Journal of the American Heart Association

ORIGINAL RESEARCH

Longitudinal Changes in Health-Related Quality of Life in Patients With Atrial Fibrillation

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BACKGROUND: Optimizing health-related quality of life (HRQoL) is an important aim of atrial fibrillation (AF) treatment. Little is known about patients' long-term HRQoL trajectories and the impact of patient and disease characteristics. The aim of this study was to describe HRQoL trajectories in an observational AF study population and in clusters of patients with similar patient and disease characteristics.

METHODS AND RESULTS: We used 5-year follow-up data from the Swiss–Atrial Fibrillation prospective cohort, which enrolled 2415 patients with prevalent AF from 2014 to 2017. HRQoL data, collected yearly, comprised EuroQoL-5 dimension utilities and EuroQoL visual analog scale scores. Patient clusters with similar characteristics at enrollment were identified using hierarchical clustering. HRQoL trajectories were analyzed descriptively and with inverse probability-weighted regressions. Effects of postbaseline clinical events were additionally assessed using time-shifted event variables. Among 2412 (99.9%) patients with available baseline HRQoL, 3 clusters of patients with AF were identified, which we characterized as follows: "cardiovascular dominated," "isolated symptomatic," and "severely morbid without cardiovascular disease." Utilities and EuroQoL visual analog scale scores remained stable over time for the full population and the clusters; isolated symptomatic patients showed higher levels of HRQoL. Utilities were reduced after occurrences of stroke, hospitalization for heart failure, and bleeding, by −0.12 (95% CI, −0.18 to −0.06), −0.10 (95% CI, −0.13 to −0.08), and −0.06 (95% CI, −0.08 to −0.04), respectively, on a 0 to 1 utility scale. Utility of surviving patients returned to preevent levels 4 years after heart failure hospitalization; 3 years after bleeding; and 1 year after stroke.

CONCLUSIONS: In patients with prevalent AF, HRQoL was stable over time, irrespective of baseline patient characteristics. Clinical events of hospitalization for heart failure, stroke, and bleeding had only a temporary effect on HRQoL.

Key Words: atrial fibrillation ■ health-related quality of life

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This article was sent to Luciano A. Sposato, MD, MBA, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.123.031872

For Sources of Funding and Disclosures, see page 11.

JAHA is available at: www.ahajournals.org/journal/jaha

RESEARCH PERSPECTIVE

What Is New?

- In a heterogeneous population of patients with atrial fibrillation, health-related quality of life remained stable during 5 years of follow-up.
- Average health-related quality of life was lower in patients with older age and more comorbidities and higher in younger, healthier patients.
- Clinical events, such as hospitalization for heart failure, stroke, and bleeding, only led to temporary declines in health-related quality of life.

What Question Should Be Addressed Next?

- Further longitudinal studies with even larger samples and more frequent measurements are needed to characterize and understand the effects of clinical events on the health-related quality of life of patients with atrial fibrillation in a more granular manner.

Nonstandard Abbreviations and Acronyms

EQ VAS EuroQoL visual analog scale

The prevalence of atrial fibrillation (AF) is increasing globally and in Europe. In Europe in 2010, ≈9 million individuals aged >55 years experienced AF, a number that is expected to reach 14 million by 2060.[1] The consequences of AF include increased stroke and systemic embolism rates, leading to increased morbidity and mortality.[2] AF treatment aims include preventing these complications and improving and maintaining patients' health-related quality of life (HRQoL).[3]

Several studies found that the burden of AF and related complications reduces HRQoL[4–6] and that available treatment options can lead to HRQoL improvements.[7–9] However, HRQoL improvement was shown to vary between patients, dependent on their characteristics.[10] Specifically, treatable AF risk factors were shown to be associated with significant 1-year HRQoL improvements, whereas patients with difficult-to-treat or less reversible comorbidities, such as prior stroke/transient ischemic attack, chronic obstructive pulmonary disease, or peripheral arterial disease, were less likely to have HRQoL improvements.[10] Nonetheless, only limited information is available on longitudinal HRQoL trajectories in patients with AF. Most studies concentrate on examining the impact of particular treatment options (eg, by comparing catheter ablation with medical therapy)[7,11] and therefore capture only specific patient groups.

Patients with AF have heterogeneous profiles as AF affects not only older patients with multiple combinations of comorbidities, such as heart failure, diabetes, and cardiovascular diseases. There are also patients, often younger, for whom lifestyle factors, such as smoking, alcohol, obesity, extreme sports, and psychological stress, seem to modulate AF occurrence.[1] In addition, symptom severity and the type of AF are highly variable, and patients undergo different therapeutic approaches to reduce their AF burden.

Using data from a large prospective cohort study, we aimed to better capture and characterize this heterogeneity by classifying the studied AF population into more homogeneous clusters defined by patient and disease characteristics representing previously described phenotypes[12] and to present longitudinal trajectories of HRQoL over a 5-year follow-up period in both the full population and the identified clusters. We were also interested in the HRQoL impact of distinct, clinical events.

METHODS

Patient Population and Data Source

We analyzed data from the Swiss–Atrial Fibrillation (Swiss-AF) cohort. This prospective, multicenter, observational cohort study enrolled patients with documented AF between April 2014 and August 2017 across 14 clinical centers in Switzerland. Patients were enrolled if they were at least aged 65 years. In addition, the study population comprised a group of 228 patients aged between 45 and 65 years who were enrolled to include patients with AF in the working age. At Swiss-AF enrollment, the median (interquartile range [IQR]) time since diagnosis was 3.6 (0.9–8.5) years; 6% of the patients were diagnosed within 3 months before enrollment. Besides a large variety of patient and clinical characteristics, the study collects health economic data, including data on HRQoL, during yearly study visits. The detailed study setup has been described earlier.[13] Patients were included in this analysis if they had baseline data on HRQoL.

Swiss-AF was approved by Ethikkommission Nordwest- und Zentralschweiz (2014-067, PB_2016-00793), and written informed consent was obtained from all participants. The patient informed consent forms state that the data, containing personal and medical information, are exclusively available for research institutions in an anonymized form and are not allowed to be made publicly available. Researchers interested in obtaining the data for research purposes can contact the Swiss-AF scientific lead. Contact information is provided on the Swiss-AF website (http://www.swissaf.ch/contact.htm). Authorization of the responsible ethics committee is mandatory before the

requested data can be transferred to external research institutions.

Outcome Measures

The study's primary outcome was HRQoL measured with the 3-level version of the European Quality of Life-5 Dimensions Instrument,[14] a standardized instrument to assess generic HRQoL with questions on the 5 dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. For each dimension, 3 response categories (no problems, some problems, and extreme problems) are offered, leading to 243 possible health states.[14] These health states are converted into preference-based index values (utilities representing HRQoL) by applying country-specific valuation algorithms. In the absence of a Swiss valuation algorithm, we used the European valuation algorithm.[15] Utilities usually range from 0 (representing death) to 1 (representing perfect health); negative values are technically possible to represent health states perceived as worse than death.

In addition, the questionnaire contains the EuroQoL visual analog scale (EQ VAS) on which respondents can indicate their health status between 0 (worst imaginable health state) to 100 (best possible health state). All quality-of-life analyses were run using utilities and, alternatively, EQ VAS scores as outcomes.

Statistical Analysis

Trajectories of HRQoL were analyzed in the entire study population and clusters of patients with similar baseline characteristics. To identify clusters, a hierarchical cluster analysis was run, as previously described.[12,16] Hierarchical clustering is a multivariate statistical approach to create a classification of observations using information on their characteristics.[17] It is performed in such a way that groups are as homogeneous as possible within their class and as dissimilar as possible between the classes. In the previous study focusing on costs, the hierarchical clustering was performed on the whole Swiss-AF population and considered a large variety of baseline covariates: age, sex, body mass index, smoking, alcohol consumption, education, type of AF, AF symptoms, disease duration, the Congestive heart failure or left ventricular dysfunction, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled)-Vascular disease, Age 65-74, Sex category (CHA2DS2-VASc) score, prior interventions (percutaneous coronary angioplasty, coronary artery bypass grafting, electroconversion, or pulmonary vein isolation), medical history (previous major bleeding, stroke or transient ischemic attack, systemic embolism, heart failure, myocardial infarction, diabetes, hypertension, renal insufficiency, or sleep apnea), medical therapy (platelet-inhibiting drugs [excluding aspirin], statins, diuretics, β-blockers, digoxin, aspirin, direct-acting oral anticoagulants, or vitamin K antagonists), and history of cardiac device implantation. The present study also considered physical activity (sports), defined as engagement in any regular sporting activity (eg, jogging/walking, cycling, aerobics, or ball games). The analysis was run for different numbers of clusters, and the optimal number of clusters was then chosen using the elbow and silhouette methods.[17,18]

Baseline characteristics of the total population and by cluster are presented with mean and SD for normally distributed variables, median and IQR for continuous nonnormally distributed variables, and number (percentage) for categorical ones.

Unadjusted trajectories of utilities and EQ VAS scores, only considering patients who survived until a given follow-up time point, were depicted using a combination of box plots and smoothed line plots showing mean estimates and 95% CIs.

We adjusted for missing HRQoL values and differential censoring through inverse probability weighting[19] to estimate cluster-specific utility and EQ VAS score trajectories. Censoring could occur due to end of observation because of late enrollment, death, loss to follow-up, or other reasons. The inverse probability weights were calculated for each patient visit using the propensity for the availability of HRQoL data at each visit as a function of visit number, age, and the date of enrollment. Inverse probability-weighted linear regression allowed for interaction between the clinical visits (representing time in the study) and the clusters. Robust SEs were calculated to account for repeated measurements. Alternative inverse probability-weighted regression analyses were performed using the variable "time since diagnosis" instead of visit number to reveal possible effects of disease duration. For this regression, only patients with a time since diagnosis of up to 20 years were included, because of a low number of patients with a disease duration of >20 years. This model was fitted using natural splines for time since diagnosis with 5 *df*.

To assess the utility and EQ VAS score effects of events occurring after baseline, an additional linear regression was performed where we included time-shifted event variables. Precisely, we denoted all follow-up visits where a postbaseline event of a specific type (stroke, bleeding, hospitalization for heart failure, or myocardial infarction) was recorded for the first time as time point 0 and set the visits before and after the event in relation to it (leading to a value range of −5 to 4). Bleeding was defined as major bleeding[20] or clinically relevant nonmajor bleeding. For patients without a postbaseline event of the respective type, all visits were denoted as −1. In the regression model, −1 was set as a reference value, and the variables "cluster" and "age at visit" were included as covariates. Our analytical approach is to be interpreted conditional on patients surviving the events previously described.

Table 1. Baseline Characteristics of the Full Swiss-AF Population and by Cluster

Characteristic	No.	Total (N=2412)*	Cardiovascular dominated (N=597)*	Isolated symptomatic (N=1296)*	Severely morbid without cardiovascular disease (N=519)*
Sex	2412				
Female		660 (27.4)	66 (11.1)	361 (27.9)	233 (44.9)
Male		1752 (72.6)	531 (88.9)	935 (72.1)	286 (55.1)
Age, y	2412	73.6 (68.2–79.0)	76.2 (71.5–80.5)	71.1 (66.1–75.9)	77.9 (72.8–82.9)
Type of AF	2412				
Paroxysmal		1077 (44.7)	224 (37.5)	688 (53.1)	165 (31.8)
Permanent		595 (24.7)	219 (36.7)	150 (11.6)	226 (43.5)
Persistent		740 (30.7)	154 (25.8)	458 (35.3)	128 (24.7)
Utility	2412	0.8 (0.7–1.0)	0.8 (0.7–1.0)	0.8 (0.8–1.0)	0.8 (0.7–1.0)
EQ VAS score	2412	75.0 (60.0–85.0)	70.0 (50.0–80.0)	80.0 (70.0–90.0)	70.0 (55.0–80.0)
Previous PVI	2412	489 (20.3)	48 (8.0)	416 (32.1)	25 (4.8)
AF symptoms	2409	1491 (61.9)	299 (50.2)	950 (73.4)	242 (46.6)
Previous stroke	2411	318 (13.2)	104 (17.4)	136 (10.5)	78 (15.0)
Status after device	2412	480 (19.9)	182 (30.5)	152 (11.7)	146 (28.1)
Diabetes	2412	421 (17.5)	228 (38.2)	91 (7.0)	102 (19.7)
Hypertension	2412	1689 (70.0)	524 (87.8)	739 (57.0)	426 (82.1)
Previous heart failure	2410	627 (26.0)	301 (50.6)	118 (9.1)	208 (40.1)
Coronary heart disease	2412	732 (30.3)	542 (90.8)	164 (12.7)	26 (5.0)
Time since first AF, y	2389	3.6 (0.9–8.5)	4.2 (1.2–10.4)	3.2 (0.8–6.8)	4.4 (1.1–10.7)
Previous electroconversion	2412	861 (35.7)	202 (33.8)	522 (40.3)	137 (26.4)
Previous major bleeding	2412	152 (6.3)	60 (10.1)	56 (4.3)	36 (6.9)
Previous MI	2412	389 (16.1)	330 (55.3)	49 (3.8)	10 (1.9)
Previous renal insufficiency	2410	511 (21.2)	232 (38.9)	101 (7.8)	178 (34.4)
Previous stroke/ TIA	2410	480 (19.9)	154 (25.9)	216 (16.7)	110 (21.2)
Previous systemic embolism	2411	126 (5.2)	49 (8.2)	41 (3.2)	36 (6.9)
Sleep apnea	2411	360 (14.9)	153 (25.7)	140 (10.8)	67 (12.9)
Device	2412				
CRT		29 (1.2)	13 (2.2)	6 (0.5)	10 (1.9)
CRT-ICD		45 (1.9)	29 (4.9)	9 (0.7)	7 (1.3)
ICD		75 (3.1)	46 (7.7)	16 (1.2)	13 (2.5)
Loop recorder		24 (1.0)	2 (0.3)	21 (1.6)	1 (0.2)
None		1932 (80.1)	415 (69.5)	1144 (88.3)	373 (71.9)
Pacemaker		307 (12.7)	92 (15.4)	100 (7.7)	115 (22.2)
Smoking	2410				
Former		1180 (49.0)	380 (63.7)	576 (44.5)	224 (43.2)
Yes, active		175 (7.3)	47 (7.9)	96 (7.4)	32 (6.2)
Never		1055 (43.8)	170 (28.5)	622 (48.1)	263 (50.7)
Sport	2410	1111 (46.1)	209 (35.0)	754 (58.3)	148 (28.5)

AF indicates atrial fibrillation; CRT, cardiac resynchronization therapy; EQ VAS, EuroQoL visual analog scale; ICD, implantable cardioverter-defibrillator; MI, myocardial infarction; PVI, pulmonary vein isolation; and TIA, transient ischemic attack.

*Data are given as number (percentage) or median (interquartile range).

Table 2. Utility and EQ VAS Score Values by Cluster and Follow-Up Time Point

Characteristic	Cardiovascular dominated						Isolated symptomatic						Severely morbid without cardiovascular disease					
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Utilities																		
Median (IQR)	0.78 (0.69–1.00)	0.78 (0.71–1.00)	0.78 (0.71–1.00)	0.78 (0.71–1.00)	0.78 (0.71–1.00)	0.78 (0.71–1.00)	0.83 (0.78–1.00)	1.00 (0.78–1.00)	1.00 (0.78–1.00)	1.00 (0.78–1.00)	1.00 (0.78–1.00)	1.00 (0.78–1.00)	0.78 (0.69–1.00)	0.78 (0.69–1.00)	0.78 (0.69–1.00)	0.78 (0.69–1.00)	0.78 (0.69–1.00)	0.78 (0.69–1.00)
Mean (SD)	0.80 (0.17)	0.80 (0.18)	0.80 (0.18)	0.80 (0.18)	0.80 (0.16)	0.79 (0.17)	0.86 (0.16)	0.86 (0.16)	0.87 (0.15)	0.86 (0.16)	0.86 (0.16)	0.88 (0.15)	0.78 (0.19)	0.77 (0.19)	0.77 (0.19)	0.78 (0.20)	0.76 (0.18)	0.77 (0.21)
Range	0.00–1.00	0.04–1.00	0.05–1.00	0.15–1.00	0.27–1.00	0.27–1.00	0.12–1.00	0.12–1.00	0.19–1.00	0.04–1.00	0.12–1.00	0.18–1.00	0.04–1.00	0.19–1.00	0.13–1.00	0.00–1.00	0.15–1.00	0.18–1.00
Unknown	0	65	90	104	176	278	0	59	98	113	333	647	0	63	77	97	152	218
EQ VAS score																		
Median (IQR)	70 (50–80)	70 (60–80)	70 (60–80)	70 (50–80)	70 (56–80)	70 (55–80)	80 (70–90)	80 (70–90)	80 (70–90)	80 (70–90)	80 (70–90)	80 (70–90)	70 (55–80)	70 (50–80)	70 (54–80)	70 (50–80)	70 (60–80)	70 (60–80)
Mean (SD)	67 (18)	69 (18)	69 (17)	69 (18)	68 (18)	67 (17)	76 (16)	78 (16)	78 (16)	78 (16)	78 (16)	78 (17)	68 (18)	68 (18)	68 (18)	69 (18)	69 (17)	69 (17)
Range	10–100	5–100	3–100	10–100	10–100	20–100	0–100	1–100	0–100	5–100	0–100	0–100	0–100	0–100	0–100	10–100	20–100	20–99
Unknown	0	65	87	105	174	278	0	55	99	120	325	646	0	64	78	97	147	215
Cumulative No. of deaths		31	63	40	103	142		18	37	55	70	96		24	50	80	114	135

Unknown values are attributable to death, loss to follow-up, or administrative censoring (ie, patients did not yet reach the respective follow-up time point). EQ VAS indicates EuroQoL visual analog scale; and IQR, interquartile range.

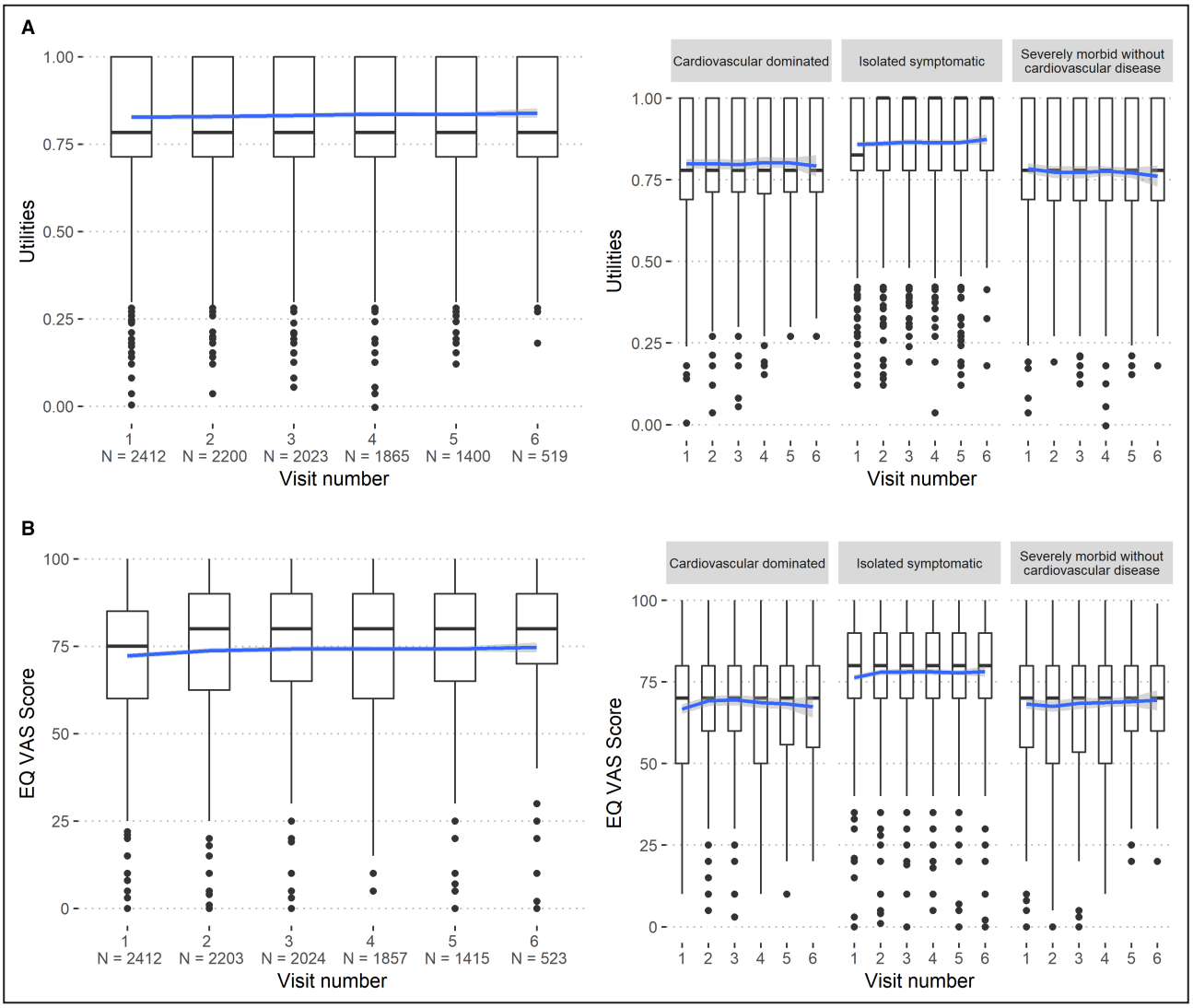

Figure 1. Unadjusted trajectories of utilities and EQ VAS scores.
A, Unadjusted trajectories of utilities. Follow-ups were performed in yearly steps. **B**, Unadjusted trajectories of EQ VAS scores. Visits were performed in yearly steps. Numbers of observation are indicated above the visit numbers. EQ VAS indicates EuroQoL visual analog scale.

All analyses were performed using R, version 4.0.5.[21]

RESULTS

Patients and Patient Clusters

Of 2415 Swiss-AF patients, 2412 (99.9%) had baseline data on HRQoL and were included in the analysis. Table 1 describes the baseline characteristics of the total population and in the 3 patient clusters, which the clustering algorithm implied to be the optimal number (Table 1).

The first cluster included 597 patients and was characterized by the highest proportion of men (88.9%) and the highest presence of previous heart failure (50.6%), previous coronary artery diseases (90.8%), and myocardial infarction (55.3%), compared with the other clusters.

Cluster 2 included 1296 patients, of whom 72.1% were men. These patients were the youngest, with a median (IQR) age of 71.1 (66.1–75.9) years, and they had primarily paroxysmal AF (53.1%). They had the highest proportion of patients with AF symptoms (73.4%) and were further characterized by a low presence of comorbidities, such as previous heart failure (9.1%), diabetes (7.0%), and renal insufficiency (7.8%).

The third cluster included 519 patients (55.1% men), who had the highest median (IQR) age of 77.9 (72.8–82.9) years and experienced most permanent AF (43.5%). In this cluster, we noted a low rate of previous pulmonary vein isolation (4.8%) at baseline and a high

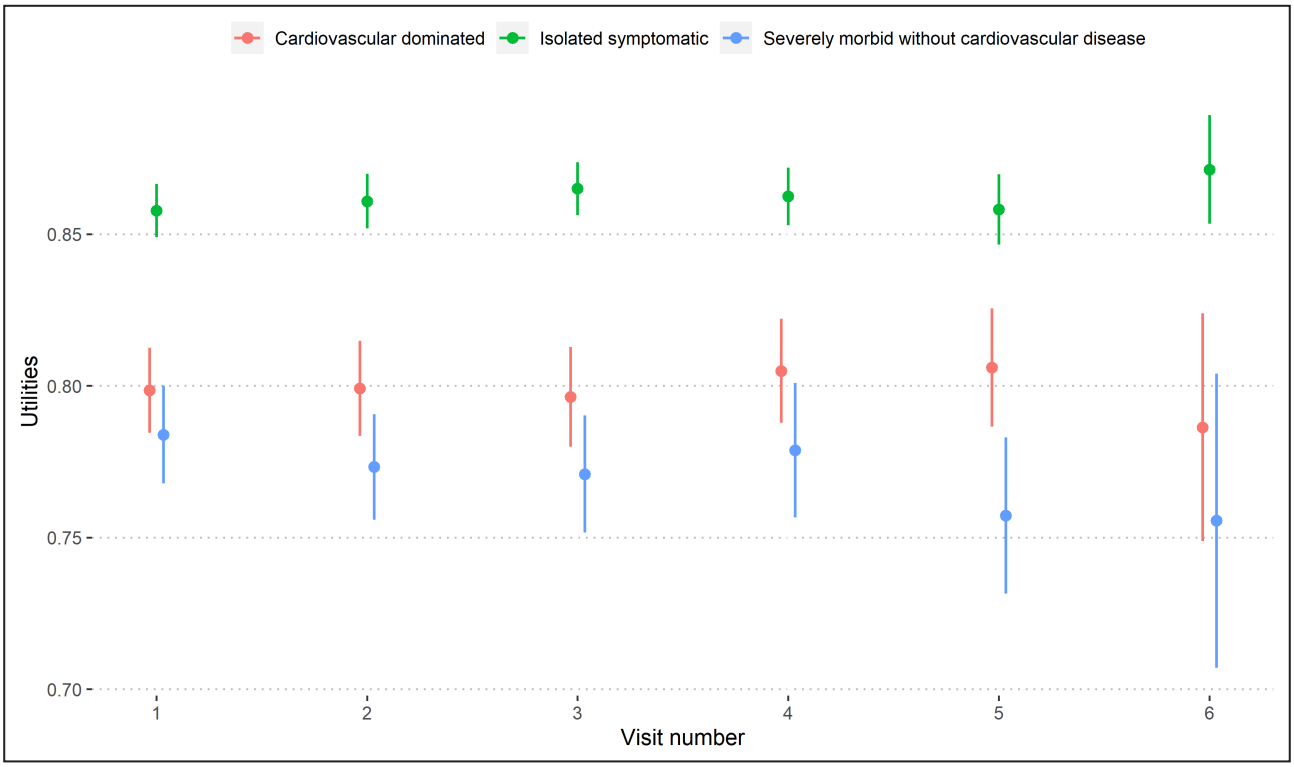

Figure 2. Predicted utility values by cluster.
Visits occurred in yearly steps. Utilities were predicted on the basis of an inverse probability-weighted model, including an interaction term between visit number and cluster.

rate of prior heart failure (40.1%), similar as in cluster 1. However, compared with cluster 1, the presence of previous coronary heart disease (5.0%) and myocardial infarction (1.9%) was low.

According to these cluster characteristics, we named cluster 1 cardiovascular dominated, cluster 2 isolated symptomatic, and cluster 3 severely morbid without cardiovascular disease.

HRQoL Trajectories

Starting with 2412 included patients at visit 1, utility data were available for 92.2%, 89.0%, 87.0%, 72.6%, and 52.6% of the patients, and EQ VAS data were available for 92.4%, 89.1%, 86.7%, 73.2%, and 52.8% of the patients at visits 2 to 6, respectively. Missing values were mainly attributed to patients who had not yet reached the different follow-up time points (Table 2). In the total study population, the unadjusted trajectories of utilities and EQ VAS scores remained stable over the 5 years of follow-up, with no apparent time trend. Similarly, HRQoL did not change significantly within the clusters over time (Figure 1A and 1B; Table 2).

The results of the inverse probability-weighted regression are shown in Table S1 and indicated that the isolated symptomatic patients started at a significantly higher utility level (0.06 [95% CI, 0.04–0.08]) than those in the cardiovascular-dominated cluster. The starting utility level of the severely morbid without cardiovascular disease cluster did not differ significantly from that in the cardiovascular-dominated cluster. As in the unadjusted analysis, the trajectories of the 3 groups remained stable during the 5-year follow-up (Table S1; Figure 2). The significantly better starting HRQoL of the isolated symptomatic cluster was also observed in the model using the EQ VAS scores as the outcome variable (9.61 [95% CI, 7.90–11.32]). This model also showed a significant increase in HRQoL for visits 2 (2.56 [95% CI, 1.18–3.94]), 3 (2.78 [95% CI, 1.19–4.38]), 4 (2.18 [95% CI, 0.35–4.00]), and 5 (2.18 [95% CI, 0.02–4.35]) compared with visit 1 (baseline) in cardiovascular-dominated patients (Table S1; Figure 3).

HRQoL and Time Since Diagnosis

HRQoL trajectories were also analyzed as a function of time since diagnosis. Median (IQR) time since AF diagnosis was 3.6 (0.9–8.5) years at study entry for the total population and 4.2 (1.2–10.4), 3.2 (0.8–6.8), and 4.4 (1.1–10.7) years for the patients in the cardiovascular-dominated, isolated symptomatic, and severely morbid without cardiovascular disease clusters, respectively.

No significant utility changes could be identified in any cluster, implying that the HRQoL remained stable without being substantially influenced by time since diagnosis (Table S2; Figure 4). When using EQ VAS

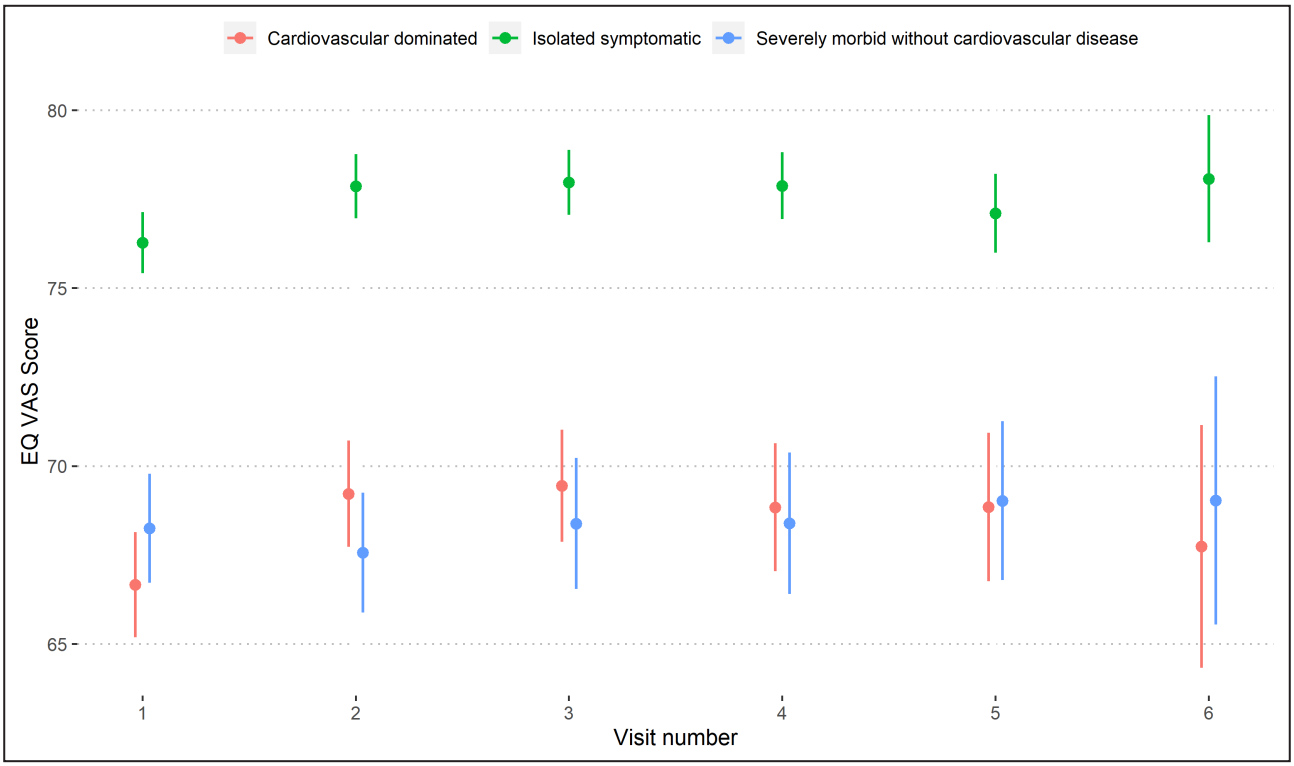

Figure 3. Predicted EQ VAS scores by cluster.
Visity occurred in yearly steps. EQ VAS scores were predicted on the basis of an inverse probability-weighted model, including an interaction term between visit number and cluster. EQ VAS indicates EuroQoL visual analog scale.

scores, we estimated a higher starting value for the isolated symptomatic cluster (7.15 [95% CI, 2.80–11.50]) with stable trajectories for all 3 clusters (Table S2; Figure 5).

Impact of Postbaseline Events on HRQoL

Figure 6 shows the effects of different postbaseline events on utility, independent of cluster membership. Events of hospitalization for heart failure (–0.10 [95% CI, –0.13 to –0.08]) and stroke (–0.12 [95% CI, –0.18 to –0.06]) entailed the most substantial reductions in utility if compared with the preevent visit. Bleeding events also reduced utility significantly (–0.06 [95% CI, –0.08 to –0.04]), whereas we observed no significant decrease in utility after myocardial infarctions. The utilities of surviving patients reincreased over time and reached their preevent values after 4 years in the case of hospitalization for heart failure, after 3 years in the case of bleeding, and after 1 year in the case of stroke (Table S3).

Findings for the EQ VAS score outcome were similar (Figure S1). Hospitalization for heart failure (–10.21 [95% CI, –12.87 to –7.56]) and stroke (–8.34 [95% CI, –12.63 to –4.05]) led to the strongest reductions, and preevent levels were reached after 2 years. Bleeding events led to a EQ VAS score change of –4.2 (95% CI, –6.11 to –2.28), with preevent levels never being restored during follow-up. HRQoL measured with the EQ VAS score was also not associated with myocardial infarction (Table S4).

DISCUSSION

This longitudinal study on the HRQoL of patients with AF brought 2 critical findings. First, we found that, in a heterogeneous population of patients with AF, the HRQoL remained stable over a 5-year follow-up independent of patients' characteristics at the first study visit. As expected, patients with older age and more comorbidities had a lower average HRQoL level than younger, healthier patients. Second, we found that the occurrence of events of stroke, hospitalization for heart failure, or bleeding reduced HRQoL substantially, with patients returning to the preevent status after ≈1 to 4 years. These results were mostly consistent regardless of whether utilities or EQ VAS scores were used to represent HRQoL. We observed, however, that bleeding events led to a longer impairment of HRQoL and that HRQoL returned faster to preevent levels after a hospitalization for heart failure, but more slowly after a stroke, if the EQ VAS metric was used.

The improvement and maintenance of HRQoL is a primary goal of AF treatment. We observed stable HRQoL trajectories over 5 years for our total study

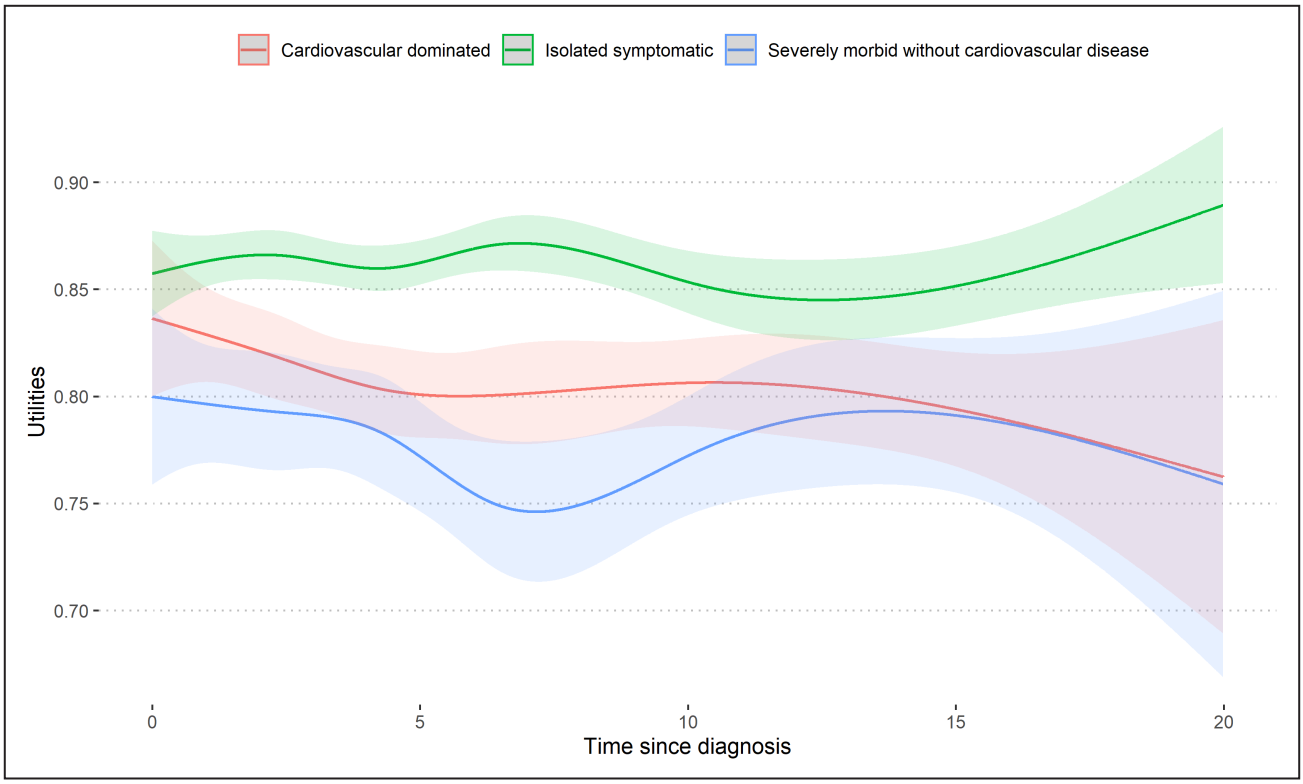

Figure 4. Predicted utitlity values according to cluster, dependent on time since diagnosis.
Utilities were predicted on the basis of an inverse probability-weighted model, including an interaction term between time since diagnosis and cluster.

population and 3 clusters of patients with AF representing cardiovascular-dominated, isolated symptomatic, and severely morbid without cardiovascular disease patients. Canadian research investigating the variability of health trajectories in patients with AF started a latent class clustering analysis based on HRQoL outcomes, an alternative approach. The authors identified trajectory classes and patient characteristics associated with these classes. They found 3 categories of trajectories (namely, "poor but improving," "good and stable," and "excellent and stable").[22] Patients in the poor but improving class were younger (aged <60 years) and had a higher likelihood of having received an ablation within 6 to 12 months after the initial consultation, compared with the patients in the other classes. The fact that in our case, most included patients were aged >65 years might explain why we did not find a patient cluster with improving HRQoL. In addition, our study population comprised only few recently diagnosed patients; a significant proportion of the patients probably already received HRQoL-improving treatments before enrollment into Swiss-AF. Nevertheless, because age and event rates increased over the 5-year study period, the stability of HRQoL in all clusters we identified is remarkable and may indicate adequate treatment. Awareness of quality-of-life differences between patient groups may help clinicians to develop realistic expectations, at least for patients matching typical cluster characteristics well. This may help them to provide more individualized care that enhances patient well-being and satisfaction. One important aim for patients in the isolated symptomatic group with high and stable HRQoL levels would be to prevent them from switching into the cardiovascular-dominated or severely morbid without cardiovascular disease group.

The observation that events of stroke, hospitalization for heart failure, and bleeding reduced HRQoL is in line with previous studies of patients with AF[23] and studies of events independent of AF.[24,25] However, to our knowledge, there are no previous data that provide estimates of the degree of utility reduction in patient populations with AF. We found the strongest impairment of HRQoL was attributable to stroke (–0.12 on the 0 to 1 utility scale), followed by hospitalization for heart failure (–0.10) and bleeding (–0.06). A previous study reported a mean minimal important difference for utilities of 0.074 across 8 different disease conditions (eg, including myocardial infarction, chronic obstructive pulmonary disease, and early rheumatoid arthritis).[26] On the basis of this, the utility changes after

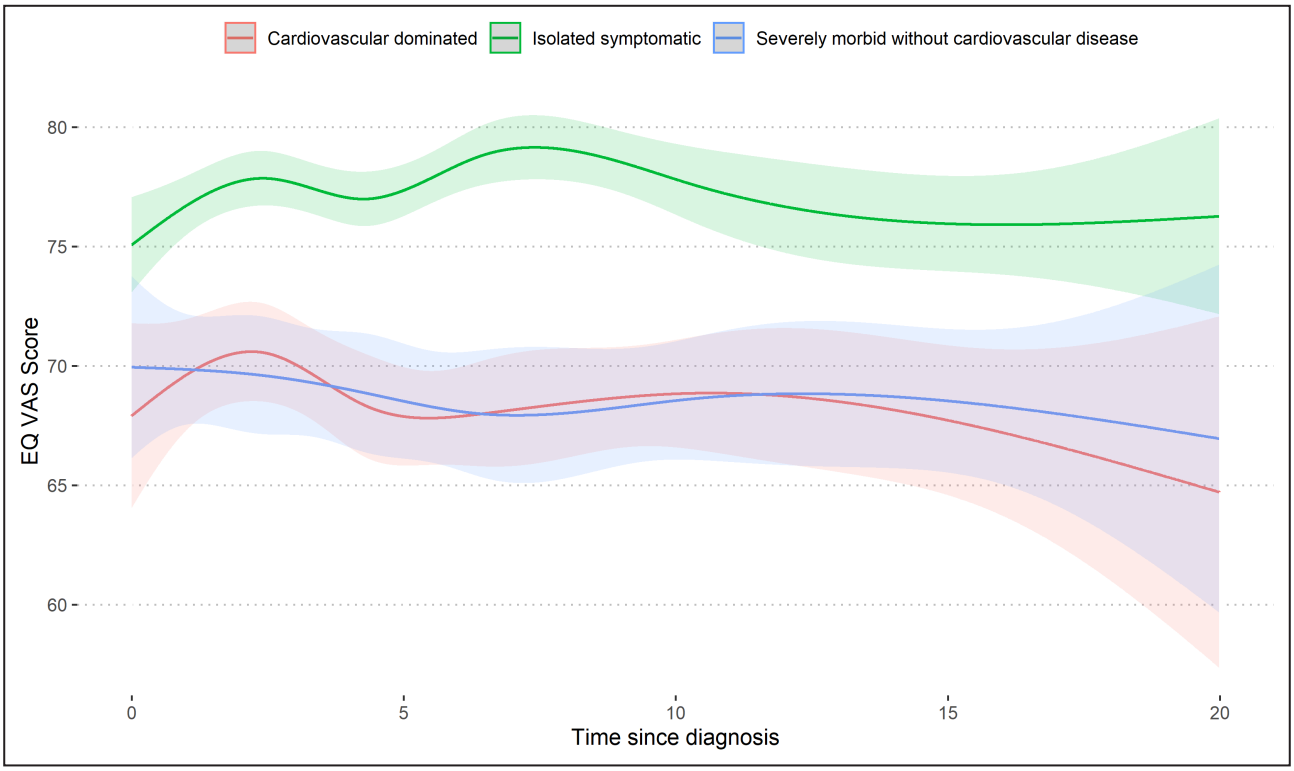

Figure 5. Predicted EQ VAS scores according to cluster, dependent on time since diagnosis.
Utilities were predicted on the basis of an inverse probability-weighted model, including an interaction term between time since diagnosis and cluster. EQ VAS indicates EuroQoL visual analog scale.

events of heart failure hospitalization and stroke were clinically meaningful, whereas the utility change after bleeding events was not. We could also show that the HRQoL increased again after an event and was restored in surviving patients. A study by Sadlonova et al also showed an improvement in HRQoL after stroke in patients with AF. The authors showed improved utilities within 12 months after the event, with the most significant improvement in patients with severe stroke.[27] However, they did not examine the dynamics of HRQoL across time. Our findings may inform other health economic analyses in need of data on the HRQoL impact of clinical events.

Strength and Limitations

The strengths of this study are the long observation period and the numerous patient, disease, and clinical characteristics that were considered. The number of included patients is large, and because of the broad inclusion criteria of Swiss-AF, the study population represents many aspects of the heterogeneity of patients with AF well. However, given the focus on recruitment in specialized clinical centers, the results may not be fully generalizable to the full population of patients with AF. Only a limited number of patients aged <65 years were included in the study, which may have led to lower HRQoL values than when considering the full population with AF of all ages. In addition, we used the European value set to calculate utilities as no Swiss value set was available, and results may therefore not fully capture the Swiss situation. As the Swiss-AF study included mainly patients from Europe, the results may be not fully generalizable to other populations. Furthermore, the time between a clinical event and the next HRQoL measurement was not standardized and could be up to 1 year if an event occurred shortly after 1 of the yearly follow-up visits. We would probably have observed stronger effects if all next HRQoL measurements had been done shortly after the event. Finally, although our hierarchical clustering analysis identified 3 well-defined groups of patients, other methods might come to alternative solutions for the grouping of patients with AF.

CONCLUSIONS

In conclusion, we found high stability of HRQoL in patients with prevalent AF. Clinical events of hospitalization for heart failure, stroke, and bleeding were associated with a temporary decline in HRQoL, but surviving patients recovered to preevent levels after 1 to 4 years. Our findings provide evidence on the long-term course of HRQoL that is to be expected

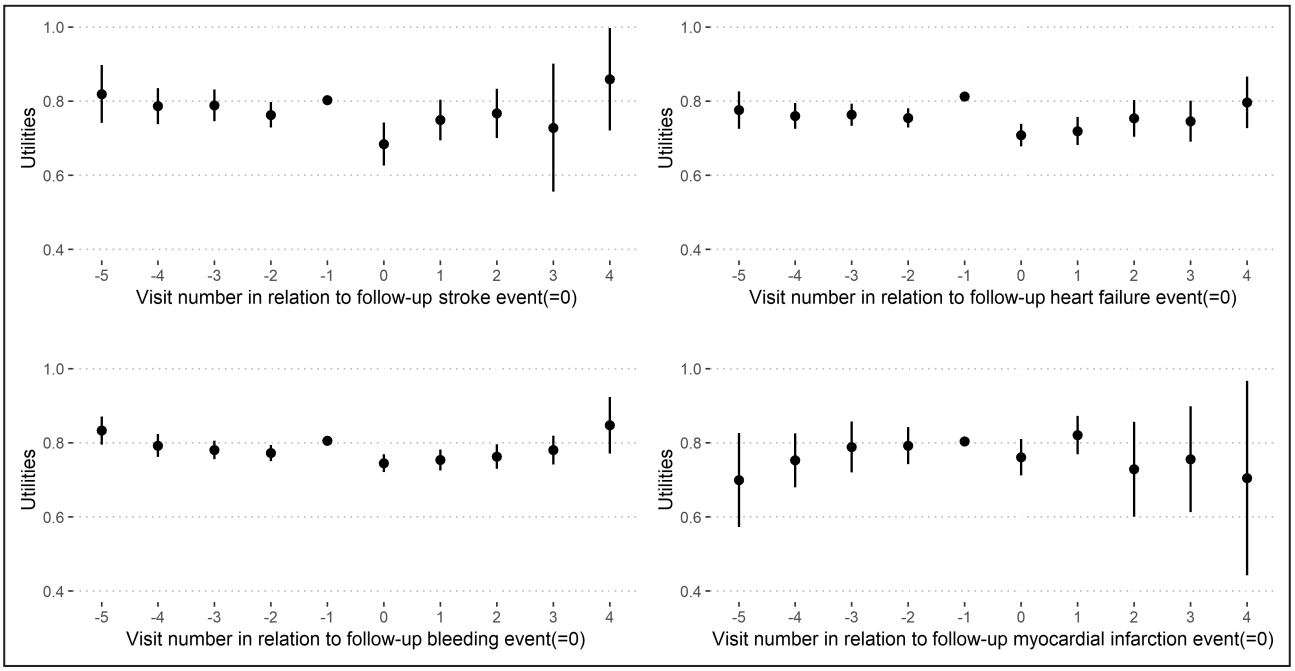

Figure 6. Effects of follow-up events on utility.
The effects were predicted on the basis of an inverse probability-weighted model. The time point 0 indicates the follow-up visit at which the first follow-up event of the relevant type was recorded. For patients without a follow-up event, all visits were denoted as –1. Time point –1 was set as the reference time point. Effects were adjusted for cluster and for age at study visit.

dependent on patients' characteristics and can inform future health economic analyses.

ARTICLE INFORMATION

Received August 14, 2023; accepted October 2, 2023.

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Sources of Funding

This work is supported by grants of the Swiss National Science Foundation (grants 105318_189195/1, 33CS30_148474, 33CS30_177520, 32473B_176178, and 32003B_197524), the Swiss Heart Foundation, the Foundation for Cardiovascular Research Basel, and the University of Basel.

Disclosures

S. Aeschbacher received speaker's fees from Roche outside of the submitted work. Dr Beer reports grant support from the Swiss National Foundation of Science, the Swiss Heart Foundation, and the Stiftung Kardio; grant support and speaker's and consultation fees to the institution from Bayer, Sanofi, and Daiichi Sankyo. Dr Blozik reports grants from the Swiss Cancer research Foundation, Amgen, MSD, Novartis, and Vifor, all outside the submitted work. Dr Moschovitis has received advisory board and/or speaker's fees from Astra Zeneca, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Gebro Pharma, Novartis, and Vifor, all outside of the submitted work. Dr Müller reports fellowship and training support from Biotronik, Boston Scientific, Medtronic, Abbott/St. Jude Medical, and Biosense Webster; speaker honoraria from Biosense Webster, Medtronic, Abbott/St. Jude Medical, AstraZeneca, Daiichi Sankyo, Biotronik, MicroPort, Novartis, Zoll, and Bristol Myers Squibb; and consultancy for Biosense Webster, Medtronic, Abbott/St. Jude Medical, and Biotronik. Dr Reichlin has received research grants from the Swiss National Science Foundation, the Swiss Heart Foundation, and the sitem insel support fund, all for work outside the submitted study; speaker/consulting honoraria or travel support from Abbott/SJM, AstraZeneca, Brahms, Bayer, Biosense Webster, Biotronik, Boston Scientific, Daiichi Sankyo, Medtronic, Pfizer/BMS, and Roche, all for work outside the submitted study; and support for his institution's fellowship program from Abbott/SJM, Biosense Webster, Biotronik, Boston Scientific, and Medtronic, for work outside the submitted study. Dr Sticherling has received speaker honoraria from Biosense Webster and Medtronic; and research grants from Biosense Webster, Daiichi Sankyo, and Medtronic. Dr Conen received consulting fees from Roche Diagnostics and Trimedics; and speaker's fees from Servier, all outside of the current analysis. Dr Kühne reports grants from the Swiss National Science Foundation (grants 33CS30_148474, 33CS30_177520, 32473B_176178, and 32003B_197524), the Swiss Heart Foundation, the Foundation for Cardiovascular Research Basel, the University of Basel, Bayer, Pfizer, Boston Scientific, BMS, and Biotronik; and grants and personal fees from Daiichi Sankyo. M. Schwenkglenks reports grants from Swiss National Science Foundation, for the conduct of the study; grants from Amgen, MSD, Novartis, Pfizer, and Roche; grants and personal fees from BMS; and personal fees from Sandoz, all outside the submitted work. The remaining authors have no disclosures to report.

Supplemental Material

Data S1
Tables S1–S4
Figure S1

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