Digoxin is Associated with Increased Mortality but Decreased Radiofrequency Ablation Rates in Patients with Atrial Fibrillation without Concomitant Heart Failure

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Background

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. It is a significant risk factor for ischemic stroke and death. Digitalis has been used for more than 200 years to treat heart conditions, including AF [1,2]. Even though it has been used for a long time, its effect on long-term morbidity and mortality remains controversial [3,4,5].

Methods

We conducted a cohort study of hospitalized patients with AF assessing the effects of digoxin on long-term all-cause mortality and radiofrequency ablation rates. Patients were divided into two groups: with and without heart failure (HF). We performed multivariable Cox regression analysis to assess hazard ratios (HR) for all-cause mortality depending on digoxin treatment and used propensity score matching to adjust for differences in background characteristics between treatment groups.

Results

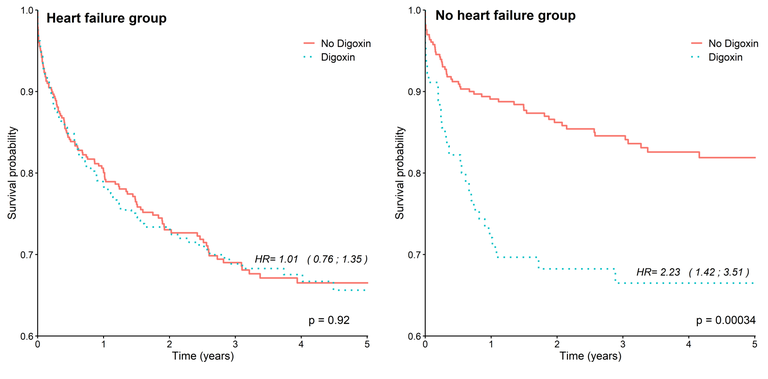
Among 2179 consecutive patients, the median age was 73 ± 14, 52.5% patient were male, 49% had HF, 18.8% were discharged on digoxin (Table 1). The mean follow-up time was 3 ± 2.05 years. After adjustment, in patients with HF, there was no statistically significant difference in mortality between the digoxin subgroups (p=0.92, Figure 1). In contrast, after adjustment, in patients without HF there was a statistically significant increased mortality in the digoxin subgroup (HR=2.23, p<0.001). In patients without HF, the radiofrequency ablation rate was 3.6% for patients in the digoxin subgroup, significantly lower than 14.8% in patients not on the medication (p=0.002).

Table 1

	All patients (n=2179)	Heart Failure (n= 1071)			No Heart Failure (n= 1108)		
		Without digoxin (n=773)	With digoxin (n=298)	p-value	Without digoxin (n=996)	With Digoxin (n=112)	p-value
Demographics							
Age, years	71.31 (14.35)	72.31 (13.78)	71.85 (12.70)	0.615	69.90 (15.17)	75.42 (13.51)	**<0.001**
Male sex, n (%)	1144 (52.5)	420 (54.3)	171 (57.4)	0.406	502 (50.4)	51 (45.5)	0.381
BMI, kg/m²	26.8 (23.1-32.2)	26.8 (23.0-32.2)	27.0 (23.4-32.6)	0.608	27.0 (23.4-32.3)	25.4 (21.3-30.2)	**0.015**
GFR Cockcroft-Gault, mL/min	79.33 (61.42)	69.81 (49.34)	75.24 (77.33)	0.186	87.33 (50.95)	87.90 (124.93)	0.929
LVEF (%)	60 (40-65)	40 (20-60)	35 (20-60)	**0.004**	60 (60-65)	60 (60-65)	0.367
Comorbidities, n (%)							
Hypertension	1691 (77.7)	644 (83.3)	237 (79.5)	0.173	727 (73.3)	83 (74.1)	0.941
DM	590 (27.1)	255 (33.0)	87 (29.2)	0.263	224 (22.6)	24 (21.4)	0.875
CAD	173 (8.0)	65 (8.4)	30 (10.1)	0.462	76 (7.7)	2 (1.8)	0.035
Hyperlipidemia	921 (42.3)	351 (45.4)	118 (39.6)	0.099	411 (41.4)	41 (36.6)	0.377
Smokers	911 (41.8)	349 (45.1)	141 (47.3)	0.569	377 (37.9)	44 (39.3)	0.846
Home medications, n (%)							
Aspirin	1002 (46.2)	379 (49.2)	140 (47.0)	0.556	437 (44.1)	46 (41.1)	0.603
Clopidogrel	189 (8.7)	85 (11.0)	20 (6.7)	0.044	76 (7.7)	8 (7.1)	0.989
Beta-Blockers	1259 (58.0)	531 (69.0)	192 (64.4)	0.178	480 (48.5)	56 (50.0)	0.838
Digoxin	234 (10.8)	33 (4.3)	135 (45.3)	**<0.001**	29 (2.9)	37 (33.0)	<0.001
ACEI/ARB	936 (43.1)	395 (51.2)	151 (50.7)	0.923	349 (35.3)	41 (36.6)	0.857
Statins	891 (41.0)	377 (48.9)	117 (39.3)	**0.006**	357 (36.1)	40 (35.7)	1
Length of Stay, days	5 (3-9)	6 (4-10)	9 (5-13)	**<0.001**	4 (2-7)	8 (4.75-16)	**<0.001**
Time to readmission, days	983.35 (798.56)	802.14 (809.93)	938.85 (838.26)	**0.014**	1119.90 (752.14)	1138.08 (757.49)	0.809
Mortality during follow-up, n (%)	462 (21.2)	209 (27.0)	92 (30.9)	0.240	125 (12.6)	36 (32.1)	**<0.001**
RFA during follow-up, n (%)	241 (11.1)	71 (9.2)	19 (6.4)	0.173	147 (14.8)	4 (3.6)	**0.002**

Note: Values represent mean ± standard deviation, median (IQR; 25th –75th percentiles), or number (%). Bold values indicate statistical significance.
Abbreviations: *ACEI/ARB* = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, *BM*= body mass index, *CAD*=coronary artery disease, CCB=calcium channel blockers, DM=Diabetes Mellitus, LV*EF*=left ventricular ejection fraction, *HDL*=high density lipoprotein, *IQR*=interquartile range, *LDL*=low density lipoprotein

Figure 1



Conclusions

Digoxin use was associated with increased mortality in patients with AF and without concomitant HF. However, there were significantly lower radiofrequency ablation rates in the digoxin subgroup suggestive of better symptom control of AF.

References

1. Page RL. Clinical practice. Newly diagnosed atrial fibrillation. The New England journal of medicine 2004;351:2408-16.
2. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. The American journal of medicine 2002;113:359-64.
3. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). European heart journal 2010;31:2369-429.
4. Fuster V, Ryden LE, Cannom DS, et al. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation 2011;123:e269-367.
5. Gheorghiade M, Adams KF, Jr., Colucci WS. Digoxin in the management of cardiovascular disorders. Circulation 2004;109:2959-64.