnostic workup was unnecessary, especially the tests of neurological function. These suggestions were based on the low yield in establishing an etiology of syncope for many of the tests. However, no studies have tried to correlate the diagnostic testing with an effect on outcome.

Recent Developments in Diagnostic Testing

Over the last ten years, the literature has focused on the evaluation of syncope using various testing modalities in select populations, with several tests having been suggested to identify which syncopal events were cardiovascular in origin, and thus individuals at risk for potentially fatal events. The optimal use of these tests has not been determined.

The use of prolonged ECG monitoring was found to be helpful in the early studies. The limitations in establishing diagnoses related to the inherently episodic and intermittent nature of arrhythmic syncope. Newer devices have been developed to address this, both event monitors and loop recorders[16-17]. The patient can wear either of these for extended periods of time in order to 'capture' a syncopal event. Neither has been extensively studied in syncope patients, and there is some suggestion that monitoring beyond the initial 24 to 48 hours[18] has a low yield in establishing new, clinically important diagnoses.

One of the newer non-invasive tests is the signal averaged EKG. This test identifies areas of slow conduction in the ventricle that may provide substrate for re-entrant ventricular arrhythmias. It appears to be sensitive in predicting the presence of ventricular tachycardia during EP study, but is plagued by false positive results and is of no value in the evaluation of other causes of syncope. It has been studied in syncope primarily in patients referred for EP study.[19]

Some authors have suggested using an assessment of left ventricular (LV) systolic function to evaluate patients with syncope. Middlekauff et al. found that the presence of

severe LV dysfunction was better than the presence of cardiac syncope in predicting poor outcome in syncope patients referred for EP testing.[20] Other studies have also found that LV dysfunction is a significant predictor of mortality in patients with syncope, but the studies have been small, and not all patients have had documentation of the left ventricular function.

Another diagnostic evaluation is the tilt table test, which attempts to reproduce neurocardiogenic syncope. This test has been studied at length in small groups of patients, but its sensitivity and specificity remain controversial[21]when applied to larger groups of patients. Additionally, the long-term outcome of patients with this diagnosis does not appear to be worse than the general population, raising the issue of cost-effectiveness of the diagnostic and therapeutic intervention.

The most invasive test is the electrophysiology study (EPS). EPS attempts to induce the cardiac arrhythmia which produced the preceding syncopal event, and has moderate (30-50%) success in establishing a diagnosis in the workup of unexplained syncope[22-24]. The limitations of EPS lie in its expense, its invasiveness, its lack of sensitivity for bradyarrythmias, and its limited sensitivity and specificity for induced ventricular arrhythmias. In general, patients with no history of cardiac disease and structurally normal hearts have a low yield of diagnoses from EPS.

Therapies for Cardiac Syncope

There are no data on patients with syncope that definitively prove that survival is affected by the therapeutic interventions. However, if a cardiac etiology of the syncopal event has been established, therapy can be tailored. It is generally accepted that the use of

pacemakers[25-26] to treat certain bradyarrhythmias and valve replacement for aortic stenosis[27] can improve survival. The treatments for tachyarrhythmias are quite varied, but also frequently successful[28-29]. There have been a number of advances in drug and device therapy, culminating in the development of implantable defibrillators (ICD). The treatments for neurocardiogenic syncope have been less successful[30], but have included both drug therapy and pacemaker implantation. There have been no randomized trials of interventions for all patients with syncope.

Current Management

This recent literature has focused mainly on the role of diagnostic tests in populations referred for EP study, but these tests have not been validated in the original less selected groups studied in the early 1980's. To the best of our knowledge, these tests are being performed on a wide range of patients in the community who may not fall into the narrowly defined study groups. For all of the newer diagnostic and therapeutic modalities, there have been no large scale data reporting an effect on patients' clinical outcomes, nor on the cost burdens that screening tests (which lead to invasive testing) and expensive treatments might impose. A recent review article[2] has stressed this in stating that "further research is needed to assess the validity, the clinical usefulness, and the cost effectiveness of these and other diagnostic test in syncope."

B. Variation in Health Care Delivery

Variability In The Process Of Care

Over the last 20 years, more importance has been paid to the process of medical care, and to the resulting outcomes. The issue of variation in patient management dates back to the differences observed in tonsillectomy rates in the 1970's[31], and earlier in the century. Recently, there has been much data[32-37] published on the variation in cardiac surgery rates, the use of cardiac catheterization and angioplasty, and in the use of proven drugs for the treatment of common cardiovascular disorders. This variation has been documented in different geographical areas, between different physicians and across health care systems. It is clear that a great deal of variability in health care delivery occurs in the United States, even for specific diseases whose management strategies are well defined in the published literature.

More recently, attention has been paid to the variation in management of common medical illnesses and syndromes. The management of low back pain[38] was recently evaluated with respect to the type of practitioner initially seeing the patient. In this prospective study, there was a significant difference in management, with primary care practitioners providing the lowest cost care. Overall, the clinical outcomes were no different in patients seen by various specialists.

Another important issue is the changing health care system, which has altered the incentives for delivering care. As many physician's reimbursement changes from fee-for-service to capitation, managed care, or pre-paid health maintenance organizations, financial factors may influence their behavior. There is evidence[33-34, 39] that specialty physicians and fee-for-service plans are associated with increased utilization of resources.

In some health care delivery systems, there are administrative and organizational obstacles that may alter patterns of care. The increased use of easily available services has been well-documented recently[40] for the use of cardiac catheterization after acute myocardial infarction. As long as scientific evidence remains controversial, we suspect that these other factors will be especially pertinent to the care that is currently being delivered.

Variability in the Evaluation and Management of Syncope

Syncope is a heterogeneous syndrome, and similar to low back pain, the causes can range from benign to life threatening. Because patients are seen by many different types of physicians, both generalists and specialists, there is a potential for wide variability in management. Generalist physicians may not be aware of the data on prognosis of syncope and may be under-evaluating their patients, failing to use the most sophisticated technology. Alternatively, specialists may be using the newer diagnostic modalities excessively, and not relying on the time honored history and physical examination. In rural settings, the access to specialists and specialized testing may be limited.

The legal, financial and social sequelae of a syncopal episode can be enormously important to both patients and their physicians. Often, patients are not allowed to drive, which may effect their ability to earn a living, and in the elderly, may lead to increasing social isolation and a loss of community supports. The fear of recurrent events may lead some patients to markedly reduce their social and recreational activities. Because of the associated poor outcome, physicians do not want to miss the diagnosis of cardiac

syncope, both out of concern for the patient's health, and (in the current legal climate) to avoid liability. These factors may increase the incentives for patients and their physicians to undergo extended evaluations, in pursuit of the pathophysiologic diagnosis, which may not be cost effective, and paradoxically, increase the risk to the patient from over testing.

The amount of variation in the delivery of care has never been addressed with respect to syncope. Because of the syndrome's heterogeneity; the multiple physicians who evaluate these patients; the social, financial and legal sequelae; and the changes in the US health care system, it is imperative to define the magnitude of the variation. It is also imperative to address whether this variability is having an effect on patients' outcomes.

We were able to identify three separate and distinct models of health care delivery in Oregon. The Portland VA is a teaching hospital that provides care to Veterans throughout the Pacific Northwest as a tertiary care medical center, as well as providing primary care to a large number of individuals. Kaiser Permanente is the only group model Health Maintenance Organization (HMO) in Oregon, and, treats patients in HMO facilities with health care delivery strictly coordinated by primary care providers. Medicare patients in Oregon are treated throughout the state in a relatively uncoordinated system of care; and primarily through fee-for-service reimbursement. We felt that these three health care delivery systems would provide a natural experiment on the different management patterns for syncope, and the resulting effects on outcomes. The purpose of our project was to define the management patterns for individuals admitted to the hospital for syncope, to define their clinical outcomes, and to determine the relationship between the initial management and subsequent outcomes.

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Long-Term Survival after an Admission for Syncope

The impact of diagnostic testing, etiology of syncope and health care system on mortality

METHODS

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Study Design and Source of Patients

This study employed an observational cohort design. We selected three health care systems in Oregon: a tertiary care Veteran Affairs Medical Center (VA), a group model Health Maintenance Organization (HMO) and Medicare. We reviewed the discharge databases at the VA, the HMO and Medicare from January 1, 1992 to Dec. 31, 1994, identifying patients with ICD-9-CM code 780.2 (Syncope and Collapse) in the admission diagnosis position, or any of the discharge diagnosis positions. The first admission in the time frame for a patient was defined as the index syncopal admission, and was the admission that was reviewed. Subsequent admissions for the same patient were flagged as re-hospitalizations, but were not reviewed in depth.

Patient Identification

There were 324 patients identified at the VA (0.98% of total admissions), 823 at the HMO (0.93%) and 5314 (1.70%) at Medicare. At the VA and the HMO, all inpatient and outpatient records were requested for review on each patient identified. In the Medicare system, patients admitted through group model HMO's hospitals were excluded (n=561), and 600 of the remaining 4753 patients were randomly selected using SPSS (version 7.5, SPSS Inc. Chicago, IL). Of these 600 patients, 46 (7.7%) were not able to be matched with names and social security numbers, thus the records from 554 patient admissions were requested from the Medicare hospitals. Claims data on the 46 individuals who were not requested revealed no difference in age, sex, ethnicity, length of stay, hospital characteristics or crude mortality when compared with the 554 patients whose charts were requested.

Chart Review Database

Medical records on the 1701 selected individuals were requested for review. Each chart was reviewed by one individual (WSG), and data was directly entered into a Microsoft Access relational database (Microsoft Corporation, Redmond WA) which was specifically created for this project. The database was pilot tested on both VA and HMO charts for ease of use and applicability. The data entry format consisted primarily of binary response fields, with occasional free text data entry, and incorporated automatic error checking and reminders for completeness. For confidentiality, all database files were password protected, and remained on stand-alone computers without network access until identifiers had been removed.

Inclusion and Exclusion Criteria

The inclusion criterion was a documented syncopal event that occurred prior to admission to the hospital. We defined syncope as a transient loss of consciousness that did not require chemical or electrical conversion. Exclusion criteria were cardiac arrest; bradycardia requiring emergent intervention (temporary pacemaker or atropine); persistently altered level of consciousness; and age less than 13 years. For individuals transferred to another hospital during their initial admission, both hospitals' records were requested and reviewed, and considered one prolonged hospitalization (all were available.) For example, we included individuals who had been admitted for a presumed syncopal event, even if the final discharge diagnosis was a fall without loss of consciousness. We excluded individuals when each physician stated that there was a fall

without loss of consciousness.

Chart Review Conventions and Definitions

For each individual, the entire admission was reviewed in detail, collecting information using standard, predetermined definitions. Comorbidities included in the Charlson Index[1] were tabulated in standard fashion. For other pre-existing comorbidities, specific definitions were created. New findings and active issues addressed during the syncope admission were recorded separate from preexisting comorbidities.

A predetermined list of tests thought to be important to the evaluation of syncope was available for binary response, as well as space for entering other diagnostic tests. A test was considered complete if there was a final report, or if there was documentation in the chart that the test was performed. The number of times a test was performed was not recorded, only whether it was or was not done. The use of telemetry was determined by reviewing the physician orders and the telemetry records. Rule out myocardial infarction was defined as the use of telemetry and ordering at least one CPK (creatine phosphokinase) blood test after admission.

The admitting vital signs were defined as those documented by the admitting physician's history and physical exam. If not documented in that location, then the first documented vital signs after the syncopal event were recorded. Major therapies were unambiguous, and were recorded if performed. Minor therapies were recorded if they were plausibly related to the episode of syncope. Physician, nursing and social work notes were used to determine where the patients lived prior to admission and at discharge.

Left Ventricular Systolic Function

The only results documented were for tests of left ventricular systolic function, and included the means of testing, as well as the result. For results listing a range (*i.e.* mildly to moderately reduced, ejection fraction 45-50%) we recorded the most favorable portion (in the example: mildly reduced, ejection fraction 50%). If there was more than one test of left ventricular function we recorded the result from the test using the following hierarchy (left ventriculogram, nuclear multi-gated acquisition scan (MUGA), echocardiogram).

Physician Specialty

Physicians were identified by name, and specialty if documented in the chart. Resident physicians were not identified specifically; rather the attending physician's name and specialty were recorded. All consultants seeing the patient and documenting a visit were also recorded. If the specialty could not be determined from the chart, the specialty was listed as unknown. These names were later linked with the lists of physicians and their specialties from the Oregon Board of Medical Examiners dating back to 1993.

Etiology of Syncope

The final cause of the syncopal event was the etiology stated by the primary or discharging physician. The final syncopal diagnosis was later categorized as cardiovascular, non-cardiovascular or unexplained, using the standard definitions[2]. Cardiovascular causes included tachycardia, bradycardia, heart block, aortic stenosis and

pulmonary embolus. Non-cardiovascular causes include vasodepressor, situational, medication-related, orthostasis and neurologic events.

Outpatient Records

In the VA and the HMO, all outpatient records for 90 days after discharge were also reviewed to determine the use of diagnostic tests and therapies. The outpatient tests were documented separate from the inpatient information. Additionally, the date and specialty of physician visits in a clinic or emergency room were recorded. As a matter of convention, visits to anticoagulation clinic, ophthalmology and otolaryngology were not included in the outpatient data. This convention was established in the pilot phase after noting that there were frequently many visits to a single provider, who often was not a physician. Similarly, home visits and nursing home visits were not included unless there was documentation that a physician was present. For individuals readmitted to the hospital within 90 days, each physician seeing the patient was recorded once on the date of admission or first consultation. In the instance were an alternate diagnosis of the syncopal event was identified, it was recorded separate from the initial diagnostic impression.

Readmissions

The date of the first readmission to the hospital was determined from the medical records at the VA and the HMO: this initial readmission was briefly reviewed, and the principle diagnosis was recorded. This data was obtained via claims records for the Medicare patients. The readmissions were classified as related to syncope, possibly

related to syncope and unrelated to syncope. The total number of readmissions between the date of discharge and 9/1/96 was determined from the same sources.

Other Data

The distance from the patients stated home address and the admitting hospital was determined using a map of Oregon and Washington, and recorded to the nearest five miles. The characteristics of each of the hospitals were incorporated from the criteria used by the Oregon Medical Professional Review Organization (OMPRO). The hospital's location was considered urban or rural, while the hospital peer group ranges from 1 to 5, with 1 being the large all capability hospital, and 5 being small rural hospitals.

Deaths

The primary study outcome was death. All names and social security numbers (available for 92% of individuals) were submitted to the National Death Index (NDI) to match with deaths through December 31,1996. The NDI is 99.9% specific and 97% sensitive when the Social Security number is available[3]. No systematic biases between systems would be expected. Overall the NDI identified 522 matches. Three out of 444 individuals confirmed to have died by chart review (death certificate, autopsy or Medicare files) were not identified by the NDI, suggesting a very high sensitivity. Individuals not identified as deceased by either method are assumed to have been alive on December 31, 1996, and their survival times are censored as of that point.

Among the 1516 names submitted there were 244 perfect matches, of which 220

had already been identified by chart review. All dates of death were the same, plus or minus one day. The remaining 24 perfect matches had not been identified in the charts as deceased (10%). Partially matched individuals identified in class 2 were reviewed, and another 263 individuals were identified as deceased, of which 53 had not been identified in the charts as deceased (20%). Partially matched individuals identified in class 4 were also reviewed, and five individuals were identified as deceased, of whom two were not identified by chart review (40%). Partially matched individuals identified in class 5 were all explicitly reviewed, and 10 more individuals were accepted as deceased, one of which was not identified by chart review (10%). The cause of death as delineated on the death certificates provided by the NDI Plus were differentiated into sudden cardiovascular, non-sudden cardiovascular and non-cardiovascular using customary distinctions. As a comparison, we calculated four-year mortality rates, adjusting for age and sex, using 1995 vital statistics for the general U.S. population [4].

Chart Review Reliability

Records were re-reviewed by a second individual in a 5% random selection of the 1516 patients. Weighted Kappa scores between the two reviewers for comorbidities, tests & therapies, physician specialty and etiology of syncope were excellent (0.71, 0.79, 0.83 and 0.91 respectively). A Kappa score above 0.7 indicates excellent reliability.

Kappa scores for individual comorbidity items ranged from 0.47 (history of syncope) and 0.49 (any tumor) to 1.00 (peripheral vascular disease, renal disease and liver disease.) The Kappa scores for individual tests ranged from 0.50 (telemetry) and 0.57 (12 lead EKG) to 1.00 (electroenchalogram, Pacemaker placement, cardiac catheterization,

thallium study, electrophysiology study, lumbar puncture and coronary artery bypass surgery.) The reliability of the specialty of the physicians involved was excellent, ranging from 0.74 (Medicine) to 0.92 (Neurology.) Kappa score for active diagnoses was excellent for the first, second and third, with much less reliability for the subsequent diagnoses.

Resource Indices

To compare the different patterns of testing in individuals, we developed an index of diagnostic tests based in 1997 dollars. For each of the diagnostic tests, we assigned the value of 1997 Medicare Relative Value Units (RVU)[13]. We used the total RVU, including physician work, practice expense and malpractice components, but ignored the geographic indices. The RVUs were converted to 1997 dollars using the standard conversion factors listed in the federal register. There were no RVUs available for two items: telemetry and rule out myocardial infarction. For telemetry, we assigned $135 for individuals with one-day hospital stays, and $260 for all other durations. For "rule out myocardial infarction", we assigned $69 as the cost of two separate tests for CPK and CPKMB. For each physician who saw the patient, we assigned the RVU for a single comprehensive evaluation. The diagnostic tests performed plus the physician visits were combined into the Diagnostic Testing Index (DTI). This index is independent of length of stay, and is the purest measure of resources involved in diagnosis.

To evaluate the overall resources used in the hospital management of syncope, we separated individuals into quartiles based on their length of stay (LOS) for the primary analysis.

We also developed a Total Resource Index (TRI). For individuals undergoing major cardiac therapies, we identified the Medicare DRG associated with the procedure, for example "DRG 106: CABG with Catheterization". To estimate the TRI, we combined each Medicare DRG (using a conversion factor of $4000 times the DRG weight) with professional fees for both the procedure and the subsequent days in the hospital and an estimated cost of durable medical supplies. For the remainder of the patients who did not have a clearly identified DRG group, the TRI was estimated as the diagnostic testing index (DTI) plus length of stay charges and physician fees for additional days in the hospital. We assigned a hospital room charge of $610 for each day in the hospital. Additional physician fees were estimated as a brief visit by one physician for each day in the hospital, with the exception of the first day comprehensive visit charge included in the DTI. We did not attempt to estimate many items such as pharmacy and laboratory charges, intensive care and any indirect costs, but we did capture most of the major expenses. The TRI is our best estimate of the overall resources used to evaluate and manage the individual with syncope from the perspective of the health care system. Although we used two approaches to estimating TRI, we do not think that we have biased our data. The TRI was not used as a continuous variable, but rather separated into quartiles for analysis. All individuals receiving major cardiac therapies were in the upper quartile of TRI. For the rest of the individuals, the second method of estimating total resource use should provide discrimination in an unbiased manner.

In our final analyses, we used the LOS quartiles as they were not subject to investigator bias, and showed similar relationships with survival as our estimate of TRI.

Statistical Analysis

Statistical testing was performed using SPSS version 7.5 (SPSS Inc., Chicago, IL) Continuous variables were compared with analysis of variance. When necessary, non-normal variables were transformed using natural log or ranking. The Kruskal-Wallis test was used for comparisons between ranked variables. Dichotomous variables were compared using Chi square, and the method of multiple subgroup comparisons from Fleiss[6]. Survival was estimated using the method of Kaplan and Meier[7], with differences between factors tested with the log rank statistic. Post hoc analysis of power associated with the log rank test was estimated using the method of Freeman[8]. All tests of hypotheses were considered significant when the 2-sided probability values were <0.05.

Cox proportional hazards analysis[9] was used to evaluate survival after hospital discharge with respect to health care system and the etiology of syncope, adjusting for age, co-morbidity and other prognostic factors. The model was built in a hierarchical fashion with the first block using demographic and study variables. Study variables forced into the model included syncope etiology and health care system. Multiple variations of age and comorbidity were tested using likelihood ratios to determine which was the best fit. Empiric observation of the data showed that age was not linearly related to survival. Therefore, we tested age in its polynomial form: age, age-squared and age-cubed were significant, while age to the fourth was not. Comorbidities were combined into the Charlson Index, which was then grouped into four categories (0, 1-2, 3-4, 5 or more) and used as a continuous variable. Other predetermined candidate variables were tested in univariate fashion against mortality using Kaplan-Meier survival and the log rank test. Variables reaching significance at $p <= 0.20$ were included in the second block

using forward stepwise regression, requiring p<=0.05 for entry. To examine the model for parsimony, the same variables were also tested using backward stepwise regression. The final models were identical. The issue of multiplicative hazards was addressed by testing interaction variables with age, sex and health care system. The only interactions that reached significance were age (in its polynomial form)-by-comorbidity. This interaction did not significantly change any other variables. As a sensitivity analysis, the model was re-tested limiting the analysis to individuals 65 years of age or older, and using only two of the systems: HMO and Medicare.

The primary exposure variable in another analysis of survival was diagnostic testing. We separated individuals into quartiles of diagnostic (DTI) and length of stay (LOS). Because the DTI and LOS were highly correlated and Kaplan-Meier survival plots of the quartiles of LOS quartiles suggested unequal baseline hazards, we used a stratified Cox model, allowing for different baseline hazards in each quartile of LOS. Cox proportional hazards analysis was used to estimate the relative risks (RR) of dying after discharge associated with varying quartiles of DTI. In all analyses, we defined the reference category as the lowest quartile of DTI. The DTI was entered into the model as a dummy variable based on quartiles. The first model included the DTI in an unadjusted, unstratified Cox model. Subsequently, we stratified by LOS quartile, and then adjusted for age and comorbidity only. Our final model adjusted for all factors found to be prognostically important previously, and allowed us to evaluate survival after hospital discharge with respect to quartiles of diagnostic resource use, adjusting for age, the presence of specialists, co-morbidity, health care system and final cause of syncope.

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Long-term survival after syncope in three health care systems.

Running Head: Long-term survival in syncope

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Abbreviations used in the text:

HMO	Health Maintenance Organization
VA	Veterans Affairs
RR	Relative Risk
CI	Confidence Interval

Key Words: syncope, prognosis, mortality, delivery of health care

ABSTRACT

Background: The impact of different health care systems on the diagnostic evaluation of patients with syncope, the identification of cardiovascular etiologies and the effects on survival is unknown.

Methods: Using an observational cohort design, we identified patients in three health care delivery systems (VA teaching hospital, Medicare population and group model HMO) with an admission or discharge diagnosis of syncope (ICD9 780.2) in 1992, 1993 or 1994. We reviewed medical records to document comorbidity, diagnostic testing, treatment and etiology of syncope. The primary outcome, mortality, was collected through the National Death Index (2 to 5 year follow up).

Results: The VA (n=285) patients were younger and had more comorbidity than the patients in the HMO (n=744) or Medicare (n=487). Diagnostic testing was higher at the VA, but intervention rates were similar in all three systems: 5.6% pacemaker implantation and 1.1% valve replacement. Overall, cardiovascular causes of syncope were found in 19% of individuals (more often at Medicare), while 41% had unexplained syncope. All cause mortality was 13% at one year and 41% at four years. In multivariate analysis, there was no significant relationship between the cause of syncope and mortality (p=0.23). Compared to Medicare (RR 1.0), the relative risk for dying was lower in the HMO (RR 0.79, 95%CI 0.65-0.96), but similar in the VA (RR 1.13, 95%CI 0.83-1.50).

Conclusions: Mortality after an admission for syncope was independent of the etiology of syncope. The improved survival seen at the group model HMO needs to be clarified by future study.

BACKGROUND

The prognosis after syncope, which accounts for 1% to 6% of all hospital admissions[1], was described in the 1980's[2-6]. Individuals with syncope of cardiovascular origin had a higher one-year mortality (18-33%) than individuals with non-cardiovascular or unexplained syncope (6-12%), and this increased risk continued for five years[7]. However, syncope represented a diagnostic challenge, and its etiology remained unexplained in as many as 47% of individuals[2-6]. Recent literature on the evaluation of syncope has focused on identifying which syncopal events were cardiovascular in origin, using single center referral populations and a single diagnostic test[8-13]. A consensus conference has distilled this literature and presented a diagnostic algorithm[14,15], yet the impact of these guidelines on outcome has never been described.

As health care delivery in the United States undergoes rapid change, there is concern about the impact on the process of care and on clinical outcomes[16]. The incentives for providing care may differ among different health care delivery systems, and the management of syncope is particularly likely to be affected by these differences, since there is no definitive algorithm for evaluation.

We felt that health care system differences would provide a natural experiment on the effect on outcomes of different management patterns for syncope. Therefore, we identified three distinct models of health care delivery: a Veterans Affairs (VA) hospital, a group model health maintenance organization (HMO) and a standard Medicare population. The VA provides tertiary care in a teaching environment. The group model HMO provides coordinated care delivered in HMO facilities. Medicare patients in Oregon are primarily treated through a fee-for-service system, and their health care is not

strictly coordinated. We hypothesized that there would be increased resource use in the Medicare system compared to the VA, and reduced resource use in the HMO, but overall survival in each of the systems would be the same.

The objective of this analysis was to identify prognostic factors affecting long-term survival after an admission for syncope. Specifically, our aims were to determine if the prognosis associated with cardiovascular syncope remained as dismal as previously reported, to determine whether different health care delivery systems evaluated syncope differently, and whether there were differences in survival for patients with syncope.

METHODS

Study Design and Source of Patients

This study employed an observational cohort design. We selected three health care systems in Oregon: a tertiary care VA hospital, a group model HMO and Medicare. We reviewed the discharge databases of these organizations from January 1, 1992 through December 31, 1994, identifying patients with ICD-9-CM code 780.2 (Syncope and Collapse) as an admission or discharge diagnosis. The first admission in the time frame for a patient was identified for review; subsequent admissions were not included. There were 324 patients identified at the VA (0.98% of total admissions), 823 at the HMO (0.93%) and 5314 (1.70%) at Medicare. After excluding Medicare patients admitted to the group model HMO's hospitals, a sample of the remaining Medicare charts was selected at random (n=554).

Chart Review Data Collection

Medical records on the 1701 individuals were reviewed by one individual. The inclusion criterion was a documented syncopal event that occurred prior to admission to the hospital. We defined syncope as a transient loss of consciousness that resolved spontaneously. Exclusion criteria were cardiac arrest, a persistently altered level of consciousness, and age less than 13 years. For individuals transferred to another hospital during their admission, both hospitals' records were reviewed, and considered as one hospitalization (all were available).

Each admission was reviewed in detail. The comorbidities included in the Charlson Index[17] were recorded. For other comorbidities, standard definitions were used.

New findings addressed during the admission were recorded separately from pre-existing conditions. Diagnostic test use was listed; however, results were recorded only for left ventricular systolic function measurements. Interventions such as pacemaker placement or cardioversion were also recorded. Physician, nursing and social work notes were used to determine where patients lived prior to admission and at discharge.

The etiology of the syncopal event was defined as that stated by the primary physician, and was later categorized as cardiovascular, non-cardiovascular or unexplained using the definitions of Kapoor[2]. Cardiovascular causes included tachycardia, bradycardia, and aortic stenosis. Non-cardiovascular causes included vasodepressor, medication-related, and neurologic events.

Deaths

The primary study outcome was death due to any cause. All names and social security numbers (available for 92% of individuals) were submitted to the National Death Index to match with deaths through December 31, 1996. This index is 99.9% specific and 97% sensitive when the social security number is available[18]. Partial matches were all explicitly reviewed. Among the 1516 names submitted, there were 522 matches. Only three out of 444 individuals identified as deceased by chart review (death certificate, autopsy or Medicare files) were not identified by the index, suggesting a very high sensitivity. Individuals not identified as deceased are assumed to have been alive on December 31, 1996, and their survival times are censored on that date. For comparison, we calculated expected four-year mortality rates, adjusting for age and sex, using 1995 vital statistics for the general U.S. population [19].

Chart Review Reliability

Records were re-reviewed by a second individual in a 5% random selection of the 1516 patients. Weighted Kappa scores between the two reviewers for comorbidities, tests and therapies, and etiology of syncope were 0.71 and 0.79, and 0.91 respectively. A Kappa score above 0.7 indicates excellent reliability.

Statistical Analysis

Statistical testing was performed using SPSS version 7.5 (SPSS Inc., Chicago, IL). Continuous variables were compared with analysis of variance, and the Kruskal-Wallis test. The χ^2 test was used to compare dichotomous variables[20]. Survival was estimated using the Kaplan-Meier method[21], and the log rank test was used to compare factors. All tests of hypotheses were considered significant when two-sided probability values were <0.05.

Cox proportional hazards analysis[22] was used to evaluate survival after hospital discharge with respect to health care system and the etiology of syncope, adjusting for age, comorbidity and other prognostic factors. We used a hierarchical model where the first block included demographic variables, health care system and etiology of syncope. Multiple variations of age and comorbidity were tested using likelihood ratios to determine the best fit. Age was entered into the model as a polynomial through the third power (Age^4 was not significant). Comorbidities were combined into the Charlson index and grouped into four categories (0, 1-2, 3-4, 5 or more) for use as an ordinal variable. Other predetermined variables were tested in univariate fashion against mortality using Kaplan-Meier survival and the log rank test. Variables reaching significance at $p \leq 0.20$

were included in the second block using forward stepwise regression, requiring $p \leq 0.05$ for entry. We tested multiple variables for interactions with age, sex and health care system. The only interaction that reached significance was age (in its polynomial form)-by-comorbidity.

RESULTS

Demographics and Comorbidity

There were 823 individuals identified at HMO, 554 at Medicare and 324 at VA. After review, 185 individuals (11%) were excluded, similar in each system (p=0.26). The main reason for exclusion was that there was no true syncopal event prior to admission (n=147). Other reasons for exclusion were miscoding (n=22), unavailable charts (n=11) and age less than 13 years (n=5). We have no direct means of assessing the accuracy of case ascertainment, yet the low rate of false positive miscoding would suggest that the number of false negatives (cases missed) due to miscoding is equally small. There were 1516 patients with syncope available for analysis.

The mean age was lowest in the VA, and highest in Medicare, with significant differences among the groups (Table 1). The Medicare population was skewed toward the very old (85 years or older). Individuals at the HMO were primarily drawn from the Portland metropolitan area, while the VA and Medicare populations were distributed throughout the state. Almost all patients (91%) were living at home prior to admission, and most patients were admitted through the emergency room, although this was less common at the VA.

Cardiac disease was common in the population (Table 2). One in six individuals had previously documented congestive heart failure or myocardial infarction and one third had a history of coronary artery disease. An episode of syncope prior to the index event was documented more often at the VA than the other systems. Overall, the Charlson comorbidity index scores were highest at the VA ($p < 0.001$).

Inpatient Management

A 12 lead electrocardiogram and telemetry monitoring were performed frequently in all systems, but the VA used markedly more advanced cardiac tests, including echocardiograms, cardiac catheterizations and electrophysiology studies, and more neurologic tests (Table 3). There were minimal differences between the HMO and Medicare in the use of diagnostic tests.

There were no significant differences in the major therapies provided in the different systems (Table 4). The most common intervention was permanent pacemaker placement, while other interventions, including valve replacement, bypass surgery and angioplasty were performed in less than 1% of the admissions, and no patient in any system received an implantable defibrillator. Anti-arrhythmic agents were used more often in Medicare and the VA than the HMO. Few patients required cardioversion or temporary pacemaker placement.

Cause of Syncope

Cardiovascular causes of syncope were assigned in 19% of admissions and non-cardiovascular causes were found in 40%. The remaining 41% of individuals were discharged without a diagnosis for their syncopal event (Table 5). Despite similar diagnostic testing, cardiovascular etiologies were identified more often in Medicare patients ($p=0.002$). The most common cardiovascular etiologies were arrhythmias, with more bradycardias than tachycardias. Obstructive cardiac causes were rare. The most common non-cardiovascular causes assigned by physicians were vasovagal syncope, orthostasis/dehydration, and medication-induced syncope. Neurologic etiologies

accounted for 4% of patients.

Survival

The median follow-up time after hospital discharge was 2.8 years with a maximum of 5.0 years. Follow up time in each system was similar. Mortality (±SE) for the study population was 13.4±0.9% at 1 year and 40.6±1.6% at 4 years. The expected four-year mortality for this population[19] (adjusted for age and sex) was 26.5%, yielding a standardized mortality rate of 1.55 for the cohort. Thus, the cohort of patients with syncope had a 55% higher risk of dying than would be expected over four years.

At four years, the mortality for cardiovascular syncope was 46.3±3.8%, for non-cardiovascular syncope 40.8±2.6%, and for unexplained syncope 38.2±2.3% (Figure 1). Although there was an 8.1% difference in mortality at four years, the overall differences ($p=0.16$ by log rank) were not significant. The four-year mortality was identical in the HMO (35.6±2.2%) and VA (35.9±3.4%) populations ($p=0.68$). Both were lower than in the Medicare (50.5±2.8%) population. Survival analysis (not age-adjusted) showed significant differences between the Medicare system and both the VA ($p=0.02$) and HMO ($p<0.001$) systems (Figure 2). The Charlson comorbidity index was significantly related to outcome: four-year mortality for individuals with scores of 0 was 19.0±2.1% versus 77.5±4.9% for individuals with scores of 5 or greater (Figure 3).

Because age and comorbidity were related to survival and differed by health care system and etiology of syncope, a multivariate model of survival was used (Table 6, Figure 4). In addition to age, gender and comorbidity, independent adverse prognostic effects were seen for impaired left ventricular systolic function, congestive heart failure,

aortic stenosis and for individuals discharged to assisted care facilities or nursing homes. After adjusting for these variables, the etiology of syncope was unrelated to mortality, with no differences between cardiovascular, non-cardiovascular or unexplained syncope (p=0.23). In contrast, the health care system was a significant predictor of mortality (p=0.01). Compared with Medicare, patients in the HMO had a 21% reduced risk of dying (Relative Risk [RR]=0.79, 95%CI 0.65-0.96). The VA population was at slightly higher risk than Medicare (RR=1.13, 95%CI 0.83-1.50), but the difference was not significant.

Limiting the multivariate analysis to individuals 65 years or older did not change these findings. Excluding the individuals at the VA did not significantly change the relative risk for dying at the HMO compared to Medicare (RR=0.77, 95%CI 0.63-0.94). Changing the reference category for etiology of syncope to unexplained or non-cardiovascular syncope did not markedly change the results for cardiovascular syncope (RR=1.20, 95%CI 0.95-1.51).

DISCUSSION

There are three major findings from our cohort of admitted patients with syncope: (1) the etiology of the syncopal event did not have prognostic significance; (2) the management of syncope was similar in three different health care systems; and (3) mortality was lower in patients cared for in the group model HMO as compared to the VA and Medicare populations.

Prognosis Unrelated to the Etiology of Syncope

In this study, individuals with cardiovascular syncope had the same long-term prognosis as individuals with non-cardiovascular and unexplained syncope in both unadjusted and adjusted analyses. In a post hoc analysis[23], our power was at least 83% to detect a 30% increased hazard of dying for patients with cardiovascular syncope, as compared to other etiologies.

One reason why our results might differ from previously reported data is that we relied on clinicians to establish the etiology of syncope, reviewing their findings retrospectively. While some authors[2, 6] studied subjects prospectively, others[3-5] used retrospective analyses. The frequencies of specific etiologies of syncope in our population are similar to this published data, so we doubt there is significant bias. Another possibility is that clinicians effectively treated cardiovascular syncope so that the mortality was reduced to the rates for non-cardiovascular or unexplained syncope. This seems unlikely, since only 7% of individuals received any major intervention during this admission, despite 18% being diagnosed with cardiovascular syncope. A third possibility is that because individuals with cardiovascular syncope were sicker, our adjustment for

multiple prognostic factors was more effective than in previous analyses, which only controlled for selected comorbidities[2,3,24]. A final possibility is that because we studied only admitted patients, and primarily an elderly population[24], we had a truly different population than the previously studied individuals with syncope.

The finding that the syncope etiology does not confer prognostic significance supports a recent case-control study where syncope was not a risk factor for mortality, after controlling for underlying cardiac disease[25]. Our study cannot address this issue directly, as we did not evaluate any patients without syncope; however the four-year mortality of our population was 55% greater than expected in the US population, an absolute mortality of 41% over four years. We don't know whether this increased mortality relates specifically to syncope or results from associated comorbid conditions.

From this retrospective assessment, it is not possible to define the appropriate evaluation and treatment for all patients with syncope. However, since mortality was so strongly related to comorbidity, and less to the etiology of syncope, our findings support an emphasis on aggressively managing underlying diseases and optimizing the use of appropriate therapies. Future research on improving survival for patients admitted to the hospital with syncope should be focused on the whole individual, not just the diagnosis and treatment of the syncopal event.

Evaluation and Treatment Similar in Three Health Care Systems

In our study, the differences in the evaluation of syncope among health care delivery systems were small, and reassuringly, there were no differences in the provision of major interventions. Individuals at the VA underwent more diagnostic testing, which

may be related to its status as a teaching and tertiary care center. Given the equivalent use of diagnostic tests, there did not appear to be any rationing of resources in the HMO, nor financially driven over-testing in the Medicare population. Whether or not there is a relationship between diagnostic testing, interventions and outcomes will need to be explored in the future.

Improved Survival in the Group Model HMO

After controlling for multiple risk factors, individuals evaluated for syncope at the group model HMO had a 21% reduced risk of dying when compared to the Medicare population and a greater risk reduction when compared to the VA population. The etiology of this benefit is not obvious and is not readily explained by the inpatient data collected in this study.

As with any observational study, unmeasured confounders may have created a spurious association. For example, our study relied on documented medical conditions to assess comorbidity, which may have been more rigorously recorded in one health care system and consequently biased the results. Additionally, there may be differential selection factors for individuals to enroll in an HMO (such as marketing or perceived benefit) that would independently impact survival. Another possibility is that the group model HMO provided a more coordinated system of care in the years after discharge.

Previously published data on the effects of HMO care on outcome have been mixed. Improved short-term mortality was seen in HMO patients compared with fee-for-service patients in a population of individuals referred for bypass surgery[26]. Also, in one geographic area, HMO patients had a ten-year adjusted risk ratio for breast cancer death

of 0.78 when compared with a fee-for-service population, but a different geographic area had no difference[27]. Similarly, no differences in outcome between HMO and fee-for-service were found in individuals with strokes[28], nor in individuals with myocardial infarction[29]. In contrast, for patients with a variety of diseases[30], worse health outcomes were found in the HMO for selected subgroups (the poor and the elderly). Overall, there is no consensus for which model of health care delivery provides the best outcomes and our results must be considered in their context. However, our data support the view that HMO care does not impair, and may enhance, health outcomes.

Limitations

This study included only admitted patients who were predominantly white Caucasian; thus, generalizing these results to all individuals suffering a syncopal event may be incorrect. The retrospective identification of individuals through coding may miss some individuals with syncope, but coding errors were rare and our case ascertainment strategy included all individuals admitted with syncope, even when syncope was not coded at discharge. Therefore, the number of missed cases must be very small, and should not be significant enough to affect the results. Involvement of medical residents may affect the process of care, but is unlikely to have altered the etiology of syncope or the long-term outcomes.

Conclusion

Mortality after an admission for syncope was 41% over four years, and was independent of the etiology of syncope. Despite minor differences in the management of

individuals in different health care systems, survival was best in the group model HMO. We believe that efforts to determine the etiology of syncopal events should be supplemented with increased attention to the overall medical care of these individuals. Future research should explore prospectively the value of diagnostic evaluations for patients with syncope.

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Table 1: Baseline Demographics for Individuals with Syncope

	HMO n= 744	Medicare n= 487	VA n= 285	p value*
Age-Years mean (SD)	72.0 (14.8)	78.7 (8.0)	66.1 (12.8)	<0.001
Age Group				<0.001
less than 55 years	90 (12.1)	1 (0.2)	44 (15.4)	
55-64 years	64 (8.6)	13 (2.7)	71 (24.9)	
65-74 years	181 (24.3)	131 (26.9)	106 (37.2)	
75-84 years	280 (37.6)	217 (44.6)	63 (22.1)	
85 or more years	125 (16.8)	122 (25.1)	8 (2.8)	
Male	343 (46.1)	225 (46.2)	279 (97.9)	<0.001
Non-Hispanic White	707 (95.0)	479 (98.4)	269 (94.4)	0.01
Portland Metropolitan Statistical Area Resident	650 (87.4)	181 (37.2)	167 (58.6)	<0.001
Hospitalized More Than 50 Miles from Home	22 (3.0)	15 (3.1)	102 (35.8)	<0.001
Prior to Admission				0.02
Independent Living	673 (90.5)	431 (88.5)	262 (91.9)	
Assisted Living	66 (8.9)	48 (9.9)	15 (5.3)	
Nursing Home	5 (0.7)	7 (1.4)	8 (2.8)	
At Discharge				<0.001
Independent Living	630 (84.7)	360 (73.9)	250 (87.7)	
Assisted Living	77 (10.3)	67 (13.8)	14 (4.9)	
Nursing Home	33 (4.4)	48 (9.9)	18 (6.3)	
Deceased	4 (0.5)	9 (1.8)	3 (1.1)	
Admitted through the:				
Emergency Room	650 (87.4)	431 (88.5)	201 (70.5)	<0.001
Clinic	61 (8.2)	44 (9.0)	18 (6.3)	
Hospital Transfer	26 (3.5)	0 (0.0)	32 (11.2)	
Other	7 (0.9)	12 (2.5)	34 (11.9)	

All values are n (%) except where described otherwise

* P value is for overall Chi square across systems

Table 2: Medical Conditions Present Prior to the Admission

	HMO n= 744	Medicare n= 487	VA n= 285	p value*
Cardiac Disease				
Coronary Artery Disease	243 (32.7)	159 (32.6)	116 (40.7)	0.04
History of Myocardial Infarction	118 (15.9)	72 (14.8)	60 (21.1)	0.06
Congestive Heart Failure	123 (16.5)	85 (17.5)	50 (17.5)	0.88
Aortic Stenosis	35 (4.7)	27 (5.5)	15 (5.3)	0.80
Arrhythmias				
Sinus Bradycardia	55 (7.4)	37 (7.6)	11 (3.9)	0.09
Second Degree Heart Block	7 (0.9)	6 (1.2)	5 (1.8)	0.56
Complete Heart Block	12 (1.6)	5 (1.0)	4 (1.4)	0.69
Atrial Fibrillation/Flutter	127 (17.1)	100 (20.5)	50 (17.5)	0.29
Supraventricular Tachycardia	32 (4.3)	23 (4.7)	16 (5.6)	0.67
Ventricular Tachycardia	16 (2.2)	14 (2.9)	10 (3.5)	0.44
Sudden Death	8 (1.1)	6 (1.2)	5 (1.8)	0.68
Pacemaker	28 (3.8)	23 (4.7)	6 (2.1)	0.18
Defibrillator	3 (0.4)	1 (0.2)	3 (1.1)	0.23
Other Vascular Disease				
Hypertension	352 (47.3)	214 (43.9)	122 (42.8)	0.32
Peripheral Vascular Disease	44 (5.9)	37 (7.6)	29 (10.2)	0.06
Cerebrovascular Disease	148 (19.9)	111 (22.8)	71 (24.9)	0.18
Prior History of Syncope	137 (18.4)	101 (20.7)	87 (30.5)	<0.001
Charlson Comorbidity Index				<0.001
0	284 (38.2)	130 (26.7)	76 (26.7)	
1 or 2	299 (40.2)	239 (49.1)	118 (41.4)	
3 or 4	124 (16.7)	85 (17.5)	64 (22.5)	
5 or more	37 (5.0)	33 (6.8)	27 (9.5)	

All values are n (%)

* P value is for overall Chi square across systems

Table 3: Tests Performed During the Syncope Admission

	HMO n= 744	Medicare n= 487	VA n= 285	p value*
Standard Cardiac Tests				
12 Lead Electrocardiogram (ECG)	733 (98.5)	465 (95.5)	277 (97.2)	0.01
Telemetry Monitoring	690 (92.7)	422 (86.7)	243 (85.3)	<0.001
Rule Out Myocardial Infarction**	354 (47.6)	184 (37.8)	97 (34.0)	<0.001
Exercise Test	50 (6.7)	6 (1.2)	22 (7.7)	<0.001
Holter Monitoring	1 (0.1)	19 (3.9)	21 (7.4)	<0.001
Advanced Cardiac Tests				
Echocardiogram	83 (11.2)	95 (19.5)	75 (26.3)	<0.001
Cardiac Catheterization	30 (4.0)	10 (2.1)	24 (8.4)	<0.001
Electrophysiology Study	3 (0.4)	12 (2.5)	14 (4.9)	<0.001
Signal Averaged ECG	1 (0.1)	6 (1.2)	6 (2.1)	0.01
Tilt Table	1 (0.1)	7 (1.4)	3 (1.1)	0.02
Stress Thallium	12 (1.6)	13 (2.7)	6 (2.1)	0.44
MUGA Scan	7 (0.9)	2 (0.4)	4 (1.4)	0.33
Neurologic Tests				
Computed Tomography: Head	137 (18.4)	99 (20.3)	64 (22.5)	0.32
Carotid Ultrasound	46 (6.2)	55 (11.3)	45 (15.8)	<0.001
MRI: Brain	13 (1.7)	8 (1.6)	30 (10.5)	<0.001
Lumbar Puncture	7 (0.9)	4 (0.8)	6 (2.1)	0.21
Electroencephalogram	66 (8.9)	57 (11.7)	44 (15.4)	0.01

All values are n (%)

* P value is for overall Chi square across systems

** Rule Out Myocardial Infarction was defined as the use of telemetry and the measurement of at least one creatine phospokinase (CPK) blood test after admission

Table 4: Interventions During the Syncope Admission

	HMO n= 744	Medicare n= 487	VA n= 285	p value*
Major Cardiac Therapy	50 (6.7)	32 (6.6)	22 (7.7)	0.81
Pacemaker Placement	41 (5.5)	27 (5.5)	17 (6.0)	0.96
Valve Replacement	4 (0.5)	2 (0.4)	2 (0.7)	0.86
Coronary Artery Bypass Surgery	4 (0.5)	2 (0.4)	5 (1.8)	0.07
Angioplasty	2 (0.3)	2 (0.4)	0 (0.0)	0.56
Defibrillator	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Minor Therapy	257 (34.5)	202 (41.5)	74 (26.0)	<0.001
Cardioversion	0 (0.0)	7 (1.4)	3 (1.1)	0.01
Temporary Pacemaker	6 (0.8)	5 (1.0)	3 (1.1)	0.90
New Anti-Arrhythmia Medication	37 (5.0)	55 (11.3)	25 (8.8)	<0.001
Blood Transfusion	33 (4.4)	32 (6.6)	6 (2.1)	0.02
New Seizure Medication	11 (1.5)	11 (2.3)	1 (0.4)	0.11

All values are n (%)

* P value is for overall Chi square across systems

Table 5: Etiology of the Syncopal Event

	TOTAL n= 1516	HMO n= 744	Medicare n= 487	VA n= 285
Cardiovascular#	284 (18.7)	121 (16.3)	111 (22.8)	52 (18.2)
Bradycardia- unspecified	52 (3.4)	28 (3.8)	15 (3.1)	9 (3.2)
Complete Heart Block	36 (2.4)	21 (2.8)	10 (2.1)	5 (1.8)
Ventricular Tachycardia	35 (2.3)	11 (1.5)	13 (2.7)	11 (3.9)
Atrial Fibrillation or Flutter	34 (2.2)	10 (1.3)	19 (3.9)	5 (1.8)
Supraventricular Tachycardia	25 (1.6)	6 (0.8)	14 (2.9)	5 (1.8)
Sick Sinus Syndrome	23 (1.5)	11 (1.5)	12 (2.5)	0 (0.0)
Myocardial Ischemia	16 (1.1)	8 (1.1)	5 (1.0)	3 (1.1)
Aortic Stenosis	14 (0.9)	5 (0.7)	5 (1.0)	4 (1.4)
Pulmonary Embolus	10 (0.7)	6 (0.8)	3 (0.6)	1 (0.4)
Mobitz 2 Heart Block	9 (0.6)	6 (0.8)	1 (0.2)	2 (0.7)
Pacemaker Dysfunction	3 (0.2)	1 (0.1)	1 (0.2)	1 (0.4)
Other Cardiovascular*	27 (1.8)	8 (1.1)	13 (2.7)	6 (2.1)
Non-Cardiovascular	602 (39.7)	300 (40.3)	204 (41.9)	98 (34.4)
Vasovagal	175 (11.5)	124 (16.7)	35 (7.2)	16 (5.6)
Orthostasis or dehydration	166 (10.9)	64 (8.6)	73 (15.0)	29 (10.2)
Drug Induced	55 (3.6)	34 (4.6)	9 (1.8)	12 (4.2)
Bleeding or Anemia	33 (2.2)	10 (1.3)	21 (4.3)	2 (0.7)
Seizures	29 (1.9)	12 (1.6)	12 (2.5)	5 (1.8)
Transient Ischemic Attack	18 (1.2)	7 (0.9)	5 (1.0)	6 (2.1)
Micturation or Tussive	18 (1.2)	5 (0.7)	6 (1.2)	7 (2.5)
Cerebrovascular Accident	13 (0.9)	9 (1.2)	3 (0.6)	1 (0.4)
Psychiatric	9 (0.6)	2 (0.3)	3 (0.6)	4 (1.4)
Other Non-Cardiovascular**	86 (5.7)	33 (4.4)	37 (7.6)	16 (5.6)
Unexplained	630 (41.6)	323 (43.4)	172 (35.3)	135 (47.4)

All values are n (%)

Chi square for the differences in cardiovascular, non-cardiovascular and unexplained syncope between systems=16.9 with 4 df, $p = 0.002$

* Includes unspecified arrhythmias, carotid sinus syncope, ruptured aorta and miscellaneous

** Includes infections, vertigo, hypoglycemia, sub-clavian steal, and miscellaneous

Table 6: Cox Proportional Hazards Model: Predictors of Long-Term Mortality After a Syncope Admission*

Variable	Reference	Beta**	S.E.	p value#	RR***	95% C.I.
Etiology of Syncope	Unexplained			0.225		
Non-Cardiovascular		-0.061	0.105		0.94	(0.77 ,1.16)
Cardiovascular		0.162	0.125		1.18	(0.92 ,1.50)
Health Care System	Medicare			0.012		
Group Model HMO		-0.237	0.101		0.79	(0.65 ,0.96)
VA Hospital		0.121	0.159		1.13	(0.83 ,1.54)
Living at Discharge	Independent			0.000		
Assisted Care Facility		0.361	0.125		1.43	(1.12 ,1.83)
Nursing Home		0.599	0.146		1.82	(1.37 ,2.42)
Left Ventricle Function	Normal or Mildly Reduced			0.033		
Moderately or Severely Reduced		0.424	0.187		1.53	(1.06 ,2.20)
Unknown or Not Stated		0.247	0.118		1.28	(1.02 ,1.61)
Congestive Heart Failure	No	0.490	0.119		1.63	(1.29 ,2.06)
Aortic Stenosis	No	0.458	0.172		1.58	(1.13 ,2.21)

hospitalization, 4 had missing values, so were excluded
* from the model

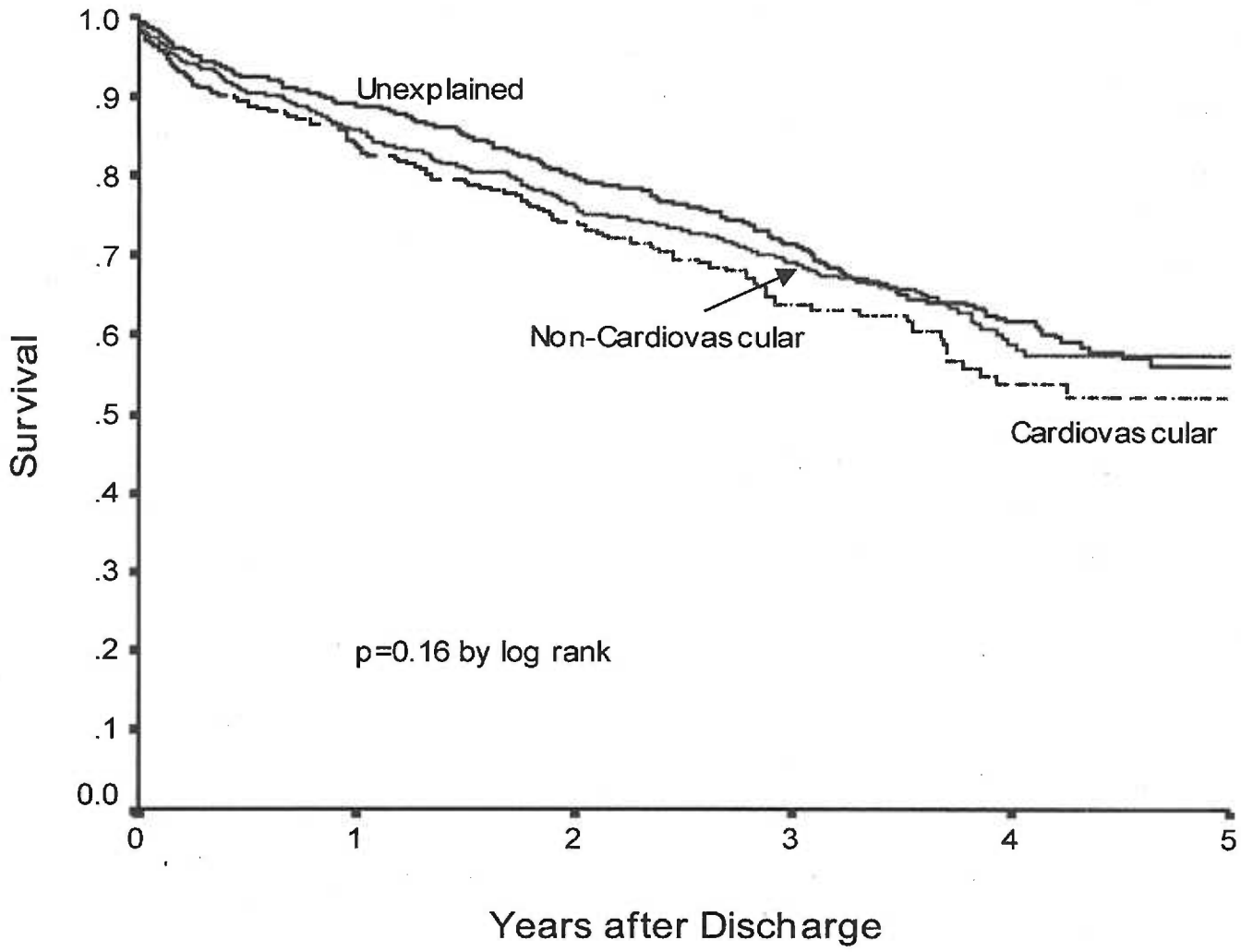
** Beta refers to coefficient from Cox model, SE is the standard error of the coefficient

*** Relative risk of dying compared to reference category

P value refers to the overall Chi square for the categorical variable with 2 df

The other variables in the final multivariate Cox model were Age (converted to z score: (age-73.0)/13.4), Age squared, Age cubed, Charlson index (grouped as 0, 1-2, 3-4, 5 or more and used as a continuous variable), Age-Comorbidity Interaction, Gender (Female/Male), Number of active diagnoses (continuous), Active diagnoses of malignancy (Yes/No) or volume/bleeding (Yes/No) and Distance from the hospital (more/less than 50 miles)

The variables which were candidates for, but did not remain in, the final multivariate model were Ethnicity (white/other), Coronary Artery Disease (Yes/No), History of Syncope (Yes/No), Hospital Location (Urban/Rural), Site of Admission (ER/Other), Non Cardiac Chest Pain (Yes/No), Neurologic Diagnosis (Yes/No), Minor Therapy (Yes/No), Major Therapy (Yes/No), Cardiology MD (Yes/No) and Neurology MD (Yes/No).

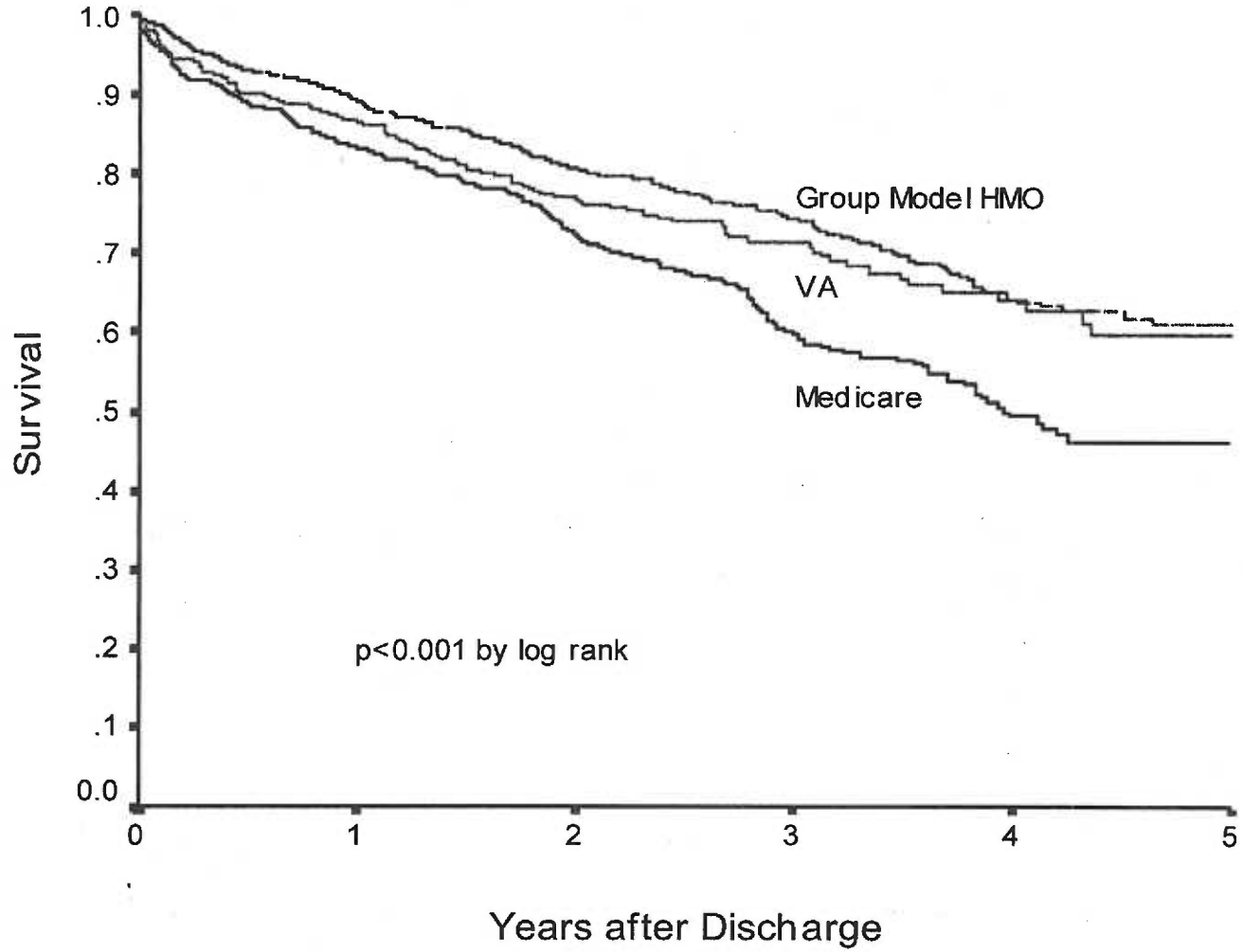


Number at Risk					
Cardiovascular	284	237	211	115	44
Non-Cardiovascular	602	516	458	279	94
Unexplained	630	560	503	299	139

Figure 1: Kaplan-Meier Survival after Syncope: Influence of the Etiology of the Syncopal Event

LEGEND FOR FIGURE 1:

N=1516 patients admitted to the hospital in three health care systems in Oregon. No overall differences in survival are seen for the different etiologies of the syncopal event. Pairwise log rank statistics, adjusted for multiple comparisons, also show insignificant differences: cardiovascular vs. non-cardiovascular syncope p=0.44, cardiovascular vs. unexplained syncope p=0.16, unexplained vs. non-cardiovascular syncope p=0.76

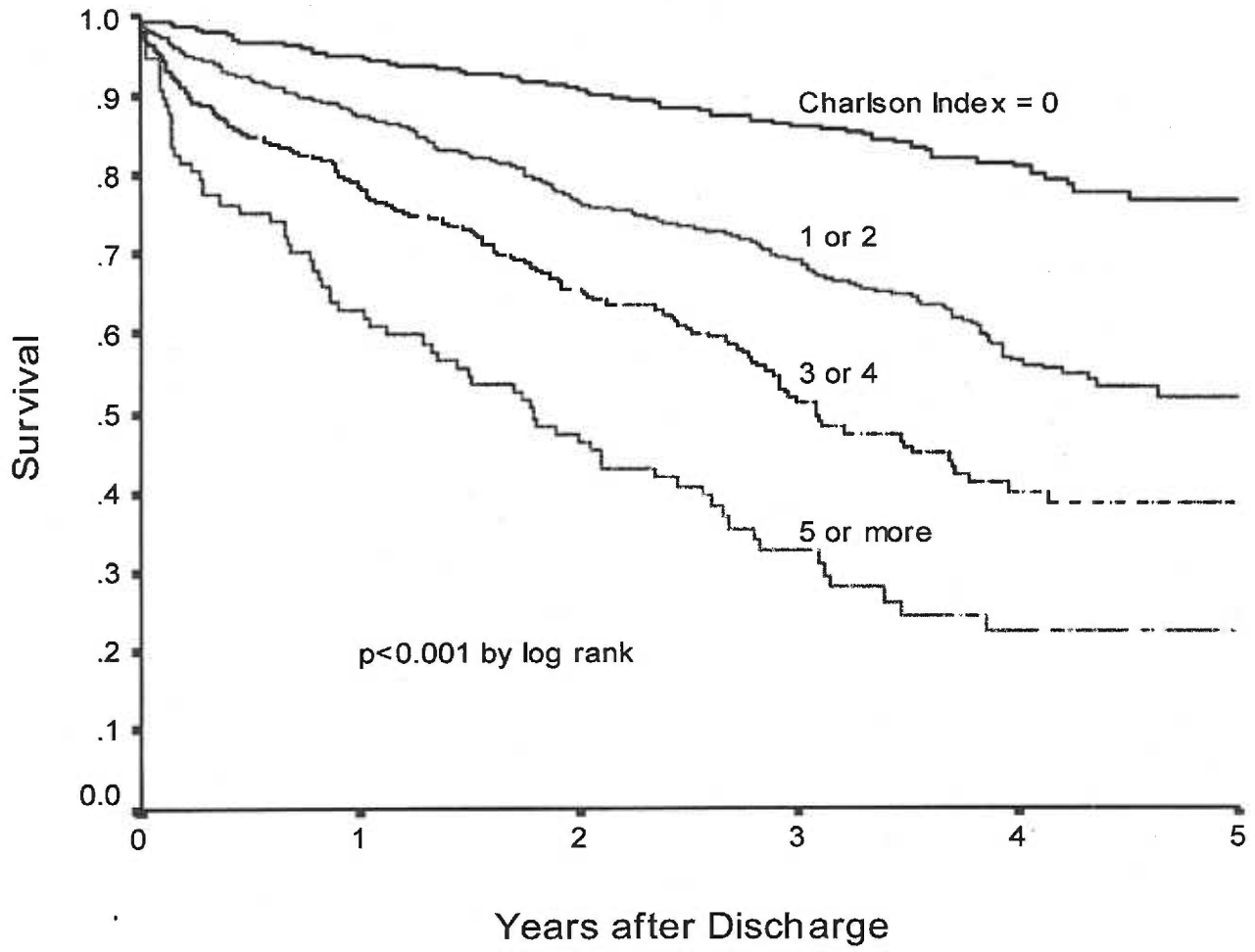


Number at Risk					
Medicare	487	405	352	202	78
Group Model HMO	744	662	601	372	144
VA	285	246	219	119	55

Figure 2: Kaplan-Meier Survival after Syncope: Influence of the Health Care System

LEGEND FOR FIGURE 2:

N=1516 patients admitted to the hospital in three health care systems in Oregon. A significant difference in survival is seen for the different health care systems. These are unadjusted survival curves, and partially reflect significant age differences between the three health care systems. The overall difference is significant. Pairwise log rank tests, adjusted for multiple comparisons, are HMO vs. Medicare $p<0.001$, HMO vs. VA $p=0.68$ and VA vs. Medicare $p=0.02$



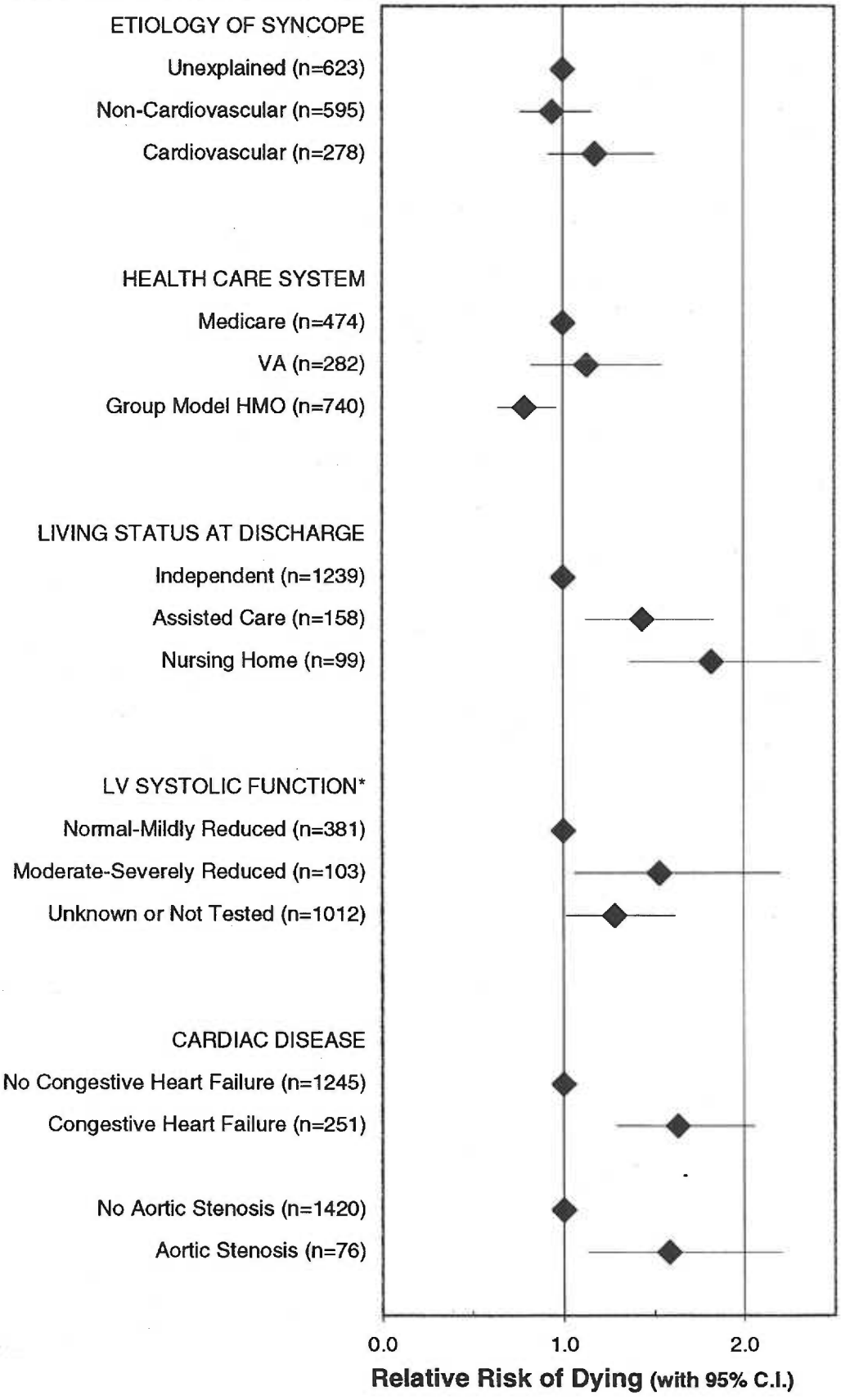
Number at Risk					
Charlson Index = 0	489	465	445	282	126
1 to 2	655	574	502	299	111
3 to 4	272	213	179	90	31
5 or more	96	61	45	22	9

Figure 3: Kaplan-Meier Survival after Syncope: Influence of Charlson Comorbidity Index

LEGEND FOR FIGURE 3:

N=1516 patients admitted to the hospital in three health care systems in Oregon. A marked difference in survival is seen for increasing Charlson comorbidity Index. These differences continue for the entire period of follow up.

Figure 4: Prognostic Factors after an Admission for Syncope



LEGEND FOR FIGURE 4:

Results of a Cox proportional hazards model including N=1496 individuals admitted to the hospital for syncope who survived to discharge and had no missing values. The relative risks [RR] for these prognostic factors are adjusted for age, gender and comorbidity. See Table 6 for exact values of estimated RR and Confidence Intervals (C.I.) * LV refers to left ventricular.

Diagnostic evaluation of individuals with syncope.
Does the initial inpatient evaluation affect 4-year survival?

Running Head: Diagnostic testing in syncope

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4 Tables
1 Figure

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Abbreviations Used in the Text:

DTI = Diagnostic Testing Index
LOS = Length of Stay
HMO = Health Maintenance Organization
RR = Relative Risk
CI = Confidence Interval

Key Words: syncope, diagnosis, survival analysis, delivery of health care

ABSTRACT

Context: Syncope is a common syndrome, yet no diagnostic algorithm has been established. It is unknown whether an aggressive evaluation with more diagnostic testing improves long-term survival when compared to a conservative approach.

Objective: To describe the relationship between the initial diagnostic resource use for individuals admitted to the hospital with syncope and 4-year survival.

Design: Retrospective cohort study

Participants: Patients with an admission or discharge diagnosis of syncope (ICD9 780.2) in the calendar years 1992,1993 or 1994 in Oregon .

Outcome Measure: All cause mortality through December 1996, obtained using the National Death Index.

Results: The mean age in our cohort was 73 years, with a mean comorbidity index of 1.6. We separated individuals into quartiles based on the amount of diagnostic testing. Increased diagnostic testing was seen for individuals in the VA system and for individuals with cardiovascular syncope. Multivariate analysis suggested that there was an inverse relationship between diagnostic testing and mortality, adjusting for other important prognostic variables. The relative risk of dying (compared to the lowest quartile) was reduced in increasing quartiles of diagnostic resource use: 0.89 (95% C.I. 0.69-1.16) in quartile 2, 0.72 (0.54-0.95) in quartile 3, and 0.65 (0.47-0.90) in the highest quartile of diagnostic resource use (overall $p = 0.036$).

Conclusions: Increased amounts of diagnostic testing for individuals with syncope were associated with improved long-term survival. The mechanism of this benefit is unclear, yet would support aggressive attention to the overall health status for individuals suffering syncopal events.

BACKGROUND

Syncope continues to stress the diagnostic abilities of clinicians[1,2]. The difficulties in the evaluation of syncope lie in the complexity and variety of the underlying pathophysiologic mechanisms, its intermittent nature, the frequent absence of abnormalities after the index event and the lack of effective and accurate tests to re-induce symptoms. In the last two decades, there have been several approaches suggested for evaluating individuals with syncope[1-6], yet as many as 47% of individuals will not have an etiology of their syncopal event identified[4,7-10]. This raises the issue as to if there is or is not a benefit from diagnostic testing in these individuals, whether defined in terms of identifying an etiology of syncope, or more importantly in improving their outcomes.

We have recently described prognostic factors for long-term survival in individuals admitted to the hospital with syncope[11]. The etiology of the syncopal event did not provide independent prognostic information as to four-year survival, after adjustment for independent predictors of mortality such as age, comorbid illness, living arrangements, gender and health care system. The finding of a lack of prognostic value for the etiology of syncope suggests that an aggressive diagnostic evaluation would be unlikely to provide a long-term survival benefit for these individuals.

We hypothesized that, among patients with syncope, the amount of diagnostic testing would not be related to long-term survival. This analysis was designed to define the initial evaluation of individuals with syncope in a broad range of health care settings in Oregon, and to describe the relationship between this initial diagnostic evaluation and long-term survival.

METHODS

Study Design and Source of Patients

This study used an observational cohort design. We identified three health care systems in Oregon: a tertiary care VA hospital, a group model HMO and Medicare. We reviewed the discharge databases of these organizations from January 1, 1992 through December 31, 1994, selecting patients with ICD-9-CM code 780.2 (Syncope and Collapse) as an admission or discharge diagnosis. The first admission in the time frame for a patient was identified for review; subsequent admissions were not included. There were 324 patients identified at the VA (0.98% of total admissions), 823 at the HMO (0.93%) and 5314 (1.70%) at Medicare. After excluding Medicare patients admitted to the group model HMO's hospitals, a sample of the remaining Medicare charts was selected at random (n=554).

Chart Review Data Collection

Medical records on the 1701 individuals were reviewed by one individual [WSG]. The inclusion criterion was a documented syncopal event that occurred prior to admission to the hospital. We defined syncope as a transient loss of consciousness that resolved spontaneously. Exclusion criteria were cardiac arrest, a persistently altered level of consciousness, and age less than 13 years. For individuals transferred to another hospital during their admission, both hospitals' records were reviewed, and considered as one hospitalization (all were available).

Each admission was reviewed in detail. The comorbidities included in the Charlson Index[12] were recorded. For other comorbidities, standard definitions were used.

New findings addressed during the admission were recorded separately from pre-existing conditions. Diagnostic test use was listed. Interventions such as pacemaker placement or cardioversion were also recorded. All physicians seeing the patient were identified by specialty. Resident physicians were not identified specifically; rather the attending physician's specialty was recorded. Physician, nursing and social work notes were used to determine where patients lived prior to admission and at discharge. The distance from each patient's stated home address and the admitting hospital was determined using a map of Oregon and Washington, and recorded to the nearest five miles. The hospital's location was categorized as urban or rural.

The etiology of the syncopal event was defined as that stated by the primary physician, and was later categorized as cardiovascular, non-cardiovascular or unexplained using the definitions of Kapoor[7]. Cardiovascular causes included tachycardia, bradycardia, and aortic stenosis. Non-cardiovascular causes included vasodepressor, medication-related, and neurologic events.

Resources

To compare the different patterns of testing in individuals, we developed an index of diagnostic tests based in 1997 dollars. For each of the diagnostic tests, we assigned the value of 1997 Medicare Relative Value Units (RVU)[13]. We used the total RVU, including physician work, practice expense and malpractice components, but ignored the geographic indices. The RVUs were converted to 1997 dollars using the standard conversion factors listed in the federal register. There were no RVUs available for two items: telemetry and rule out myocardial infarction. For telemetry, we assigned $135 for

individuals with one-day hospital stays, and $260 for all other durations. For "rule out myocardial infarction", we assigned $69 as the cost of two separate tests for CPK and CPKMB. For each physician who saw the patient, we assigned the RVU for a single comprehensive evaluation. The diagnostic tests performed plus the physician visits were combined into the Diagnostic Testing Index (DTI). This index is the purest measure of resources involved in diagnosis.

In order to control for differences in patient characteristics and severity of illness that were not captured by standard confounding variables, we grouped individuals into quartiles of length of stay (LOS). LOS loosely estimates the resources used in the hospital management of syncope. Although we are underestimating the overall resource use (for example, ICU care, pharmacy and laboratory) LOS assists in differentiating between individuals requiring significantly different amounts of hospitalization.

Death Data

The primary study outcome was death due to any cause. All names and social security numbers (available for 92% of individuals) were submitted to the National Death Index to match with deaths through December 31, 1996. This index is 99.9% specific and 97% sensitive when the social security number is available[14]. Partial matches were all explicitly reviewed. Among the 1516 names submitted, there were 522 matches. Only three out of 444 individuals identified as deceased by chart review (death certificate, autopsy or Medicare files) were not identified by the index, suggesting a very high sensitivity. Individuals not identified as deceased are assumed to have been alive on December 31, 1996, and their survival times are censored on that date.

Chart Review Reliability

Records were re-reviewed by a second individual in a 5% random selection of the 1516 patients. Weighted Kappa scores between the two reviewers for comorbidities, tests and therapies, and etiology of syncope were 0.71 and 0.79, and 0.91 respectively. A Kappa score above 0.7 indicates excellent reliability.

Statistical Analysis

Statistical testing was performed using SPSS version 7.5 (SPSS Inc., Chicago, IL) Continuous variables were compared with analysis of variance. When necessary, non-normal variables were transformed using ranking. The Kruskal-Wallis test and Spearman Rho were used for comparisons between ranked variables. The χ^2 test was used to compare dichotomous variables, and using the method of multiple subgroup comparisons from Fleiss[15]. Survival was estimated using the Kaplan-Meier method, and the log rank test was used to compare factors. All tests of hypotheses were considered significant when two-sided probability values were <0.05.

The primary exposure variable in this analysis of survival was diagnostic testing. We separated individuals into quartiles of diagnostic testing (DTI) and length of stay (LOS). Because the DTI and LOS were highly correlated and Kaplan-Meier survival plots of the quartiles of LOS suggested unequal hazards, we used a stratified Cox model, allowing for different baseline hazards in each quartile of LOS. Cox proportional hazards analysis was used to estimate the relative risks (RR) of dying after discharge associated with varying quartiles of DTI. In all analyses, we defined the reference category as the lowest quartile of DTI.

Age was used in our models as a polynomial up to the third power. The Charlson Index was categorized into four categories (0, 1-2, 3-4, 5 or more) and used as a continuous variable. Variables with several values were re-coded as dummy variables.

Our first model included the DTI in an unadjusted, unstratified Cox model. Subsequently, we stratified by LOS, and then adjusted for age and comorbidity only. Our final model adjusted for all factors found to be prognostically important previously, and allowed us to evaluate survival after hospital discharge with respect to quartiles of diagnostic resource use, adjusting for age, the presence of specialists, co-morbidity, health care system and final cause of syncope. The analyses were repeated after creating the DTI quartiles separately for each system.

Results

Demographics and Baseline Characteristics

There were 1701 individuals identified. After review, 185 patients (11%) were excluded. The main reason for exclusion was that there was no true syncopal event prior to admission (n=147). Other reasons for exclusion were miscoding (n=22), unavailable charts (n=11) and age less than 13 years (n=5). We have no way of directly assessing the accuracy of case ascertainment, yet the low rate of false positive miscoding suggests that the number of false negatives (cases missed) due to miscoding is also small. There were 1516 patients with syncope available for analysis.

The mean age was 73 years, and there were slightly more males than females (Table 1). Typical of Oregon, most of the patients were non-Hispanic white. Individuals were primarily drawn from the Portland metropolitan area. Most patients were living at home independently prior to admission (90%). The remaining patients were almost all in assisted care. The site of the admission was usually the emergency room with smaller numbers admitted through clinic or hospital transfers. The mean Charlson comorbidity index was 1.60, with a range from 0 to 9. Cardiovascular disease was common in the population. One out of five individuals had suffered syncope in the past.

Inpatient Management

The standard tests of EKG and telemetry monitoring were used almost universally, while other tests for arrhythmias such as holter monitoring and electrophysiology study were only rarely performed (Table 2). The most common other cardiac test was an echocardiogram, performed in 17% of individuals. Neurologic tests

were also performed relatively often, with head CT scan performed in 20% of individuals, and electroencephalogram in 11%. Internists participated in the care of 3 out of 4 admissions, while family practitioners and general practice physicians cared for one in seven. Cardiologists and neurologists were often consulted (31% and 13% of admissions respectively). The median length of stay was 3 days, with a range of 1 to 37 days.

Interventions were uncommon in this population. Pacemakers were implanted in 5.6% of patients, antiarrhythmic drugs were started in 7.7%, valve replacement was performed in 0.5%, coronary artery bypass surgery was performed in 0.7% and angioplasty in 0.3%. Other interventions, such as cardioversion and temporary pacemaker placement were also performed in less than 1% of individuals.

Diagnostic Testing Quartiles

Combining the diagnostic tests and initial physician visits resulted in a median diagnostic testing index (DTI) of $643, with a range of $150 to $5642. The entire cohort was separated into quartiles based on the values of the DTI (Table 3). The lowest quartile had a median DTI of $381, the second quartile had a median DTI of $547, the third quartile had a median DTI of $813, and the highest quartile had a median DTI of $1,350.

There were significant differences in age between the quartiles ($p<0.001$), with younger patients receiving more diagnostic testing. There were no differences ($p=0.29$) in comorbidity among the quartiles. Individuals in the highest quartile of DTI were more likely to have been living at home prior to admission, were more likely to be hospitalized more than 50 miles from home and were more likely to have been admitted to the VA hospital. Individuals in the higher quartiles of diagnostic testing were more likely to have

a cardiovascular etiology of syncope identified during the admission, and had more active diagnoses documented during their admission. In this retrospective analysis, we do not know if these findings are a cause of, or an effect of, the different amounts of diagnostic testing.

As expected, there was a steep gradient of specific diagnostic tests across the four quartiles (Table 4), and there were marked differences in the involvement of cardiologists and neurologists. Strikingly, more than half of the individuals in the highest quartile underwent echocardiography, compared to none of the individuals in the lowest two quartiles. The patterns were similar for both cardiologic and neurologic tests. Cardiologists were seen by 62% of the highest quartile individuals, compared to only 4% of the lowest quartile patients. Generalist physicians were seen equally among all quartiles, suggesting that diagnostic testing was driven by specialty care.

The ranked values of length of stay (LOS) were highly correlated with DTI (Spearman Rho 0.53). The median LOS ranged from 1 in the lowest quartile of DTI to 5 in the highest quartile. There were significant differences in the rates of all major cardiac interventions, although pacemakers were implanted relatively similarly in the upper three quartiles. All cardiothoracic surgery was performed on individuals in the highest quartile of diagnostic testing.

Survival

The Kaplan-Meier estimates of survival (± SE) at one year was similar for the four quartiles of diagnostic testing- 86± 1% for the lowest quartile; 86± 2% for the second quartile; 87± 2% for the third quartile and 88± 2% for the highest quartile of diagnostic

testing. At four years there were greater differences: 56± 4% in quartile 1; 56± 3% in quartile 2; 60± 3% in quartile 3 and 65± 3% in the highest quartile of DTI, but the overall differences in survival were not significant (p=0.16 by log rank).

These results were replicated using a simple unadjusted, unstratified proportional hazards model where there were no significant differences in relative risk (RR) between the four quartiles of DTI (p=0.19). However, when a model stratified for quartile of LOS was used, the impact of increasing DTI quartiles was substantial and highly significant (p<0.001). The RR (95% Confidence Interval) of dying for the highest quartile was 0.36 (0.27–0.49) when compared to the lowest quartile. After adjusting the stratified model for age and comorbidity, the effects of increased diagnostic testing were attenuated, but highly significant (p=0.001). The RR of dying in the highest quartile was 0.53 (0.38-0.73) compared to the lowest quartile. When adjusting for all other confounders, there remained a significantly reduced risk of dying with the higher levels of diagnostic testing (p=0.035). The adjusted RR estimates with confidence intervals for the four quartiles of diagnostic testing suggest improved survival at each level of increased diagnostic evaluation (Figure 1). The model was reanalyzed after dividing the patients into quartiles separately in each health care system, yet virtually identical RR estimates were obtained [data not shown]. Additionally, we performed the same analysis separately in each health care system and recorded similar patterns, although not every quartile in every system was significant, as the number of patients in each analysis was reduced. A post hoc analysis of the different groups of etiology of syncope showed greater differences between DTI quartiles in individuals with non-cardiovascular and unexplained syncope than in individuals with cardiovascular syncope, although with smaller sample sizes the

variable was no longer significant.

Of particular interest is that the addition of the diagnostic testing index as a covariate and the stratification of the model by quartile of LOS did not markedly change any of the other major prognostic variables significantly [data not shown]. Of particular interest is that compared to Medicare, the RR of dying in the group model HMO was 0.76 (0.62-0.92) and the RR at the VA was 1.03 (0.75-1.41) [p = 0.01]. The RR of dying for cardiovascular syncope (compared to unexplained syncope) was 1.16 (0.91-1.48) and the RR for non-cardiovascular syncope was 0.92 (0.75-1.14) [p = 0.23].

DISCUSSION

The primary finding in this analysis of patients admitted to the hospital with syncope was that there was a significant relationship between the initial diagnostic evaluation and four-year survival. We found that individuals in the highest quartile of diagnostic testing during their hospitalization had a 35% reduced risk of when compared to individuals in the lowest quartile of diagnostic testing. At first glance, one might think that the mechanism that would produce this significant survival benefit was improved identification of individuals with cardiovascular syncope. However, we recently described a lack of prognostic value for the etiology of the syncopal event[11], contradicting the easy explanation. How then might the more extensive diagnostic evaluation be associated with survival?

The first possibility is that the association is spurious- a result of unmeasured confounders. In this analysis we have controlled exhaustively for age, comorbid disease, active problems during the admission and several social and administrative issues. Yet, we cannot rule out that there is a missing factor, "the eyeball test", where clinicians are able to predict who will survive in the future, and thus focus diagnostic efforts only on patients destined to survive. There is no way to definitively refute this explanation given our observational study design, and doing so would require a prospective randomized controlled trial to retest the association we have identified.

The second possibility is that our cohort of patients with syncope are at high risk of dying during the years after discharge, and the increased diagnostic testing is a surrogate measure of quality care in attending to their multiple medical problems. This

explanation is based on the assumption that more diagnostic tests are equivalent to quality care, an idea that is not universally accepted [16-18]. The impact of specialty care (more frequent in the higher quartiles) is also not known to provide a survival advantage, yet a more detailed analysis of the impact of specialists would be of interest.

The third possibility is that the individuals in the higher quartiles are simply receiving standard care, while the individuals in the lower quartiles are receiving sub-standard care. In a retrospective analysis of a syndrome like syncope, there is no way to know which amount of tests is right. Of course, the aggregate measures of association that we have used for our analyses cannot be extrapolated to determine the value of any individual tests.

Another possible reason for the association was the differential rates of therapeutic interventions in the quartiles of diagnostic testing. This explanation rests on the assumption that major cardiac interventions provide survival benefit. Although we would not argue that the use of valve replacement for aortic stenosis and the use of permanent pacemakers for complete heart block may provide a survival advantage, this is unlikely to completely explain the association. The stratification by overall resource use should have removed much of the influence of major interventions, and only 7% of individuals received these therapies anyway. Also, in our previous analysis[11], major intervention was not an independent predictor of survival.

On the surface, these results appear to contrast with our previous data that suggested that survival in the HMO was better than the other health care systems[11], despite similar or less diagnostic testing. However, simply considering the aggregate testing a system performs may be misleading, as the appropriate amount of testing may be

extensive for some individuals, but minimal in others. It may be that the HMO provided the most appropriate diagnostic evaluation for each individual, but overall performed less testing for better outcomes.

Our current findings also raise the question as to why the etiology of syncope was not associated with prognosis[11], despite the association with diagnostic testing. Our data does not allow us to assess whether more diagnostic testing resulted in more diagnoses of cardiovascular syncope, or whether cardiovascular syncope led to further diagnostic evaluations. It is also possible that since cardiac evaluations tend to be more expensive than evaluations of other etiologies of syncope, there is a natural association with cardiac syncope and higher testing. We hypothesize that the increased testing, whether a cause of or an effect of cardiovascular syncope, improved outcomes in a completely unrelated manner. It is certainly possible that the testing identified other medical problems that needed to be addressed, or clarified the degree of cardiologic disease, leading to more optimal management.

Overall, the observational nature of this study does not allow us to draw conclusions about causality. However, patients admitted to the hospital are at high risk (41%) of dying in the next four years, and we have identified an association with more extensive initial diagnostic evaluations and improved survival. Before changing current practice, we would recommend that our findings be tested prospectively in a randomized trial, comparing an aggressive diagnostic evaluation to a more conservative approach.

From the standpoint of process of care, at least 89% of individuals underwent the recommended[1-2] screening tests for arrhythmias: 12 lead electrocardiogram and telemetry monitoring. The paucity of individuals undergoing invasive electrophysiologic (EPS)

procedures (2%) suggests some uncertainty about the benefits of EPS in the initial evaluation of patients with syncope. There were also surprisingly few individuals undergoing the newer tests including signal averaged electrocardiograms and tilt table testing. Whether this is a result of a lack of data, lack of interest, or lack of availability is not known. The large number of individuals undergoing echocardiography is also somewhat puzzling. Clearly individuals with systolic murmurs consistent with aortic stenosis or IHSS should be evaluated with an echocardiogram, but for individuals without those physical findings, the reasons for performing an echocardiogram are unknown[2,19]. Whether the echocardiogram is helpful in the clinical management of these individuals separate from determining the etiology of the syncopal event is also not known.

Despite several recommendations to avoid neurologic testing in patients with syncope because of low yields for etiologies [1-6], there are still many head CT scans, carotid ultrasounds and electroencephalograms being performed. A limitation of our data is that we do not know why any of these tests were performed. It is certainly possible that much of the head CT's were performed to evaluate individuals with head contusions, as opposed to evaluating the syncopal event from a diagnostic standpoint. Thus deciding which specific tests were or were not useful in the evaluation of syncope is not possible.

Limitations

Our population was limited to patients admitted to the hospital with syncope, thus generalizing the findings to all individuals with syncope is not recommended, and may be inaccurate. In addition, the individuals in the population were primarily elderly (81% were 65 years or older), so generalizing the results to younger patients may prove

inaccurate. Although we feel that our data is representative of a wide variety of health care systems, facilities and providers, it was not a true random sample of all individuals in the state of Oregon with syncope, and specifically extrapolating the data to other populations may be inaccurate. Another factor that may limit the generalization of these results is the fact that no patient received an implanted defibrillator. We consider this a benefit, since it provides a true picture of the outcomes of syncope in an elderly population. As with any observational study, the treatment was not randomized, and we do not know the specific reasons why any test was performed, nor what benefit it provided. Particular to this study, we cannot say that the tests were truly used to evaluate syncope, as they may have been performed to assess other aspects of the individual's health status, totally unrelated to syncope. Thus we have not attempted to define which test or tests were associated with a survival benefit, but have examined broad groupings of diagnostic testing.

Conclusions

Increasing amounts of diagnostic testing for individuals admitted to the hospital with syncope were associated with improved survival. The mechanism of this benefit is unclear, yet would support aggressive attention to the overall health status of these individuals. The association that we have described should be tested formally in a prospective study.

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Table 1: Baseline characteristics for individuals admitted to the hospital with syncope.

	N= 1516
Age in Years mean (SD)	73.0 (13.4)
Non-Hispanic white	1455 (96.0)
Male	847 (55.9)
Portland Metropolitan Area	998 (65.8)
Hospital Location	
Rural	99 (6.5)
Urban	1417 (93.5)
Living Status Prior to Admission	
Independent	1366 (90.1)
Assisted Care	129 (8.5)
Nursing Home	20 (1.3)
Unknown	1 (0.1)
Admission Source	
Emergency Room	1282 (84.6)
Clinic Visit	123 (8.1)
Hospital Transfer	58 (3.8)
Elective	30 (2.0)
Other/Unknown	23 (1.5)
Health Care System	
Medicare	487 (32.1)
Group Model HMO	744 (49.1)
Veterans Affairs Hospital (VA)	285 (18.8)
Comorbidities	
Charlson Index mean(SD)	1.6 (1.7)
Coronary Artery Disease	518 (34.2)
History of Myocardial Infarction	250 (16.5)
Congestive Heart Failure	258 (17.0)
Aortic Stenosis	77 (5.1)
Atrial Fibrillation/Flutter	277 (18.3)
Supraventricular Tachycardia	71 (4.7)
Ventricular Tachycardia	40 (2.6)
Complete Heart Block	21 (1.4)
History of Syncope	325 (21.4)
Dementia	146 (9.6)
Diabetes	252 (16.6)
Hypertension	688 (45.4)

*all values are n(%) unless otherwise specified

Table 2: Diagnostic testing for individuals admitted to the hospital with syncope.

	N= 1516
Tests of Arrhythmia	
12 Lead Electrocardiogram (EKG)	1475 (97.3)
Telemetry Monitoring	1355 (89.4)
Holter Monitoring	41 (2.7)
Signal Averaged EKG	13 (0.9)
Electrophysiology Study	29 (1.9)
Cardiac Tests	
Tilt Table	11 (0.7)
Exercise Test	78 (5.1)
Echocardiogram	253 (16.7)
MUGA	13 (0.9)
Stress Thallium	31 (2.0)
Cardiac Catheterization	64 (4.2)
Neurologic Tests	
Carotid Ultrasound	146 (9.6)
Computed Tomography Head	300 (19.8)
Magnetic Resonance Image (Brain)	51 (3.4)
Lumbar Puncture	17 (1.1)
Electroencephalogram (EEG)	167 (11.0)
Other Tests	
Pulmonary Function Tests	26 (1.7)
Ventilation/Perfusion (VQ) Scan	34 (2.2)
Lower Extremity Venous Doppler	23 (1.5)
Physicians	
Internal Medicine	1166 (76.9)
Family or General Practice	217 (14.3)
Cardiology	468 (30.9)
Neurology	201 (13.3)

	25th percentile	Median	75th percentile
Diagnostic Testing Index [DTI] $	477	643	1,002
Length of Stay (LOS) days	2	3	5

*all values are n(%) unless otherwise specified

Table 3: Quartile of diagnostic testing index [DTI] for individuals admitted to the hospital with syncope. General Characteristics

	Quartile 1 n=379	Quartile 2 n=390	Quartile 3 n=368	Quartile 4 n=379	p value*
Diagnostic Testing Index [DTI]					
Median $	381	547	813	1,350	
Min, Max	(150,475)	(481,643)	(649,1000)	(1003,5642)	
Age in Years mean (SD)	74.4 (13.8)	74.6 (13.7)	73.0 (11.9)	70.0 (13.6)	0.000
Charlson Index mean (SD)	1.5 (1.6)	1.6 (1.6)	1.7 (1.7)	1.7 (1.7)	0.287
Living Status Prior to Admission					0.000
Independent	85%	88%	93%	95%	
Assisted Care	13%	11%	6%	5%	
Nursing Home	3%	1%	1%	1%	
Hospitalized More than 50 miles from Home	7%	4%	7%	20%	0.000
Health Care System					0.000
Medicare	35%	30%	32%	30%	
Group Model HMO	58%	56%	55%	38%	
VA	12%	14%	17%	32%	
Number of Active Diagnoses mean (SD)	2.4 (1.1)	2.6 (1.0)	2.7 (1.1)	2.8 (1.2)	0.000
Cause of Syncope					0.000
Cardiovascular	10%	18%	20%	27%	
Non-Cardiovascular	53%	39%	36%	30%	
Unexplained	38%	43%	44%	42%	

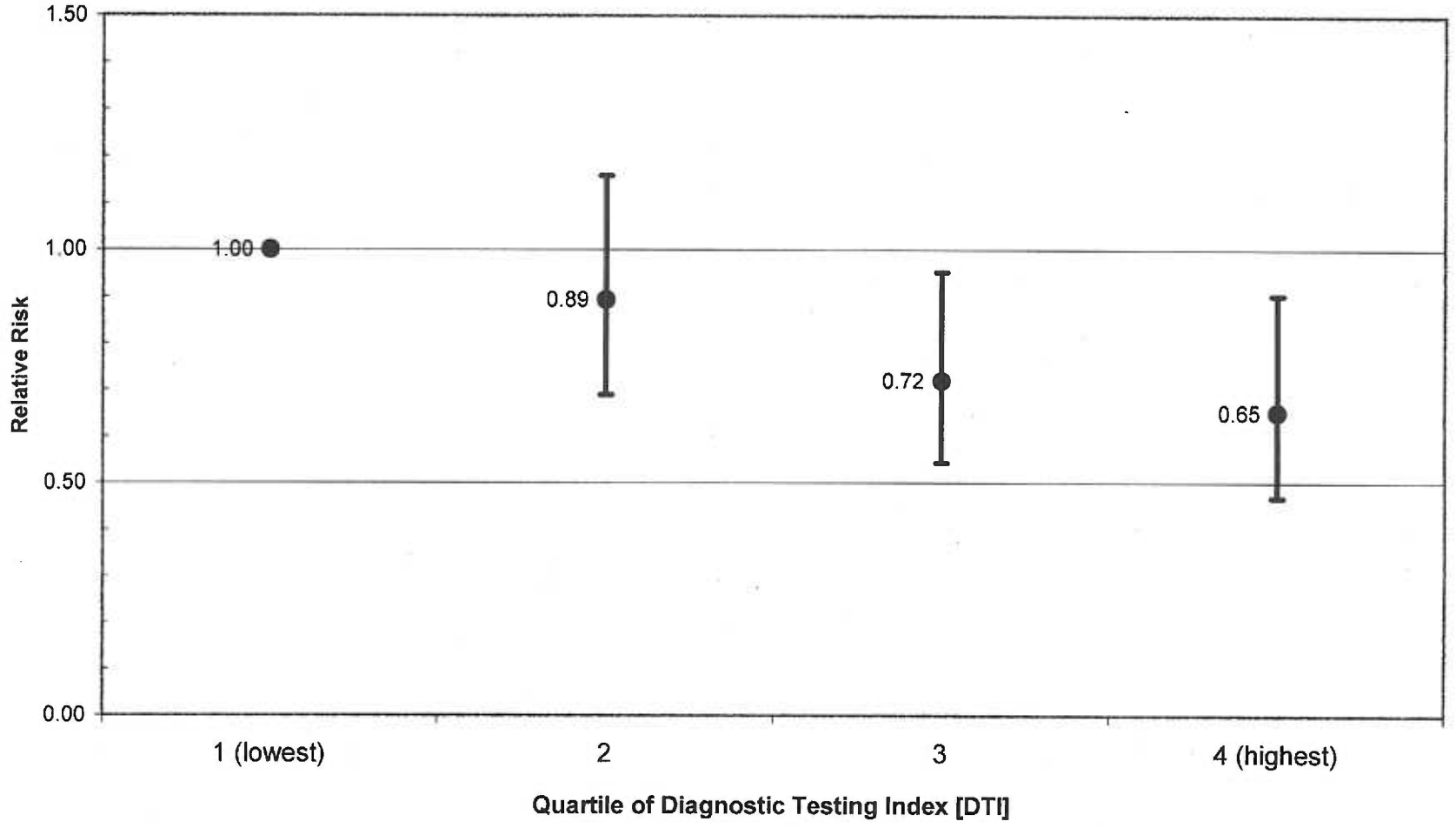
* p value for overall difference between quartiles by Chi Square

Table 4: Quartile of diagnostic testing index [DTI] for individuals admitted to the hospital with syncope. Testing and Interventions

	Quartile 1 n=379	Quartile 2 n=390	Quartile 3 n=368	Quartile 4 n=379	p value*
Selected tests performed in each quartile					
Telemetry	75%	95%	93%	95%	0.000
Holter Monitor	0%	0%	4%	6%	0.000
Electrophysiology Study	0%	0%	0%	8%	0.000
Tilt Table Test	0%	0%	1%	2%	0.003
Exercise Test	1%	5%	8%	7%	0.000
Echocardiogram	0%	0%	15%	52%	0.000
Cardiac Catheterization	0%	0%	0%	17%	0.000
Carotid Ultrasound	0%	3%	13%	22%	0.000
Head CT Scan	3%	13%	29%	35%	0.000
Electroencephalogram	1%	5%	16%	22%	0.000
Physician Involvement					
Internal Medicine	80%	79%	77%	75%	0.718
Family or General Practice	14%	16%	16%	12%	0.335
Cardiology	4%	22%	35%	63%	0.000
Neurology	1%	5%	17%	31%	0.000
Selected Interventions in each quartile					
Permanent Pacemaker	0%	5%	8%	9%	0.000
Valve Replacement	0%	0%	0%	2%	0.001
Coronary Artery Bypass Grafting	0%	0%	0%	3%	0.000
New Anti-Arrhythmic Drug	4%	6%	8%	13%	0.000
Length of Stay median (25,75)	1 (1,3)	2 (2,4)	3 (2,5)	5 (3,9)	0.000

* p value for overall difference between quartiles by Chi Square

Figure 1: Relative Risk of Dying After an Admission for Syncope: Effects of Increasing Amounts of Diagnostic Testing



Legend for Figure 1

*Relative risk of dying derived from Cox proportional hazards model, n=1496. Individuals not surviving the initial hospitalization (n=16), and individuals with missing values were excluded (n=4). The Cox model was stratified by quartile of Length of Stay- allowing for different baseline hazards in each quartile.

**Other variables in the model were age, comorbidity, age*comorbidity interaction, left ventricular systolic function, number of active diagnoses, active malignant diagnosis, active volume/bleeding diagnosis, gender, distance from the hospital, congestive heart failure, aortic stenosis, living arrangements at discharge, etiology of syncope and health care system.