Cardiovascular related mortality in hypertensive patients who were newly prescribed perindopril or lisinopril: a 5-year cohort study of 15,622 cases

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Background

Perindopril and Lisinopril are two common ACE inhibitors prescribed for management of hypertension. Their comparative benefit on cardiovascular related mortality was not evaluated.

Objective

• To compare the incidence of cardiovascular related and all-cause mortality among patients newly prescribed these ACE inhibitors.

Methods

Data source. The Hospital Authority of Hong Kong, which provides free or low cost primary and secondary care as part of the public health-care sector, adopted a comprehensive computerized patient recording system in 2000 which captures patients' clinical and demographic parameters, as well as drug prescription details..

These databases so far consist of 7 million patient records, 1 million annual admissions and 13 million ambulatory visits.

All adult patients prescribed perindopril or lisinopril from 2001 to 2005 in all public clinics or hospitals in Hong Kong were retrospectively evaluated, and followed up until 2010.

Patients prescribed the ACE inhibitors less than a month were excluded.

The incidence of all-cause and cardiovascular-specific (i.e. coronary heart disease, heart failure and stroke) mortality was compared between the ACE inhibitors.

Cox proportional hazard regression model was used to compare the mortality, controlling for age, sex, socioeconomic status, service type, the presence of comorbidities, and medication adherence as measured by the Proportion of Days Covered.

Additional model with control for propensity score were performed to minimize indication bias.

Results

A total of 15,622 patients were included in this study, in which 6,910 were new perindopril users and 8,712 new lisinopril users.

The incidence of cardiovascular related mortality among perindopril users was lower than those prescribed lisinopril (4.7% vs. 5.4%, p<0.005) (Table 1).

The all-cause mortality among perindopril users was also significantly lower (20.8% vs 22.1%, p<0.005) (Table 1).

When compared with perindopril users, lisinopril users were 1.18-fold (95% C.I. 1.02-1.35) more likely to die from cardiovascular diseases and 1.09-fold (95% C.I. 1.01-1.16) for all-cause mortality. (Table 2 & 3)

The additional models controlled for propensity scores yielded comparable results.

Table 1. Patient Demographics of using Perindopril or Lisinopril

	Survival n=12,259	All-cause Mortality n=3,363	Cardiovascular Mortality n=798
Age			
<49	2843 (96.3%)	108 (2.7%)	24 (8%)
49-59	3044 (93.9%)	197 (6.1%)	40 (1.2%)
60-69	2838 (85.4%)	487 (14.6%)	108 (3.2%)
≥ 70	3534 (57.9%)	2571 (42.1%)	626 (10.3%)
Sex			
Male	6072 (76.8%)	1837 (23.2%)	419 (5.3%)
Female	6187 (80.2%)	1526 (19.8%)	379 (4.9%)
Public Assistance			
No	10873 (82.9%)	2244 (17.1%)	534 (4.1%)
Yes	1386 (55.3%)	1119 (44.7%)	264 (10.5%)
Service type			
In-patient	2640 (55.4%)	2122 (44.6%)	534 (11.2%)
Specialist outpatient	5158 (86.9%)	776 (13.1%)	172 (2.9%)
General outpatient	3954 (92.4%)	323 (7.6%)	60 (1.4%)
Others	507 (78.1%)	142 (21.9%)	32 (4.9%)
Presence of co-morbidities			
0	4049 (83.1%)	823 (16.9%)	213 (4.4%)
1	6653 (79.8%)	1684 (20.2%)	405 (4.9%)
2	1424 (66.2%)	728 (33.8%)	158 (7.3%)
3	133 (51.0%)	128 (49.0%)	22 (8.4%)
Drug			
Perindopril	5473 (79.2%)	1437 (20.8%)	326 (4.7%)
Lisinopril	6786 (77.9%)	1926 (22.1%)	472 (5.4%)
Proportion Days Covered			
<0.4	2903 (81.2%)	674 (18.8%)	135 (3.8%)
0.4-0.7	4008 (88.6%)	517 (11.4%)	107 (2.4%)
>0.7	5348 (71.1%)	2172 (28.9%)	556 (5.1%)

Table 2 Incidence of all-cause mortality associated with Lisinopril compared with Perindopril

	Unadjusted Hazard Ratios	Adjusted Hazard Ratios	Adjusted Hazard Ratios with propensity score**
Age (years)			
<49	1.00	1.00	
49-59	1.78 (1.40 – 2.25)*	1.57 (1.24 – 1.99)*	
60-69	4.45 (3.61 – 5.48)*	3.45 (2.80 – 4.26)*	
≥ 70	15.88 (13.10 – 19.26)*	9.17 (7.53 – 11.16)*	
Sex			
Male	1.00	1.00	
Female	1.21 (1.13 – 1.30)*	1.34 (1.25 – 1.43)*	
Public Assistance			
No	1.00	1.00	
Yes	3.11 (2.89 – 3.34)	1.53 (1.42 – 1.65)*	
Service type			
In- patient	2.37 (2.00 – 2.80)*	2.05 (1.73 – 2.43)*	
Specialist outpatient	0.52 (0.43 – 0.62)*	0.88 (0.74 – 1.06)	
General outpatient	0.34 (0.28 – 0.42)*	0.35 (0.29 – 0.43)*	
Others	1.00	1.00	
Presence of co-morbidities (No)			
1	1.00	1.00	1.00
2	1.24 (1.14 – 1.35)	1.21 (1.12 – 1.32)*	1.14 (1.05 – 1.24)*
3	2.14 (1.94 – 2.37)*	1.48 (1.32 – 1.64)*	2.06 (1.86 – 2.27)*
	3.17 (2.63 – 3.82)*	1.61 (1.33 – 1.94)*	2.88 (2.39 – 3.47)*
Drug			
Perindopril	1.00	1.00	1.00
Lisinopril	1.05 (0.98 – 1.13)	1.08 (1.01 – 1.16)*	1.09 (1.02 – 1.17)*
Proportion Days Covered			
<0.4	1.00	1.00	1.00
0.4-0.7	0.53 (0.47 – 0.60)*	0.71 (0.63 – 0.08)*	0.52 (0.46 – 0.58)*
>0.7	2.39 (2.19 – 2.62)*	2.97 (2.71 – 3.26)*	2.34 (2.14 – 2.56)*

Table 3 Incidence of cardiovascular related mortality associated with Lisinopril compared with Perindopril

	Unadjusted Hazard Ratios	Adjusted Hazard Ratios	Adjusted Hazard Ratios with propensity score**
Age (years)			
<49	1.00	1.00	
49-59	1.64 (0.99 – 2.71)	1.37 (0.82 – 2.27)	
60-69	4.67 (3.00 – 7.26)*	3.51 (2.25 – 5.48)*	
≥ 70	21.06 (14.01 – 31.67)*	11.48 (7.58 – 17.38)*	
Sex			
Male	1.14 (0.99 – 1.31)	1.32 (1.15 – 1.52)*	
Female	1.00	1.00	
Public Assistance			
No	1.00	1.00	
Yes	3.70 (3.20 – 4.29)*	1.69 (1.45 – 1.96)*	
Service type			
In- patient	2.96 (2.07 – 4.23)*	2.66 (1.86 – 3.81)*	
Specialist outpatient	0.49 (0.34 – 0.72)*	0.91 (0.62 – 1.32)	
General outpatient	0.26 (0.17 – 0.40)*	0.25 (0.16 – 0.38)*	
Others	1.00	1.00	
Presence of co-morbidities (No)			
1	1.00	1.00	1.00
2	1.17 (0.99 – 1.38)	1.23 (1.04 – 1.45)*	1.05 (0.89 – 1.24)
3	0.07 (1.65 – 2.49)*	1.47 (1.19 – 1.81)*	1.92 (1.56 – 2.36)*
	2.95 (1.90 – 4.57)*	1.35 (0.87 – 2.10)	2.56 (1.65 – 3.97)*
Drug			
Perindopril	1.00	1.00	1.00
Lisinopril	1.13 (0.98 – 1.31)	1.17 (1.02 – 1.35)*	1.17 (1.01 – 1.36)*
Proportion Days Covered			
<0.4	1.00	1.00	1.00
0.4-0.7	0.52 (0.41 – 0.67)*	0.72 (0.56 – 0.93)*	0.50 (0.39 – 0.65)*
>0.7	3.19 (2.62 – 3.89)*	4.44 (3.64 – 5.42)*	3.18 (2.61 – 3.88)*

*signifies statistical significance at p<0.05 by Cox proportional hazard regression analysis. The propensity scores were matched for age, sex, public assistance, district of residence, and service type.
**represent a separate Cox proportional hazard regression analysis where only variables not matched by the propensity scoring system were included.

Conclusion

➢ The long-term cardiovascular related and all-cause mortality of Lisinopril users was significantly higher than that of Perindopril users.
➢ These findings showed that intra-class heterogeneity among antihypertensive agents exists.