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Comparison of CHA_2DS_2-VASc and AHEAD scores for the prediction of incident dementia in patients hospitalized for heart failure: a nationwide cohort study

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Abstract
This study explores the use of the CHA_2DS_2-VASc and the AHEAD scores to predict incident dementia in patients with heart failure (HF) who need hospitalization. We used a large national database to study 387,595 adult patients hospitalized for HF from Taiwan. This registration cohort was followed to document the cumulative incidence of dementia. The area under the curve of receiver operating characteristics (AUROC) was used to evaluate the discriminative ability of CHA_2DS_2-VASc and AHEAD scores in predicting dementia, whereas the DeLong test was used to examine the difference between the predictive capacity. A higher CHA_2DS_2-VASc and AHEAD scores appear to be more strongly associated with a higher incidence of dementia. The AUROC for CHA_2DS_2-VASc score in predicting dementia (0.61, 95% CI = 0.60–0.61) is significantly higher than the AHEAD score (0.55, 95% CI = 0.54–0.55) (DeLong test $p < 0.001$). A significantly higher ability, by AUROC, of CHA_2DS_2-VASc score to predict new-onset dementia in patients hospitalized for HF is found.

Keywords AHEAD score · CHA_2DS_2-VASc score · Dementia · Heart failure

Introduction

Heart failure (HF), defined as the mismatch of supply and demand of cardiac perfusion, is recognized as a major health burden in the world [1]. The relationship linking HF and dementia has been established [2–5].

In addition to an aging society, it is also important to anticipate the onset of dementia [2–6]. Nonetheless, a score validated for dementia risk discrimination in patients with HF is currently unavailable. The existing CHA_2DS_2-VASc and AHEAD scores have been validated for risk stratification of thromboembolism and mortality in the HF population [7–10]. It would be novel to compare the CHA_2DS_2-VASc and the AHEAD scores in this HF patient population for stratifying dementia risk to see if the more recent scoring strategy is beneficial. Hence, we used such a large sample size from this huge Taiwanese national data base with adjusting for the covariates that are the familiar risk factors for dementia to examine the predictive performance of the existing two scores.

Methods

Data source

This retrospective cohort study was conducted using Taiwan's National Health Insurance Research Database (NHIRD). The National Health Insurance (NHI) program was implemented in Taiwan since 1995, and it covers nearly 99% of all residents [11]. For this study, we used a subset of the NHIRD containing health care data including files of inpatients claims, and Registry of Beneficiaries. These files record the disease based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The Research Ethics Committee of China

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Medical University and Hospital in Taiwan approved the study (CMUH-104-REC2-115).

Sampled participants

After examination of the medical claims, 387,595 patients with a diagnosis of HF (ICD-9-CM code 428) were identified from inpatients claims during 2000–2011. The dates of their first hospitalization diagnosis of HF were defined as their index dates. Patients with a history of dementia (ICD-9-CM codes 290, 294.1 and 331.0) prior to the index date, missing information for age or gender were excluded. The CHA_2DS_2-VASc score [12, 13] and AHEAD score (9, 10) were calculated for each patient to measure dementia risk. Preexisting comorbidities with hyperlipidemia, hyperthyroidism, sleep disorder, gout, chronic obstructive pulmonary disease (COPD), head injury, depression, and alcoholism-related disease were included for analyses. Follow-up began from the index date and continued until a diagnosis of dementia, withdrawal from the NHI program, or at the end of 2011.

Statistical analysis

We calculated the number and percentage for categorical variables and the mean and corresponding standard deviation (SD) and median (Q1–Q3) for continuous variables (including age, CHA_2DS_2-VASc score, AHEAD score, and follow-up period). The Kaplan–Meier method was applied to estimate the cumulative incidence of dementia stratified by CHA_2DS_2-VASc score or AHEAD score, and the Log-rank test was used to examine the statistical significance of the differences of CHA_2DS_2-VASc score or AHEAD score. The incidence density rate (per 1000 person-years) of dementia was estimated according to the CHA_2DS_2-VASc score and the AHEAD score. Univariable and multivariable Cox proportional hazard models were performed to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) of dementia associated with HF stratified by CHA_2DS_2-VASc score or AHEAD score. The multivariable model for CHA_2DS_2-VASc score was simultaneously adjusted for atrial fibrillation, hyperlipidemia, COPD, hyperthyroidism, sleep disorder, gout, chronic kidney disease, anemia, head injury, depression, and alcoholism-related disease. The multivariable model for AHEAD score was simultaneously adjusted for gender, CVA or TIA, vascular disease, hypertension, COPD, hyperlipidemia, hyperthyroidism, sleep disorder, gout, head injury, depression, and alcoholism-related disease. The proportional hazard model assumption was also examined using a test of scaled Schoenfeld residuals. In the model evaluating the dementia risk throughout overall follow-up period, results of the test revealed a significant relationship between Schoenfeld residuals for CHA_2DS_2-VASc score and follow-up time, and for AHEAD score and follow-up time, suggesting that the proportionality assumption was violated (p value = 0.047 and p value < 0.001). In the subsequent analyses, we stratified the follow-up duration by median ($<2, \geq 2$ years) to deal with the violation of proportional hazard assumption. The area under the curve of receiver operating characteristics (AUROC) was used to assess the predictive accuracy of CHA_2DS_2-VASc score and AHEAD score in predicting dementia. The DeLong test was used to examine the difference between the two scores. All statistical analyses were performed using the SAS package (Version 9.4 for Windows; SAS Institute, Inc., Cary, NC, USA). A two-tailed p value < .05 was considered significant.

Results

Table 1 displays the demographic characteristics and comorbidities of the HF patients. The mean age among HF patients is 72.0 (SD=13.7) years. More patients are male (n = 201,548; 52.0%), and hypertension is the most prevalent comorbidity (60.8%). The mean CHA_2DS_2-VASc score and AHEAD score are 4.33 and 1.63, respectively. The mean follow-up of dementia is 2.91 years.

The incidence of dementia increases from 0.26% to 3.84% when a CHA_2DS_2-VASc score increases from 1 to ≥ 6 (Fig. 1a) or increases from 0.80% to 2.96%, while an AHEAD score increases from 0 to ≥ 3 (Fig. 1b). The incidence density rate of dementia increases from 0.64 per 1000 person-years for HF patients with a CHA_2DS_2-VASc score of 1 to 18.4 per 1000 person-years for those with a CHA_2DS_2-VASc score of ≥ 6 (Table 2). The risk of dementia increases from 3.22 (95% CI = 2.37–4.37) in HF patients with a CHA_2DS_2-VASc score of 2 to 25.3 (95% CI = 18.9–33.8) in HF patients with a CHA_2DS_2-VASc score of ≥ 6 as compared with those with a CHA_2DS_2-VASc score of 1 (trend test, p < .001). The risk of dementia is still higher in HF patients with a CHA_2DS_2-VASc score of 2 to >= 6 compared to those with a CHA_2DS_2-VASc score of 1 stratified by the follow-up duration (median follow-up duration < 2 years and median follow-up duration ≥ 2 years). The incidence density rate

Table 1 Baseline characteristics of heart failure patients

Variable	Heart failure $N = 387,595$
Age (years) (*n* (%))	
≤ 64	98,837 (25.5)
65–74	98,305 (25.4)
≥ 75	190,453 (49.1)
Mean ± SD	72.0 ± 13.7
Median (Q1–Q3)	74.7 (64.7–81.7)
Gender	
Male	201,548 (52.0)
Female	186,047 (48.0)
Underlying disease (components of the CHA_2DS_2-VASc score or AHEAD score)	
Atrial fibrillation	69,863 (18.0)
Diabetes mellitus	143,961 (37.1)
CVA or TIA	97,754 (25.2)
Vascular disease	49,708 (12.8)
Hypertension	235,472 (60.8)
Chronic kidney disease	89,782 (23.2)
Anemia	80,039 (20.7)
Other underlying disease	
Hyperlipidemia	58,041 (15.0)
Hyperthyroidism	5117 (1.32)
Sleep disorder	61,535 (15.9)
Gout	33,609 (8.67)
COPD	84,606 (21.8)
Head injury	882 (7.76)
Depression	134 (1.18)
Alcoholism-related disease	635 (5.59)
Mean CHA_2DS_2-VASc score (SD)	4.33 (1.75)
Median (Q1–Q3)	4.00 (3.00–6.00)
Mean AHEAD score (SD)	1.63 (1.04)
Median (Q1–Q3)	2.00 (1.00–2.00)
Mean follow-up, year (SD)	2.91 (2.95)
Median (Q1–Q3)	1.89 (0.49–4.56)

SD denotes standard deviation, *Q1* denotes Quartile 1, *Q3* denotes Quartile 3, *CVA* denotes cerebrovascular accident, *TIA* denotes transient ischemic attack, *COPD* denotes chronic obstructive pulmonary disease

of dementia increases from 1.81 per 1000 person-years in HF patients with an AHEAD score of 0 to 15.3 per 1000 person-years in HF patients with an AHEAD score of 3 or above. Compared to patients with HF with an AHEAD score of 0, the corresponding adjusted hazard ratios (aHRs) of dementia are 4.54 (95% CI = 4.10–5.03), 5.58 (95% CI = 5.04–6.19), and 6.12 (95% CI = 5.50–6.82) for those with an AHEAD of 1, 2, and ≥ 3, respectively (trend test, $p < 0.001$). The risk of dementia is still higher in HF patients with an AHEAD score of 1 to >= 3 compared with those with an AHEAD score of 0 stratified by the follow-up duration (median follow-up duration < 2 years and median follow-up duration ≥ 2 years).

In the subgroup of HF patients with AF, compared to patients with a CHA_2DS_2-VASc score of 1, the corresponding aHRs of dementia are 4.37 (95% CI = 2.00–9.53), 13.5 (95% CI = 6.38–28.6), 21.7 (95% CI = 10.3–45.7), 25.7 (95% CI = 12.2–54.1), and 31.0 (95% CI = 14.7–65.2) for those with a CHA_2DS_2-VASc score of 2, 3, 4, 5 and ≥ 6, respectively (trend test, $p < 0.001$) (Table 3). Compared to HF patients with AF with an AHEAD score of 1, the corresponding aHRs of AF are 5.47 (95% CI = 4.44–6.73), and 6.14 (95% CI = 4.96–7.60) for those with an AHEAD score of 2, and ≥ 3, respectively (trend test, $p < 0.001$).

The cumulative incidences of dementia associated with increasing CHA_2DS_2-VASc score and AHEAD score over time are clearly demonstrated by Kaplan–Meier curves in Fig. 2a, b (Log-rank test $p < 0.001$). The AUROC for CHA_2DS_2-VASc score in predicting dementia (0.61, 95% CI = 0.60–0.61) is significantly higher than the AHEAD score (0.55, 95% CI = 0.54–0.55) (DeLong test $p < 0.001$) (Fig. 3).

Discussion

We performed a large-scale nationwide cohort investigation based on the inpatients claims and Registry of Beneficiaries provided by the National Health Research Institutes of Taiwan to identify the association between comorbidities (estimated by two scores), and incident dementia in a total of 387,595 patients hospitalized for HF.

The strength of this article appears to be that the predictive values of the CHA_2DS_2-VASc and AHEAD scores have not been tested in patients with HF using a large-scale data base providing a large study power in exchange for loss of granularity. This study is part of the growing literature on the association between HF and dementia.

Compared with serious acute medical problems such as stroke and heart attack, dementia can be underestimated or unnoticed by patients or physicians, since such illness is relatively not life-threatening. However, HF patients who have dementia are more likely to have untoward physiologically and psychologically sequelae [2–6]. Indeed, there is an increasing body of evidence that HF is associated with cognitive decline and aging brain diseases [2–6, 14–17]. In

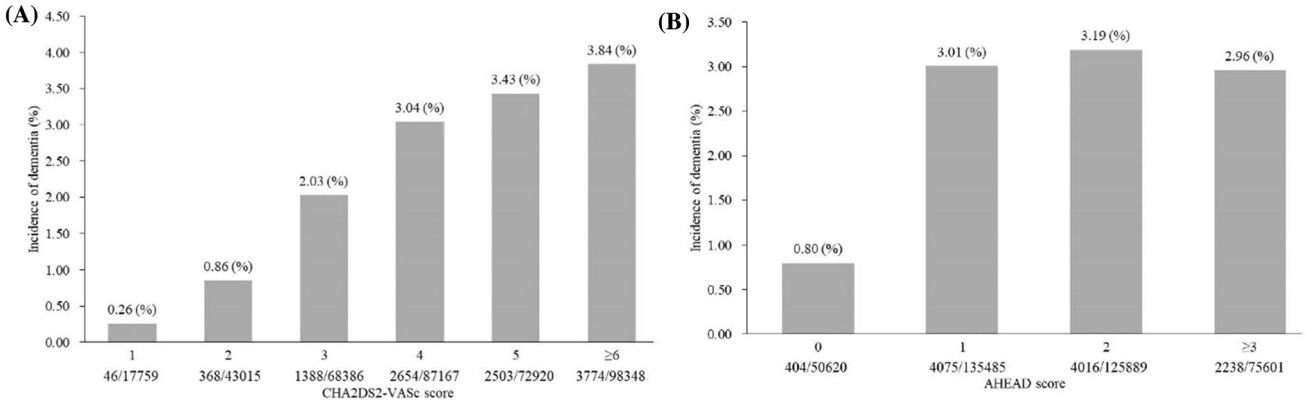

Fig. 1 The incidence of new-onset dementia continuously correlates with CHA_2DS_2-VASc score (**a**) and AHEAD score (**b**) in patients with heart failure who need hospitalization

the light of the data obtained, the implication of this study is that patients with HF have much higher rates of dementia, and those who have dementia tend to have more aggregate comorbidities. The CHA_2DS_2-VASc score, originally validated for thromboembolic stroke prediction risk in patients with AF [18–20], seems to outperform the AHEAD score for dementia risk discrimination in this population.

Interestingly, the moderate predictive ability of the CHA_2DS_2-VASc and AHEAD scores seems to be similar in patients with HF, although the former has a better stratification power based on the DeLong test. The potential mechanism for the observed difference of the predictive ability of the exist two scores might be related to the components of the scoring systems since more atherosclerotic factors are captured in the CHA_2DS_2-VASc as opposed to the AHEAD score [7–10]. Considering that the CHA_2DS_2-VASC score considers many cardiovascular risk factors, the results might simply reflect the impact of such variables on the onset of dementia, an aspect which has been widely stated in the literature. Further studies to explore other new scoring schemes including the possible risk factors not captured in CHA_2DS_2-VASc or AHEAD scores might be helpful in dementia risk stratification, and make a clinically important distinction in this group in terms of the modest predictive value of the existing scores.

Limitations

First, no information about drug therapy or clinical conditions of the patients are reported, which may affect the results of the study. Thus, several potential confounders are unmeasured, and the possibility of incomplete statistical analysis cannot be excluded. Second, even if a total of 387,595 HF patients were recruited, this is a retrospective nationwide cohort study using the NHIRD of the Taiwan NHI Program, and the retrospective nature of this registry study is subject to certain limitations. Finally, the completeness of ICD coding for the diseases is another major concern. That is, missing or incomplete coding might affect the interpretation of the results. Nevertheless, this particular national database has been previously validated and reported to be of high accuracy.

Conclusions

The CHA_2DS_2-VASc score appears to be more predictive of dementia than the AHEAD score in patients with HF who need hospitalization. The modest predictive value of both scores implies that other sophisticated models might be needed for dementia risk stratification in this population.

Table 2 Incidence and hazard ratios (HRs) of dementia in heart failure patients according to CHA_2DS_2-VASc and AHEAD scores

Score	*N*	No. of events	Person-years	Rate[a]	Crude HR	95% CI	Adjusted HR	95% CI
CHA_2DS_2-VASc score[b]								
1	17,759	46	71,510	0.64	1	(Reference)	1	(Reference)
2	43,015	368	175,220	2.10	3.26	(2.40, 4.43)***	3.22	(2.37, 4.37)***
3	68,386	1388	231,183	6.00	9.23	(6.88, 12.4)***	8.79	(6.55, 11.8)***
4	87,167	2654	253,319	10.5	16.0	(11.9, 21.3)***	15.0	(11.2, 20.0)***
5	72,920	2503	189,834	13.2	19.9	(14.9, 26.6)***	18.7	(14.0, 25.0)***
≥6	98,348	3774	205,158	18.4	27.3	(20.4, 36.5)***	25.3	(18.9, 33.8)***
p for trend					< 0.001		< 0.001	
Median follow-up duration < 2 years								
CHA_2DS_2-VASc score[b]								
1	17,759	13	25,987	0.50	1	(Reference)	1	(Reference)
2	43,015	96	64,858	1.48	2.95	(1.65, 5.26)***	2.92	(1.64, 5.21)***
3	68,386	650	95,901	6.78	13.4	(7.74, 23.2)***	12.7	(7.35, 22.0)***
4	87,167	1349	116,027	11.6	22.8	(13.2, 39.4)***	21.3	(12.4, 36.8)***
5	72,920	1334	93,881	14.2	27.8	(16.1, 47.9)***	26.0	(15.1, 44.9)***
≥6	98,348	2313	113,722	20.3	39.2	(22.8, 67.6)***	36.3	(21.1, 62.7)***
p for trend					< 0.001		< 0.001	
Median follow-up duration ≥ 2 years								
CHA_2DS_2-VASc score[b]								
1	10,769	33	45,524	0.72	1	(Reference)	1	(Reference)
2	26,653	272	110,361	2.46	3.40	(2.37, 4.88)***	3.35	(2.33, 4.80)***
3	37,308	738	135,282	5.46	7.54	(5.32, 10.7)***	7.17	(5.05, 10.2)***
4	42,911	1305	137,292	9.51	13.1	(9.30, 18.6)***	12.3	(8.72, 17.4)***
5	33,256	1169	95,953	12.2	16.9	(11.9, 23.8)***	15.8	(11.1, 22.3)***
≥6	36,577	1461	91,435	16.0	22.1	(15.7, 31.3)***	20.5	(14.5, 28.9)***
p for trend					< 0.001		< 0.001	
AHEAD score[c]								
0	50,620	404	223,006	1.81	1	(Reference)	1	(Reference)
1	135,485	4075	436,597	9.33	5.04	(4.55, 5.58)***	4.54	(4.10, 5.03)***
2	125,889	4016	320,064	12.6	6.63	(5.99, 7.35)***	5.58	(5.04, 6.19)***
≥3	75,601	2238	146,557	15.3	7.85	(7.05, 8.73)***	6.12	(5.50, 6.82)***
p for trend					< 0.001		< 0.001	
Median follow-up duration < 2 years								
AHEAD score[c]								
0		132	79,480	1.66	1	(Reference)	1	(Reference)
1		2019	187,703	10.8	6.38	(5.35, 7.61)***	6.36	(5.33, 7.58)***
2		2200	158,840	13.9	8.12	(6.82, 9.68)***	9.66	(8.07, 11.6)***
≥3		1404	84,353	16.6	9.60	(8.03, 11.5)***	15.6	(12.8, 19.0)***
p for trend					< 0.001		< 0.001	
Median follow-up duration ≥ 2 years								
AHEAD score[c]								
0		272	143,526	1.90	1	(Reference)	1	(Reference)
1		2056	248,894	8.26	4.35	(3.84, 4.94)***	4.60	(4.05, 5.23)***
2		1816	161,224	11.3	5.93	(5.22, 6.74)***	7.96	(6.97, 9.11)***
≥3		834	62,204	13.4	7.04	(6.14, 8.08)***	14.0	(11.9, 16.5)***
p for trend					< 0.001		< 0.001	

Crude HR relative hazard ratio

***$p < 0.001$

[a]Per 1000 person-year

[b]Adjusted for atrial fibrillation, hyperlipidemia, chronic obstructive pulmonary disease, hyperthyroidism, sleep disorder, gout, chronic kidney disease, anemia, head injury, depression, and alcoholism-related disease

[c]Adjusted for gender, CVA or TIA, vascular disease, hypertension, chronic obstructive pulmonary disease, hyperlipidemia, hyperthyroidism, sleep disorder, gout, head injury, depression, and alcoholism-related disease

Table 3 Incidence and hazard ratios (HRs) of dementia in heart failure patients with a history of AF according to CHA_2DS_2-VASc and AHEAD scores

Score	*N*	No. of Events	Person-years	Rate[a]	Crude HR	95% CI	Adjusted HR	95% CI
CHA_2DS_2-VASc score[b]								
1	3113	7	14,106	0.50	1	(Reference)	1	(Reference)
2	6488	62	27,860	2.23	4.47	(2.05, 9.76)***	4.37	(2.00, 9.53)***
3	10,940	271	36,575	7.41	14.7	(6.97, 31.2)***	13.5	(6.38, 28.6)***
4	15,463	525	43,277	12.1	23.9	(11.4, 50.4)***	21.7	(10.3, 45.7)***
5	13,484	497	33,851	14.7	28.8	(13.7, 60.7)***	25.7	(12.2, 54.1)***
≥ 6	20,375	733	39,787	18.4	35.5	(16.9, 74.7)***	31.0	(14.7, 65.2)***
p for trend					< 0.001		<0.001	
AHEAD score[c]								
1	11,486	99	50,925	1.94	1	(Reference)	1	(Reference)
2	31,685	1129	89,818	12.6	6.32	(5.15, 7.77)***	5.47	(4.44, 6.73)***
≥ 3	26,692	867	54,714	15.9	7.78	(6.31, 9.59)***	6.14	(4.96, 7.60)***
p for trend					< 0.001		< 0.001	

Crude HR relative hazard ratio

***$p < 0.001$

[a]Per 1000 person-year

[b]Adjusted for atrial fibrillation, hyperlipidemia, chronic obstructive pulmonary disease, hyperthyroidism, sleep disorder, gout, chronic kidney disease, anemia, head injury, depression, and alcoholism-related disease

[c]Adjusted for gender, CVA or TIA, vascular disease, hypertension, chronic obstructive pulmonary disease, hyperlipidemia, hyperthyroidism, sleep disorder, gout, head injury, depression, and alcoholism-related disease

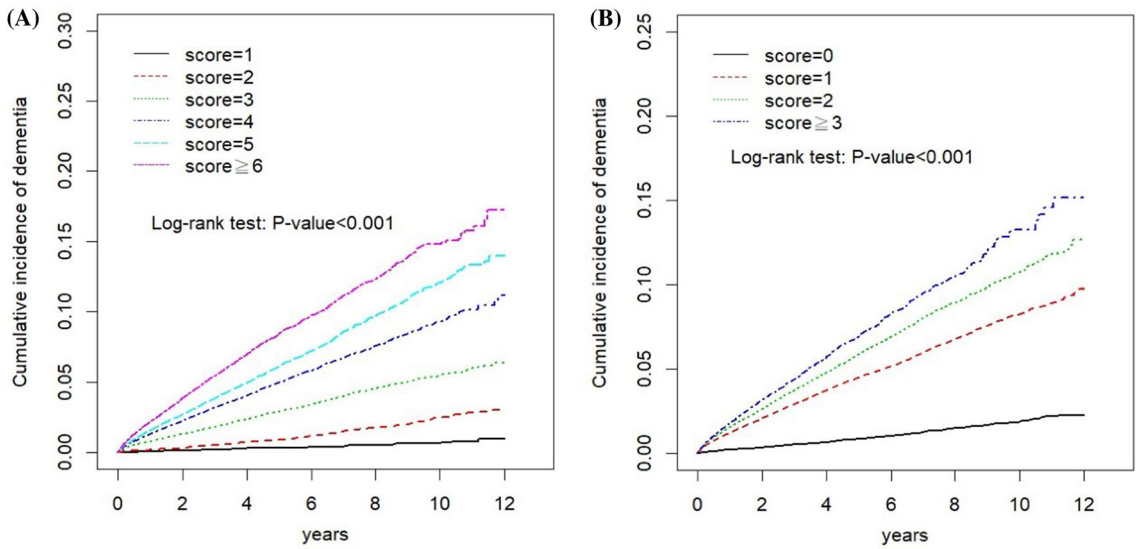

Fig. 2 Cumulative incidence curves of new-onset dementia stratified by CHA_2DS_2-VASc score (**a**) and AHEAD score (**b**) in patients with heart failure who need hospitalization

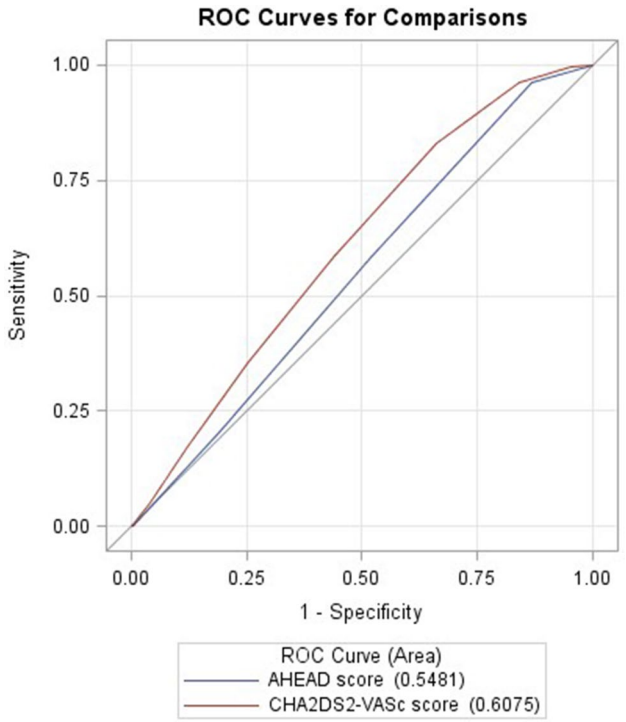

Fig. 3 Receiver operating characteristic (ROC) curve for CHA_2DS_2-VASc score and AHEAD score in predicting new-onset dementia in patients with heart failure who need hospitalization

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent None.

References

1. Roger VL (2013) Epidemiology of heart failure. Circ Res 113(6):646–659
2. Adelborg K, Horváth-Puhó E, Ording A, Pedersen L, Toft Sørensen H, Henderson VW (2017) Heart failure and risk of dementia: a Danish nationwide population-based cohort study. Eur J Heart Fail 19(2):253–260
3. Cermakova P, Lund LH, Fereshtehnejad SM, Johnell K, Winblad B, Dahlström U, Eriksdotter M, Religa D (2015) Heart failure and dementia: survival in relation to types of heart failure and different dementia disorders. Eur J Heart Fail 17(6):612–619
4. Rusanen M, Kivipelto M, Levalahti E, Laatikainen T, Tuomilehto J, Soininen H, Ngandu T (2014) Heart diseases and long-term risk of dementia and Alzheimer's disease: a population-based CAIDE study. J Alzheimers Dis 42:183–191
5. Qiu C, Winblad B, Marengoni A, Klarin I, Fastbom J, Fratiglioni L (2006) Heart failure and risk of dementia and Alzheimer disease: a population-based cohort study. Arch Intern Med 166:1003–1008
6. Murad K, Goff DC Jr, Morgan TM et al (2015) Burden of comorbidities and functional and cognitive impairments in elderly patients at the initial diagnosis of heart failure and their impact on total mortality: the Cardiovascular Health Study. JACC Heart Fail 3:542–550
7. Melgaard L, Gorst-Rasmussen A, Lane DA, Rasmussen LH, Larsen TB, Lip GY (2015) Assessment of the CHA_2DS_2-VASc score in predicting ischemic stroke, thromboembolism, and death in patients with heart failure with and without atrial fibrillation. JAMA 314(10):1030–1038
8. Ye S, Qian M, Zhao B, Buchsbaum R, Sacco RL, Levin B et al (2016) CHA_2DS_2-VASc score and adverse outcomes in patients with heart failure with reduced ejection fraction and sinus rhythm. Eur J Heart Fail 18:1261–1266
9. Spinar J, Jarkovsky J, Spinarova L, Mebazaa A, Gayat E, Vitovec J, Linhart A, Widimsky P, Miklik R, Zeman K, Belohlavek J, Malek F, Felsoci M, Kettner J, Ostadal P, Cihalik C, Vaclavik J, Taborsky M, Dusek L, Littnerova S, Parenica J (2016) AHEAD score—long-term risk classification in acute heart failure. Int J Cardiol 1(202):21–26
10. Chen YJ, Sung SH, Cheng HM, Huang WM, Wu CL, Huang CJ, Hsu PF, Yeh JS, Guo CY, Yu WC, Chen CH (2017) Performance of AHEAD score in an Asian cohort of acute heart failure with either preserved or reduced left ventricular systolic function. J Am Heart Assoc 6(5):e004297
11. National Health Research Institutes. National Health Insurance Research Database. http://nhird.nhri.org.tw/en/index.html. Accessed 14 Apr 2015
12. Hu WS, Lin CL (2017) CHA2DS2-VASc score in the prediction of ischemic bowel disease among patients with atrial fibrillation: insights from a nationwide cohort. Int J Cardiol 235:56–60
13. Hu WS, Lin CL (2018) The predictive role of CHA2DS2-VASc score between venous thromboembolism and ischemic stroke: a large-scale cohort study. J Hypertens 36(3):628–633
14. Leto L, Feola M (2014) Cognitive impairment in heart failure patients. J Geriatr Cardiol 11(4):316–328
15. Heckman GA, Patterson CJ, Demers C, St Onge J, Turpie ID, McKelvie RS (2007) Heart failure and cognitive impairment: challenges and opportunities. Clin Interv Aging 2(2):209–218 **(Review)**
16. Acanfora D, Trojano L, Iannuzzi GL, Furgi G, Picone C, Rengo C, Abete P, Rengo F (1996) CHF Italian study investigators. The brain in congestive heart failure. Arch Gerontol Geriatr 23(3):247–256
17. Alosco ML, Hayes SM (2015) Structural brain alterations in heart failure: a review of the literature and implications for risk of Alzheimer's disease. Heart Fail Rev 20(5):561–571
18. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW, American College of Cardiology/American Heart Association Task Force on Practice Guidelines (2014) 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 64(21):e1–76
19. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P, ESC Committee for Practice

Guidelines (CPG) (2012) 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 33(21):2719–2747

20. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Kay GN, Le Huezey JY, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann LS (2011) 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 developed in partnership with the European Society of Cardiology and in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. J Am Coll Cardiol 57(11):e101–e198