Does quality of life predict morbidity or mortality in patients with atrial fibrillation (AF)?

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Background
Atrial Fibrillation (AF)

- AF is the most common chronic arrhythmia
- Incidence of AF increases with advancing age affecting almost 1 in 20 people > the age of 60
- Prevalence is expected to increase 2.5 fold by the year 2050 as the general population ages
- Hospital discharges exceed 465,000 annually in the U.S.

Rosamond W et al. (2007) *Circulation;* Fuster V et al. (2006) *J Am Coll Cardiol;* Go AS et al. (2001) *JAMA*

Background
Atrial Fibrillation (AF)

- **AF is an independent risk factor for death, stroke and decreased quality of life**

  Wolfe PA (1991) *Stroke*; Ezekowitz MD (2007) *N Engl J Med*

- **Symptoms include shortness of breath, palpitations, dizziness, chest pain, fatigue**

  Levy D et al. (1999) *Circulation;* Moser & Riegel (2008) *Cardiac Nursing*

- **Patients with AF frequently have associated cardiovascular conditions, including heart failure, MI, and other cardiac arrhythmias**

  BenjaminEJ et al. (1998) *Circulation;* Fuster V et al. (2006) *J Am Coll Cardiol*

Background
Atrial Fibrillation (AF)

- AF management
  - Rate-control with anticoagulation
  - Rhythm-control with anticoagulation
  - Innovative treatments (e.g. ablation)
- No differences in mortality or QOL between treatments reported in large, multi-center clinical trials.
- Symptoms improve with treatment however patients have poorer health related quality of life (QOL) than healthy controls.
- Psychosocial impairments and poor QOL worse in AF than post angioplasty, post-myocardial infarction, or with heart failure.

Dorian P, et al. (2000) J Am Coll Cardiol; Thrall et al. (2007) Chest; Thrall et al. (2006) Am J Med
Ong L et al. (2006) Quality of Life Research

Poor QOL Predicts Morbidity or Mortality

Post Myocardial Infarction

Gorkin L et al. (1993) *Am J Cardiol;* Thomas et al. (1997) *Am j Crit Care*

Heart Failure

Thomas et al. (2003) *AACN;* Friedmann E et al (2006) *Am Heart J*

Ventricular Arrhythmia

Steinberg et al. (2008) Heart Rhythm; Piotrowicz et al. (2007) Eur Heart J

Atrial Fibrillation

None known

Purpose

- **To examine the contribution of health related quality of life (QOL) to mortality, defined as time to death, beyond those of clinical/demographic variables in patients with AF.**

- **To examine the contribution of QOL to mortality, defined as hospitalization or death within one year beyond those of clinical/demographic variables in patients with AF.**

Methodology

- **Limited Access Data base**
  - IRB approved by UMB and NHLBI/NIH

- **Database**
  - Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)
  - Secondary data analysis
  - Prospective, longitudinal study
  - Baseline
  - Patients with AF (N=693)

Description of AFFIRM

Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)

- Randomized clinical trial comparing rate versus rhythm control in patient with AF and at least 1 other risk factor for stroke or death:
  - age 65 years or older
  - systemic hypertension
  - diabetes mellitus
  - congestive heart failure
  - transient ischemic attack, or prior stroke.

- 213 clinical sites randomized 4,060 pts over 3 years (NOV 1995 - OCT 1999).

- Average follow-up 3.5 years (OCT 2001)

- No statistically significant differences according to treatment in primary end point – survival .

AFFIRM Investigators (2002) *N Engl J Med*

Description of AFFIRM QOL Sub Study

- Fifty-six (25%) of AFFIRM sites were randomly selected to recruit AFFIRM patients to participate in the QOL substudy.

- Patients in both treatment groups completed questionnaires at baseline and follow-up.

  - Short Form-36 (SF-36) Ware, et al. (1992) *Medical Care*

  - Quality of Life Index-cardiac version (QLI-CV)
    Ferrans & Powers (1985) *Advances in Nursing Science*
    AFFIRM Investigators (2005) *AHJ*

Description of AFFIRM QOL Instruments: Short Form 36 (SF-36)

- Brief, self-administered, widely used generic measure of health status

- Covers physical and mental health concepts

- Designed to be applicable to a wide range of types and severities of health conditions

- Well-documented reliability and validity

Ware JE Jr, Kosinski M, & Gandek B (2002) *SF-36 Health Survey Manual & Interpretation Guide*.

Description of AFFIRM QOL Instruments:
Quality of Life Index- Cardiac Version (QLI-CV)

- **Brief, self-administered, generic instrument with an added disease component**

- **Well-documented reliability and validity**

- **Respondents rate satisfaction with 36 aspects of QOL then rate importance of each on a 6-point Likert-type scale**

Ferrans and Powers (1985) *Advances in Nursing Science*

Ferrans and Powers (1992) *Res Nurs Health*

Methods: Independent Variables

- Clinical/Demographic
  - History of CAD, Hypertension, Diabetes, Stroke/TIA
  - Heart Failure
  - LVEF
  - Treatment Arm
  - Smoker
  - Age
  - Gender
  - Socioeconomic status

- QOL
  - SF36 Physical component score (PCS)
  - SF 36 Mental component score (MCS)
  - Quality of life Index-CV scores

Baseline Characteristics N=693

Variable	Mean (SD)	N (%)
Age	69.8 (8.2)	
Gender, male		431 (62.2)
Ethnicity		
White, not of Hispanic origin		649 (93)
Clinical history		
Coronary artery disease		257 (37)
Heart failure		116 (17)
Hypertension		489 (71)
Diabetes		129 (19)
Stroke or transient ischemic attack		94 (13.5)
Left ventricular ejection fraction < 50%		128 (24.8)
Lives Alone		141 (20.3)
Smoking (within 2 years)		79 (11.4)

Outcomes

– **Mortality (n = 93; 13.4%)**

- **Time to death (survival days)**
- **Average follow up 3.5 years**

– **Morbidity (n = 259; 37.8%)**

- **Hospitalized or died within one year**

Research Questions

1. Do clinical/demographic variables, predict **mortality** (time to death)) in patients with AF **beyond the contributions of the** clinical/demographic variables?

2. Does QOL independently predict **mortality** (time to death) in patients with AF **beyond the contributions of the** clinical/demographic variables?

Predicting Mortality

Cox regression used to examine predictors of mortality (time to death)

- Step 1: Clinical/demographic variables (clinical history CAD, hypertension, HF, diabetes, stroke/TIA, LVEF, age, gender, socioeconomic status, treatment arm) are individual predictors of mortality (time to death)

  - Any variable that predicted mortality with $p < .2$ was included in a combined analysis of clinical/demographic predictors

Cox Regression Mortality: Combined Clinical/ Demographic Predictors

	Sig.	HR	95% CI	
Hypertension	.011	1.937	1.162	3.226
Age	< .001	1.109	1.070	1.150
Female	.039	.619	.393	.975

Predicting Mortality

- Step 2: QOL variables (PCS, MCS, QLI-CV) are independent predictors of mortality.

  - QOL variables were included in a combined analysis with clinical/demographic variables that predicted mortality with $p < .20$ in step 1

- Step 3: A parsimonious model was created by removing non- significant and non-influential ($p > .20$) variables and re-running the regression iteratively.

Cox Regression Mortality: Clinical/Demographic & QOL Predictors

	Sig.	HR	95% CI	
Hypertension	.015	1.885	1.131	3.143
Age	< .001	1.099	1.060	1.139
Female	.005	.510	.318	.818
MCS Score	.846	.995	.948	1.044
PCS Score	.005	.935	.892	.980
QLI –CV Score	.625	1.014	.959	1.071

Cox Regression Mortality: Final Model
Clinical/ Demographic & QOL Predictors

	Sig.	HR	95% CI	
Hypertension	.013	1.913	1.149	3.186
Age	< .001	1.102	1.063	1.142
Female	.004	.504	.315	.807
PCS Score	.002	.940	.905	.977

Predicting Morbidity

- **Logistic regression - same steps as in analysis of mortality**

- **Outcome is presence or absence of morbidity (hospitalization or death) in the first year of the study.**

Logistic Regression Morbidity: Clinical/Demographic Predictors

	Sig.	OR	95% CI	
CAD	.160	1.274	.909	1.785
Diabetes	.060	1.481	.984	2.230
Stroke	.013	1.793	1.132	2.840
Heart Failure	.007	1.801	1.171	2.772
Rhythm Control	< .001	2.090	1.508	2.897

Morbidity: Clinical/Demographic & QOL Predictors

	Sig.	OR	95% CI	
CAD	.207	1.247	.885	1.759
Diabetes	.224	1.301	.852	1.988
Stroke	.013	1.815	1.134	2.905
Heart Failure	.020	1.681	1.083	2.608
Rhythm Control	< .001	2.239	1.604	3.126
MCS Score	.036	.960	.924	.997
PCS Score	< .001	.932	.899	.967
QLI Score	.489	.986	.947	1.026

Logistic Regression Morbidity: Clinical/Demographic & QOL Predictors Parsimonious Model

	Sig.	OR	95% CI	
Stroke	.014	1.796	1.127	2.863
Heart Failure	.007	1.807	1.175	2.778
Rhythm Control	.000	2.206	1.584	3.073
MCS Score	.021	.957	.922	.993
PCS Score	.000	.927	.896	.958

Limitations

- **Related to secondary data analysis**
  - Variables set
  - Data categories defined
- **Cannot generalize results to younger patients with AF or those excluded from AFFIRM**
- **Small number of minorities**

Strengths

- Large, well-characterized sample

- No cost

- Network of investigators available

- Complete baseline SF-36 and QLI-CV data in AFFIRM

Conclusion

- QOL contributes to morbidity and mortality in patients with AF.

- Interventions for improving QOL and helping patients adapt to treatments for AF may decrease morbidity and improve survival.

- QOL adds meaningful information beyond traditional biomedical factors to the prediction of mortality and/or morbidity of patients with AF.