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Role of CHA_2DS_2-VASc score in predicting new-onset atrial fibrillation in patients with type 2 diabetes mellitus with and without hyperosmolar hyperglycaemic state: real-world data from a nationwide cohort

Wei-Syun Hu,[1,2] Cheng-Li Lin[3]

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[1]School of Medicine, College of Medicine, China Medical University, Taichung, Taiwan
[2]Division of Cardiovascular Medicine, Department of Medicine, China Medical University Hospital, Taichung, Taiwan
[3]Management Office for Health Data, China Medical University Hospital, Taichung, Taiwan

Correspondence to
Dr Wei-Syun Hu;
weisyunhu@gmail.com

ABSTRACT

Purpose The objective of the current study was to explore the role of CHA_2DS_2-VASc score in predicting incidence of atrial fibrillation (AF) in patients with type 2 diabetes mellitus (DM). Furthermore, the use of the CHA_2DS_2-VASc score for stratifying new-onset AF risk in patients with DM and with/without hyperosmolar hyperglycaemic state (HHS) was also compared.

Methods The study subjects were identified from Longitudinal Health Insurance Database provided by the National Health Research Institutes. The patients with DM were divided into two groups based on a history of HHS or not. The predictive ability of CHA_2DS_2-VASc score for stratifying new-onset AF risk in the two groups was calculated using the area under the curve of receiver-operating characteristic (AUROC).

Results The present study involved a total of 69 530 patients with type 2 DM. Among them, 1558 patients had a history of HHS, whereas 67 972 patients did not. The AUROC of the CHA_2DS_2-VASc score as a predictor of incident AF in patients with DM and with/without HHS was 0.67 (95% CI 0.59 to 0.75) and 0.71 (95% CI 0.70 to 0.72), respectively.

Conclusions To conclude, we reported for the first time on the assessment of CHA_2DS_2-VASc score for incident AF risk discrimination in patients with type 2 DM. We further found that the predictive ability of the CHA_2DS_2-VASc score was attenuated in patients with type 2 DM and with HHS in comparison with those without HHS.

Strengths and limitations of this study

- We reported for the first time on the application of CHA_2DS_2-VASc score for stratifying incident atrial fibrillation risk among patients with type 2 diabetes mellitus (DM).
- We found that the predictive ability of the CHA_2DS_2-VASc score was attenuated in patients with DM and hyperosmolar hyperglycaemic state (HHS) compared with those without HHS.
- The use of International Classification of Disease Ninth Revision codes is a critical limitation in the current study.
- However, the codes have been used in many epidemiological studies, and the results from this big dataset have been reported with high reliability.

INTRODUCTION

Type 2 diabetes mellitus (DM) is one of the major issues in public health worldwide due to its increasing incidence and prevalence.[1 2] Indeed, hyperosmolar hyperglycaemic state (HHS) is a major acute complication in patients with DM.[3–8] The common triggers for HHS include poor medication compliance, fluctuation of blood glucose or other stress responses.[3–8] The prognostic impact of atrial fibrillation (AF) could not be overemphasised due to its associated high morbidity and mortality.[9 10] In comparison to the therapeutic strategy for AF treatment, the prevention for incident AF gained relatively less attention.[9–11]

The link between DM and AF has been investigated; indeed, DM is an important risk factor for AF development and a crucial predictor of adverse cardiovascular outcomes in patients with AF.[12–16] Several pathogenesis mechanisms underlying the link between DM and AF were proposed, including structure and electric remodelling, oxidative stress reaction, inflammatory response and autonomic dysfunction.[12–16]

CHA_2DS_2-VASc score, a simple, practical and user-friendly scoring scheme which was initially used for stroke risk discrimination among patients with AF has gained widely use for predicting different cardiovascular outcomes in different population recently.[17–19]

Hence, using a large nationwide dataset, the objective of the current study was to explore the role of CHA_2DS_2-VASc score in predicting incidence of AF in patients with DM. Furthermore, the use of the CHA_2DS_2-VASc score for discriminating new-onset AF risk in patients with DM and with/without hyperosmolar hyperglycaemic state (HHS) was also compared.

METHODS

Data source

This retrospective cohort study was assembled using data from Longitudinal Health Insurance Database (LHID) of 2000 provided by the National Health Research Institutes (NHRI). The National Health Insurance (NHI) programme in Taiwan, which started from 1 March 1995, includes approximately 99% of Taiwan's population.[20] The LHID includes longitudinal data and comprises a total of 1 000 000 people randomly selected from the NHI Registry for Beneficiaries of 2000. More details on the LHID have been described elsewhere.[21 22] Disease was operationalised using the International Classification of Disease, Ninth revision (ICD-9) codes. The Ethics Review Board of China Medical University and Hospital in Taiwan approved this study (CMUH-104-REC2-115).

Sampled participants

The study subjects were defined as those over 20 years old with a new diagnosis of type 2 DM (ICD-9-CM codes 250.x0 or 250.x2) between 1 January 2000 and 31 December 2011. The patients with DM were divided into two groups based on a history of hyperosmolar hyperglycaemic state (HHS) (ICD-9-CM codes 250.20 or 250.22) or not. The index date was assigned as the first DM diagnosis date. We excluded patients who had a diagnosis of AF (ICD-9-CM code 427.31) before the index date. All study subjects received follow-up from the index date and terminated while they were removed from the health insurance programme, death, AF occurrence or the end of the study (31 December 2011). We used the CHA_2DS_2-VASc score to measure incident AF risk among patients with type 2 DM and with and without HHS.[23 24] The CHA_2DS_2-VASc score was calculated for each patient by assigning one point for heart failure, type 2 DM, hypertension, vascular disease, sex category (female) and an age between 65 and 74 years; and two points for a history of ischaemic stroke/transient ischaemia attack (TIA) or an age 75 years or older.

Baseline comorbid medical illness, such as hyperlipidaemia (ICD-9-CM code 272), chronic obstructive pulmonary disease (COPD) (ICD-9-CM code 491, 492, 496), chronic kidney disease (CKD) (ICD-9-CM codes 585, 586, 588.8, 588.9), hyperthyroidism (ICD-9-CM code 242), sleep disorders (ICD-9-CM codes 307.4, 780.5), gout (ICD-9-CM code 274) and Charlson Comorbidity Index (CCI) score were identified and included in the current study.

Statistical analysis

To display the distribution of baseline characteristics of study population, the age, sex, underlying disease whether captured in the CHA_2DS_2-VASc score or not between patients with DM and with/without HHS were shown as number and percentage or mean and SD. The χ^2 test and t-test were applied to examine the distribution difference for category variables and for continuous

Table 1 Baseline characteristics of patients with DM and with/without HHS

	HHS		
	No	Yes	
Variable	n=67 972	n=1558	P value
Age, year	n (%)	n (%)	<0.001
≤64	48 497 (71.4)	883 (56.7)	
65–74	13 156 (19.4)	404 (25.9)	
≧75	6319 (9.30)	271 (17.4)	
Mean±SD*	57.0 (13.2)	60.8 (14.8)	<0.001
Sex			<0.001
Female	32 463 (47.8)	662 (42.5)	
Male	35 509 (52.2)	896 (57.5)	
Underlying disease(components of the CHA_2DS_2-VASc score)			
CHF	2643 (3.89)	90 (5.78)	0.001
CVA or TIA	2984 (4.39)	121 (7.77)	<0.001
Vascular disease	3315 (4.88)	90 (5.78)	0.10
Hypertension	38 497 (56.6)	917 (58.9)	0.08
Other underlying disease			
Hyperlipidaemia	31 588 (46.5)	550 (35.3)	<0.001
Chronic obstructive pulmonary disease	9147 (13.5)	247 (15.9)	0.006
Chronic kidney disease	3229 (4.75)	126 (8.09)	<0.001
Hyperthyroidism	1531 (2.25)	23 (1.48)	0.04
Sleep disorders	14 099 (20.7)	311 (20.0)	0.45
Gout	11 237 (16.5)	267 (17.1)	0.52
CCI score			<0.001
0	55 237 (81.3)	963 (61.8)	
1	8466 (12.5)	351 (22.5)	
2	2310 (3.40)	129 (8.28)	
3 or more	1959 (2.88)	115 (7.38)	
Mean CHA_2DS_2-VASc score (SD)*	2.60 (1.31)	2.89 (1.53)	<0.001
Mean follow-up, year (SD)*	6.20 (3.49)	6.64 (3.51)	<0.001

χ^2test; *t-test.
CHF, congestive heart failure; CCI, Charlson Comorbidity Index; CVA, cerebrovascular accident; DM, diabetes mellitus; HHS, hyperosmolar hyperglycaemic state; TIA, transient ischaemic attack.

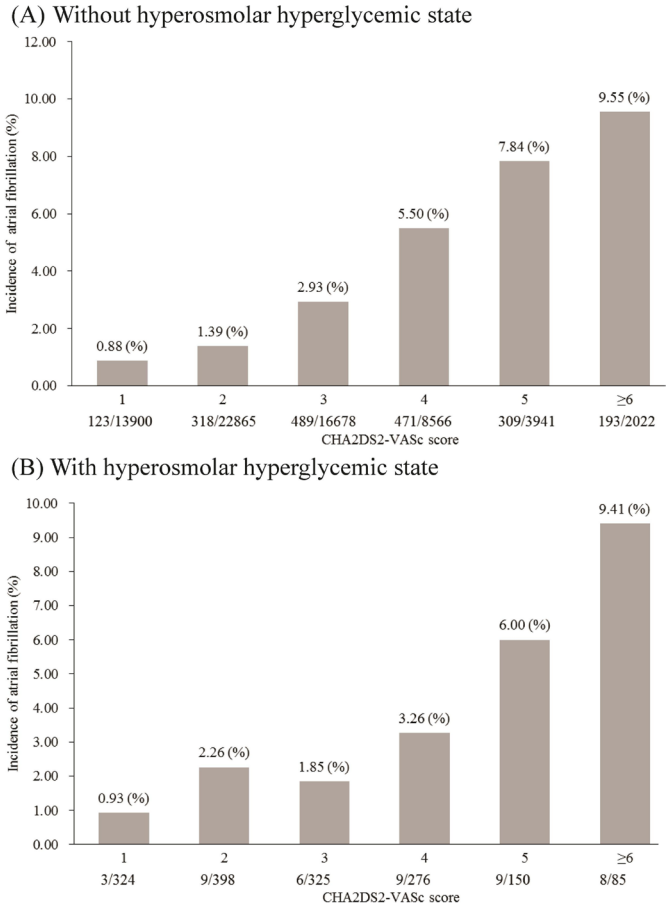

Figure 1 Incidence of new-onset atrial fibrillation in patients with type 2 diabetes mellitus without hyperosmolar hyperglycaemic state (A) and with hyperosmolar hyperglycaemic state (B) with different CHA_2DS_2-VAS scores.

variables, respectively. The CHA_2DS_2-VASc score-specific incidence density rate of new-onset AF per 1000 person-years (PYs) was calculated in each group. The cumulative incidences of new-onset AF among patients with type 2 DM and with or without HHS stratified by CHA_2DS_2-VASc score were assessed using the Kaplan-Meier method. The differences between the cumulative incidence curves were evaluated using a log-rank test. Univariable and multivariable Cox proportional hazards models were adopted to estimate the HRs and the 95% CIs for incident AF associated with the CHA_2DS_2-VASc score in the two groups. CCI score and comorbidities which were not captured in the CHA_2DS_2-VASc score were included in the multivariable models for adjustment, including hyperlipidaemia, COPD, CKD, hyperthyroidism, sleep disorders and gout. The predictive ability of CHA_2DS_2-VASc score for stratifying AF risk in the two groups was calculated using the area under the curve of receiver-operating characteristic (AUROC). The AUROC integrated measures of sensitivity and specificity of the variable range from 0 to 1. The statistical significance was accepted at a two-tailed p value lower than 0.05.

RESULTS

The study involved a total of 69 530 patients with type 2 DM. Among them, 1558 patients had a history of HHS, whereas 67 972 patients did not (table 1). The mean age of the HHS group and the non-HHS group were 60.8 and 57.0 years, respectively (p<0.001). The percentage of male gender in the HHS group was significantly higher than the non-HHS group (57.5% vs 52.2%, p<0.001). Compared with the non-HHS group, the HHS group significantly had more comorbid congestive heart failure (CHF), cerebrovascular accident (CVA) or TIA, COPD and CKD. Most study participants had a CCI score of 0 (61.8% vs 81.3%). The mean CHA_2DS_2-VASc score of the HHS group and the non-HHS group were 2.89 (SD=1.53) and 2.60 (SD=1.31), respectively (p<0.001). The mean follow-up period for the HHS group and for the non-HHS group were 6.64 (SD=3.51) years and 6.20 (SD=3.49) years, respectively. Among patients with type 2 DM and without HHS, the incidence of new-onset AF increased from 0.88% for those with a CHA_2DS_2-VASc score of 1 to 9.55% for those with a score of 6 or greater (figure 1A). The incidence of AF increased from 1.42 per 1000 PYs for patients with DM and without HHS with a CHA_2DS_2-VASc score of 1 to 22.6 per 1000 PYs for those with a CHA_2DS_2-VASc score of ≧6 (table 2). After adjusting for the comorbidities of hyperlipidaemia, COPD, CKD, hyperthyroidism, sleep disorders, gout and CCI score, the risk of incidence of AF among patients with DM and without HHS increased with increasing CHA_2DS_2-VASc score. The incidence of new-onset AF increased from 0.93% to 9.41% when the CHA_2DS_2-VASc score increased from 1 to 6 or greater among patients with DM and HHS (figure 1B). Among patients with DM and HHS, in comparison with patients with a CHA_2DS_2-VASc score of 1, the corresponding adjusted HRs of new-onset AF for those with a CHA_2DS_2-VASc score of 5 and ≧6 were 8.59 (95% CI 2.26 to 32.6) and 16.1 (95% CI 3.79 to 68.8), respectively. The cumulative incidence curves of new-onset AF stratified by CHA_2DS_2-VASc score in patients with DM without and with HHS were shown in figure 2A,B (log-rank test p<0.001). Table 3 reports the sensitivity, specificity and AUROC for the CHA_2DS_2-VASc score in relation to new-onset AF in the two study groups. Among the non-HHS group, discrimination value of the CHA_2DS_2-VASc score for incident AF results in AUROC of 0.71 (95% CI 0.70 to 0.72) (table 3 and figure 3A).The cut-off value of the CHA_2DS_2-VASc score for incident AF was 3 (sensitivity: 76.8%; specificity: 55.0%). Among HHS group, the AUROC of the CHA_2DS_2-VASc score as a predictor of AF was 0.67 (95% CI 0.59 to 0.75) (table 3 and figure 3B). The cut-off value of the CHA2DS2-VASc for incident AF was 4 (sensitivity: 59.1%; specificity: 68.0%).

DISCUSSION

To date, we reported for the first time on the application of CHA_2DS_2-VASc score for stratifying incident AF risk among patients with type 2 DM. Furthermore, we found

Table 2 Incidence and HRs of AF in DM patients with or without HHS stratified by CHA_2DS_2-VASc score

CHA_2DS_2-VASc score	N	No. of events	Person-years	Rate†	Crude HR (95% CI)	Adjusted HR (95% CI)‡
Without HHS						
1	13900	123	86889	1.42	1 (Reference)	1 (Reference)
2	22865	318	146724	2.17	1.52 (1.24 to 1.88)***	1.54 (1.25 to 1.90)***
3	16678	489	107434	4.55	3.20 (2.62 to 3.90)***	3.15 (2.58 to 3.85)***
4	8566	471	51279	9.19	6.52 (5.35 to 7.95)***	5.88 (4.80 to 7.19)***
5	3941	309	20477	15.1	10.9 (8.84 to 13.4)***	8.83 (7.11 to 11.0)***
≧6	2022	193	8554	22.6	16.5 (13.2 to 20.7)***	10.8 (8.44 to 13.9)***
P values for trend					<0.001	<0.001
With HHS						
1	324	3	2103	1.43	1 (Reference)	1 (Reference)
2	398	9	2709	3.32	2.33(0.63 to 8.62)	2.42(0.65 to 9.00)
3	325	6	2363	2.54	1.72(0.43 to 6.86)	1.96(0.49 to 7.88)
4	276	9	1915	4.70	3.24(0.88 to 12.0)	3.32(0.89 to 12.4)
5	150	9	877	10.3	7.66 (2.07 to 28.3)**	8.59 (2.26 to 32.6)***
≥6	85	8	384	20.8	17.8 (4.70 to 67.7)***	16.1 (3.79 to 68.8)***
P values for trend					<0.001	<0.001

**p<0.01; ***p<0.001.
†Rate per 1000 person-years.
‡Adjusted for hyperlipidaemia, chronic obstructive pulmonary disease, chronic kidney disease, hyperthyroidism, sleep disorders, gout and CCI score.
AF, atrial fibrillation; CCI, Charlson Comorbidity Index; DM, diabetes mellitus; HHS, hyperosmolar hyperglycaemic state.

that the predictive ability of the CHA_2DS_2-VASc score was attenuated in patients with DM and HHS compared with those without HHS.

The association between DM and AF has been addressed previously.[12–16] Early studies have discussed the prognostic impact of DM among patients with AF; indeed, one of the major players of CHA_2DS_2-VASc score, an important risk scoring scheme for predicting stroke in patients with AF, is DM.[12–19] Furthermore, the causal relationship between DM and AF has also been investigated; and currently proposed molecular mechanisms underlying the link include atrial mechanical and electrical remodelling triggered by high glucose environment, the fluctuation of the blood sugar, inflammatory response,

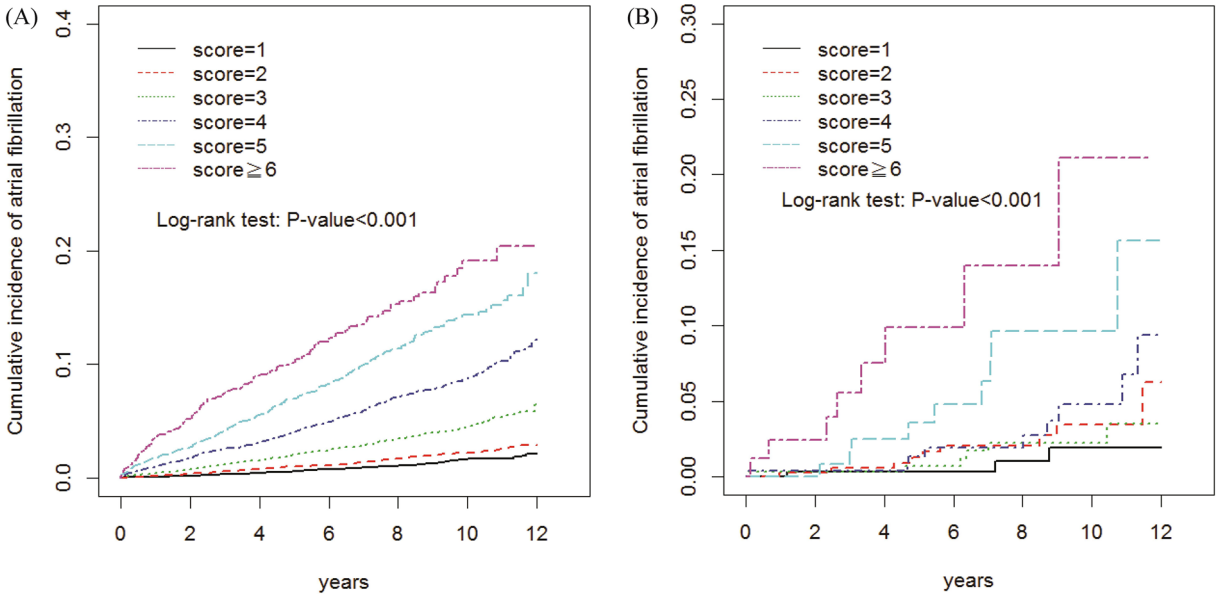

Figure 2 Cumulative incidence curves of new-onset atrial fibrillation stratified by CHA_2DS_2-VASc score in patients with type 2 diabetes mellitus without hyperosmolar hyperglycaemic state (A) and with hyperosmolar hyperglycaemic state (B).

Table 3 Sensitivity, specificity and predictive ability (AUROC and the 95% CI) for CHA_2DS_2-VASc score in relation to AF in DM patients with and without HHS

	Sensitivity	Specificity	AUROC (95% CI)	P value
Without HHS				
CHA_2DS_2-VASc score				
≧1	100.0	0.00	0.71 (0.70 to 0.72)	<0.001
≧2	93.5	20.9		
≧3	76.8	55.0		
≧4	51.1	79.5		
≧5	26.4	91.7		
With HHS				
CHA_2DS_2-VASc score				
≧1	100.0	0.00	0.67 (0.59 to 0.75)	<0.001
≧2	93.1	21.2		
≧3	72.7	46.8		
≧4	59.1	68.0		
≧5	38.6	85.6		

AF, atrial fibrillation; AUROC, area under the curve of receiver-operating characteristic; DM, diabetes mellitus; HHS, hyperosmolar hyperglycaemic state.

dysregulation of autonomic system and oxidative stress reaction.[12–16]

Compared with the management strategies for AF intervention, identification and detection for new-onset AF gained relatively less attraction.[9–11] Although prediction models for incident AF were currently available, the major limitations of the scoring system were user unfriendly and relatively complicated for clinical use.[25 26] Thus, using a large-scale nationwide dataset, we sought to identify the predictive role of CHA_2DS_2-VASc score in this population. Although patients with DM and HHS tend to have more comorbidity; after adjustment for several risk factors for AF development other than the components of the CHA_2DS_2-VASc score, the ability of the score for discriminating new-onset AF risk in patients with DM and HHS was attenuated as opposed to those without HHS. Furthermore, patients with DM and who had a history of HHS tend to be at a significantly increased risk for incident AF at a relative higher threshold. Possible explanation for our observations is that a previous exposure of HHS in patients with DM might enhance the phenomenon of oxidative injury, endothelial damage and stress response, which in turn could probably attenuate the ability of the CHA_2DS_2-VASc score for incident AF risk stratification in this population.[12–16] The results presented here should still be verified by other large prospective investigations.

Limitations

First, the use of ICD-9 codes is a critical limitation in the current study. However, the codes have been used in many epidemiological studies and the results from this big dataset have been reported with high reliability.[27 28] Second, this study lacks considerations of smoking, nutrition, obesity, family history and physical activity. Finally, the use of the therapeutic procedures, such as atrial fibrillation ablation, pacemaker implantation, cardiac catheterisation, and the severity of the diseases were not included in the current study.

CONCLUSIONS

To conclude, we reported for the first time on the assessment of CHA_2DS_2-VASc score for incident AF risk discrimination in patients with type 2 DM. We further found that the predictive ability of the CHA_2DS_2-VASc score was attenuated in patients with type 2 DM and HHS in comparison with those without HHS. The findings

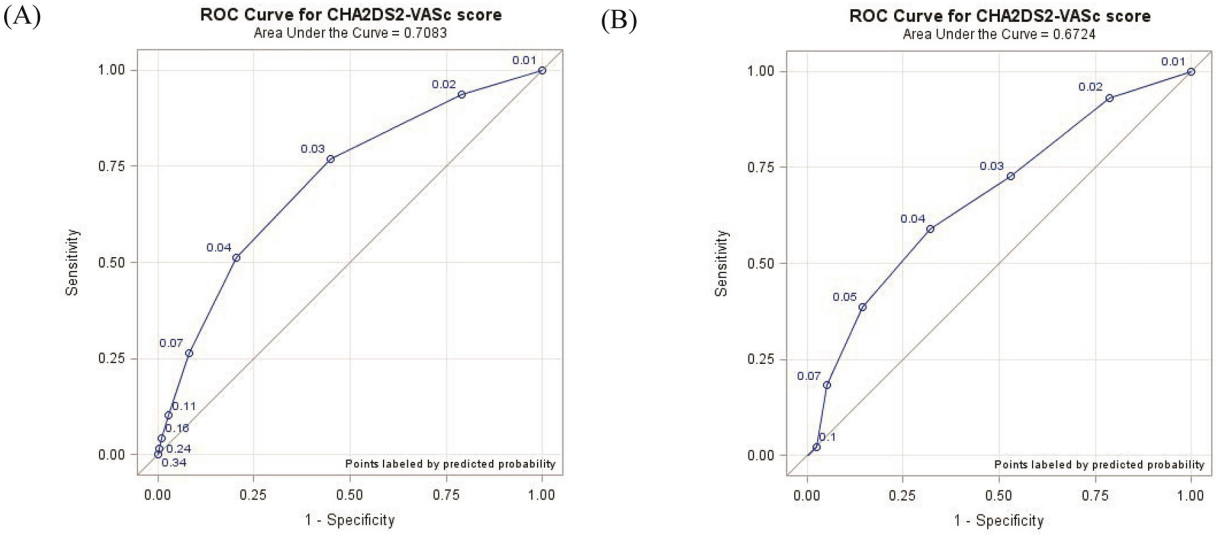

Figure 3 ROC curve for CHA_2DS_2-VASc score in predicting new-onset atrial fibrillation in patients with type 2 diabetes mellitus without hyperosmolar hyperglycaemic state (A) and with hyperosmolar hyperglycaemic state (B). ROC, receiver operating characteristic.

presented here should still be confirmed by further large prospective studies.

Contributors Wei-Syun Hu: conceptualisation, methodology, software, validation; formal analysis, investigation, resources, data curation, writing (original draft preparation), writing (review and editing), visualisation, supervision, project administration and funding acquisition.Cheng-Li Lin: formal analysis, investigation, resources and data curation.

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Competing interests None declared.

Patient consent Not required.

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REFERENCES

1. International Diabetes Federation. Key findings. 2014 http://www.idf.org/diabetesatlas/update-2014 (2 Feb 2014).
2. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, *et al*. Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength? *World J Diabetes* 2014;5:444–70.
3. Fadini GP, de Kreutzenberg SV, Rigato M, *et al*. Characteristics and outcomes of the hyperglycemic hyperosmolar non-ketotic syndrome in a cohort of 51 consecutive cases at a single center. *Diabetes Res Clin Pract* 2011;94:172–9.
4. Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin North Am* 2006;35:725–51.
5. Ceriello A, Esposito K, Piconi L, *et al*. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. *Diabetes* 2008;57:1349–54.
6. Chiasson JL, Aris-Jilwan N, Bélanger R, *et al*. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. *CMAJ* 2003;168:859–66.
7. Quagliaro L, Piconi L, Assaloni R, *et al*. Intermittent high glucose enhances apoptosis related to oxidative stress in human umbilical vein endothelial cells: the role of protein kinase C and NAD(P)H-oxidase activation. *Diabetes* 2003;52:2795–804.
8. Jones SC, Saunders HJ, Qi W, *et al*. Intermittent high glucose enhances cell growth and collagen synthesis in cultured human tubulointerstitial cells. *Diabetologia* 1999;42:1113–9.
9. January CT, Wann LS, Alpert JS, *et al*. American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 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* 2014;64:e1–76.
10. Camm AJ, Lip GY, De Caterina R, *et al*. 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* 2012;33:2719–47.
11. Benjamin EJ, Chen PS, Bild DE, *et al*. Prevention of atrial fibrillation: report from a national heart, lung, and blood institute workshop. *Circulation* 2009;119:606–18.
12. Goudis CA, Korantzopoulos P, Ntalas IV, *et al*. Diabetes mellitus and atrial fibrillation: Pathophysiological mechanisms and potential upstream therapies. *Int J Cardiol* 2015;184:617–22.
13. De Sensi F, De Potter T, Cresti A, *et al*. Atrial fibrillation in patients with diabetes: molecular mechanisms and therapeutic perspectives. *Cardiovasc Diagn Ther* 2015;5:364–73.
14. Tadic M, Cuspidi C. Type 2 diabetes mellitus and atrial fibrillation: from mechanisms to clinical practice. *Arch Cardiovasc Dis* 2015;108:269–76.
15. Movahed MR, Hashemzadeh M, Jamal MM. Diabetes mellitus is a strong, independent risk for atrial fibrillation and flutter in addition to other cardiovascular disease. *Int J Cardiol* 2005;105:315–8.
16. Benjamin EJ, Levy D, Vaziri SM, *et al*. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. *JAMA* 1994;271:840–4.
17. Fuster V, Rydén 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 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* 2011;57:e101–98.
18. Cetin M, Cakici M, Zencir C, *et al*. Prediction of coronary artery disease severity using CHADS2 and CHA2DS2-VASc scores and a newly defined CHA2DS2-VASc-HS score. *Am J Cardiol* 2014;113:950–6.
19. Paoletti Perini A, Bartolini S, Pieragnoli P, *et al*. CHADS2 and CHA2DS2-VASc scores to predict morbidity and mortality in heart failure patients candidates to cardiac resynchronization therapy. *Europace* 2014;16:71–80.
20. Database NHIR. Taiwan. 2015 http://nhird.nhri.org.tw/en/index.html
21. Hu WS, Lin CL. Association between cataract and risk of incident atrial fibrillation: a nationwide population-based retrospective cohort study. *Mayo Clin Proc* 2017;92:370–5.
22. Hu WS, Lin CL, Chang SS, *et al*. Increased risk of ischemic heart disease among subjects with cataracts: a population-based cohort study. *Medicine* 2016;95:e4119.
23. Hu WS, Lin CL. Postoperative ischemic stroke and death prediction with CHA_2DS_2-VASc score in patients having coronary artery bypass grafting surgery: a nationwide cohort study. *Int J Cardiol* 2017;241:120–3.
24. Hu WS, Lin CL. CHA_2DS_2-VASc score in the prediction of ischemic bowel disease among patients with atrial fibrillation: Insights from a nationwide cohort. *Int J Cardiol* 2017;235:56–60.
25. Chamberlain AM, Agarwal SK, Folsom AR, *et al*. A clinical risk score for atrial fibrillation in a biracial prospective cohort (from the Atherosclerosis Risk in Communities [ARIC] study). *Am J Cardiol* 2011;107:85–91.
26. Schnabel RB, Sullivan LM, Levy D, *et al*. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet* 2009;373:739–45.
27. Cheng CL, Kao YH, Lin SJ, *et al*. Validation of the National Health Insurance Research Database with ischemic stroke cases in Taiwan. *Pharmacoepidemiol Drug Saf* 2011;20:236–42.
28. Cheng CL, Chien HC, Lee CH, *et al*. Validity of in-hospital mortality data among patients with acute myocardial infarction or stroke in National Health Insurance Research Database in Taiwan. *Int J Cardiol* 2015;201:96–101.