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Atrial fibrillation and $CHADS_2$ score as mortality predictors in young versus elderly patients undergoing coronary angiography

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Initially developed to predict stroke probability in patients with atrial fibrillation (AF),[1–3] $CHADS_2$ and CHA_2DS_2VASC scores are used to predict different outcomes in cardiac patients in both acute and chronic conditions.[4–5,8–12] The scores were also demonstrated to correlate with mortality.[4,6,7,11–15] AF also has been associated with mortality in different groups of patients, including elderly.[16–18] There is little information about the prognostic value of $CHADS_2$ score in elderly versus young patients, especially in mortality prediction (taking into consideration that age is a component of the score).

We hypothesized that both atrial fibrillation and the $CHADS_2$ score are independently associated with mortality in the young as well as elderly patients and that the $CHADS_2$ score can be a useful tool to predict mortality in patients undergoing coronary angiography in both young and elderly patients.

The study was approved by the institutional review board as a prospective registry. Nine hundred eighty six patients who underwent coronary angiography in Kaplan Medical Center (Jerusalem, Israel) were enrolled in this study. The hospital database and the Israeli population authority registry were used to collect the patients' data.

The median follow up was 30 months. We divided the total cohort into two age groups: young group (< 75 years, n = 666) and the elderly group (≥ 75 years, n = 320). Baseline clinical characteristics, laboratory and procedural data and mortality were compared between patients in the two age groups. Then, we assessed mortality in the two age groups according to the $CHADS_2$ score. The chi-square test and Fisher's exact test were used for dichotomous variables, and independent t test was used for continuous variables. Data are expressed as mean ± SD or frequency and/or percentage when appropriate.

Cumulative event proportions in the two age groups were calculated by Kaplan-Meier method, and outcome differences were assessed with the Log-Rank test. The multivariate analysis of the mortality predictors in the two age groups was done with Cox regression analysis. Receiver operating characteristic (ROC) curve was used to analyze C-statistics of the relevant $CHADS_2$ score. Comparison between ROC curves was done with DeLong method. A P value < 0.05 was considered significant. Data were analyzed using SPSS statistical software version 21 and Medcalc 17.5.5.

During the follow up, 53 patients (8.0%) in the young age group and 75 (23.4%) in the elderly group died. The baseline demographic clinical and laboratory characteristics and the mortality in the two age groups are showed in Table 1. The distribution of the $CHADS_2$ score in the two age groups is described in Table 2. Due to the low number of patients with the score of 6, we combined patients with scores 5 and 6 into single category (5+).

Our data demonstrated that patients with $CHADS_2$ score of 0–1 in younger patients and score of 1–2 in the elderly patients had much lower mortality than patients with the higher scores in the relevant groups (Table 2). To further test the appropriate cutoff value for each group, we performed the ROC curve analysis for the total cohort and the two age groups and compared them using DeLong method (Figure 1). The C-statistics was optimal for $CHADS_2$ score of 2 in young group and 3 in the elderly group. On the basis of this data, we performed additional analysis using a cutoff vale of ≥ 2 in the young group and ≥ 3 in the elderly group. Mortality was significantly higher in younger group (13.6% *vs.* 3.7, P < 0.0001) if $CHADS_2$ score was ≥ 2; and in the elderly group (28.6% *vs.* 16.3%, P = 0.01) if $CHADS_2$ score was ≥ 3.

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Table 1. Baseline patient's characteristics.

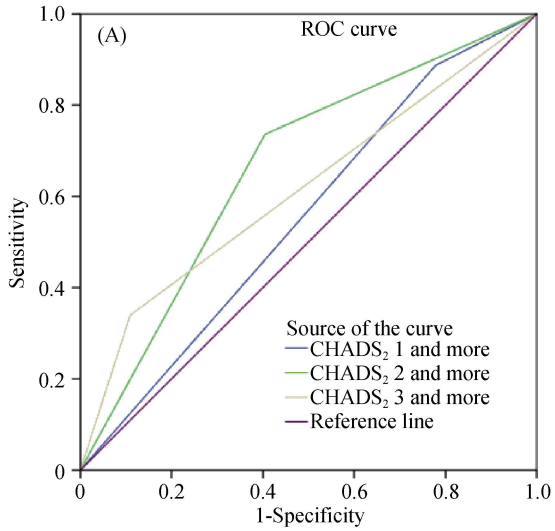
Variable	Patients with age < 75 yrs	Patients aged ≥ 75 yrs	*P* value for difference
Age, yrs	62.1 ± 9.2	80.26 ± 4.3	< 0.0001
$CHADS_2$ score	1.4 ± 1.0	2.8 ± 1.0	< 0.0001
Creatinine, mg/dL	1.15 ± 1.25	1.22 ± 0.77	0.313
HB, g/dL	13.5 ± 1.6	12.4 ± 1.5	< 0.0001
LVEF	49.6% ± 9.6%	48.5% ± 10.7%	0.238
AF	15.1%	29.0%	< 0.0001
Female	25.5%	40.0%	< 0.0001
DM	41.5%	47.5%	0.043
HTN	69.7%	88.1%	< 0.0001
Previous MI	21.4%	24.1%	0.187
Previous stroke	8.9%	11.5%	0.125
PAD	5.8%	6.4%	0.122
CHF	12.1%	18.6%	0.005
CKD	17.1%	36.2%	< 0.0001
ACS	50.9%	46.4%	0.107
Obstructive CAD	54.5%	55.8%	0.193
LVEF > 50%	49.5%	46.0%	0.201
Mortality	8.0%	23.4%	< 0.0001

Data are expressed as mean ± SD or percent. ACS: acute coronary syndrome; AF: atrial fibrillation; CAD: cardiovascular disease; CHF: chronic heart failure; CKD: chronic kidney disease; DM: diabetes mellitus; HB: hemoglobin; HTN: hypertension; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PAD: peripheral arterial disease.

Table 2. Distribution of patients according to the $CHADS_2$ score in the two age groups.

$CHADS_2$ score	*N*	Percent	Cumulative percent	Mortality
*Young age group				
0	142	21.3%	21.3%	4.2%
1	237	35.6%	56.9%	3.4%
2	202	30.3%	87.2%	10.4%
3	53	8.0%	95.2%	20.8%
4	29	4.4%	99.5%	17.2%
5+	3	0.5%	100%	66.7%
Total	666	100%	100%	8%
# The elderly group				
1	19%	5.9%	5.9%	15.8%
2	116%	36.3%	42.2%	16.4%
3	135%	42.2%	84.4%	26.7%
4	25%	7.8%	92.2%	40%
5+	25%	7.8%	100%	28%
Total	320%	100%	100%	23.4%

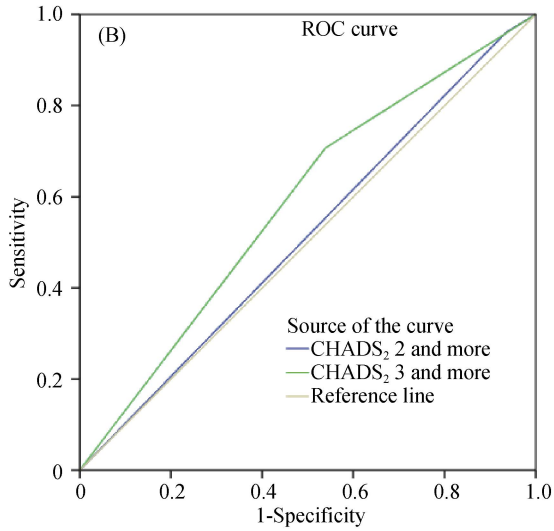
*P value < 0.001 for any difference in mortality; #P = 0.068 for any difference in mortality.



Variable	AUC	95% CI	*P* value
$CHADS_2 \geq 1$	0.554	0.516–0.593	0.189
$CHADS_2 \geq 2$	0.666	0.628–0.701	< 0.0001
$CHADS_2 \geq 3$	0.615	0.577–0.652	0.005

Comparison of ROC curves

Variable	*P* value
$CHADS_2 \geq 1$ *vs.* $CHADS_2 \geq 2$	< 0.0001
$CHADS_2 \geq 1$ *vs.* $CHADS_2 \geq 3$	0.0893
$CHADS_2 \geq 2$ *vs.* $CHADS_2 \geq 3$	0.1509



Variable	AUC	95% CI	*P* value
$CHADS_2 \geq 2$	0.513	0.456–0.569	0.740
$CHADS_2 \geq 3$	0.584	0.528–0.639	0.028

Comparison of ROC curves

Variable	*P* value
$CHADS_2 \geq 2$ *vs.* $CHADS_2 \geq 3$	0.0165

Figure 1. ROC curve analysis of different $CHADS_2$ cutoff values in the young and elderly groups. (A): ROC curve analysis of $CHADS_2$ of 1, 2 and 3 for predictive probability of mortality in the younger group; and (B): ROC curve analysis of $CHADS_2$ of 1, 2 and 3 for predictive probability of mortality in the elderly group. AUC: area under curve; ROC curve: receiver operating characteristic curve.

Univariate analysis of patients' characteristics on mortality in the two age groups is showed in Table 3. Kaplan Meier analysis demonstrated a statistically significant correlation of $CHADS_2 \geq 2$ with mortality in the young group and $CHADS_2 \geq 3$ with mortality in the elderly group (Figure 2). AF was also associated with mortality in two age groups (Figure 3).

Table 3. Univariate analysis of effect on mortality.

Variable	Alive, *n* = 613	Deceased, *n* = 53	*P* Value
Young age group			
AF	6.6%	16.0%	0.003
Female	7.7%	8.8%	0.367
Previous MI	8.0%	7.9%	0.567
CKD (creatinine > 1.1)	5.9%	17.9%	< 0.0001
ACS	6.7%	8.9%	0.186
Obstructive CAD	8.2%	7.8%	0.214
LVEF < 50%	6.8%	11.0%	0.118
$CHADS_2 \geq 2$	3.7%	13.6%	< 0.0001
Anemia (HB < 13)	4.9%	14.6%	< 0.0001
The elderly group			
AF	20.0%	32.6%	0.013
Female	20.3%	28.1%	0.07
Previous MI	23.0%	22.4%	0.522
CKD (creatinine > 1.1)	16.9%	34.2%	< 0.0001
ACS	17.9%	28.6%	0.02
Obstructive CAD	18.9%	27.4%	0.34
EF < 50%	23.0%	32.2%	0.10
$CHADS_2 \geq 3$	11.3%	28.6%	< 0.011
Anemia (HB < 13)	17.1%	27.7%	0.038

ACS: acute coronary syndrome; AF: atrial fibrillation; CAD: cardiovascular disease; CKD: chronic kidney disease; EF: ejection fraction; HB: hemoglobin; LVEF: left ventricular ejection fraction; MI: myocardial infarction.

Multivariate analysis using Cox regression model which combined $CHADS_2$ score, presence of AF, anemia (hemoglobin < 13 g/dL) and presence of renal insufficiency (creatinine > 1.1 mg/dL) demonstrated that $CHADS_2 \geq 2$ was independently associated with higher mortality in the younger group as was $CHADS_2 \geq 3$ in the elderly group. Presence of AF and renal failure were also independently associated with increased mortality in the two age groups. Anemia was independently associated with mortality only in the younger group (Table 4).

The major finding in our study is the independent association between increased $CHADS_2$ score and mortality in patients undergoing coronary angiography in both young and elderly patients.

Older patients significantly differed from the younger patients by having much greater frequency of comorbidities, including, but not limited to hypertension, diabetes, history of stroke, congestive heart failure, lower hemoglobin levels, and chronic renal failure. Thus, the age component of the $CHADS_2$ score reflects these comorbidities. Of note, LV systolic function, history of previous myocardial infarction, as well as presence of obstructive cardiovascular disease on the current angiography were not different between the two groups. By dividing patients into groups below and above 75 years of age, we nullified the effect of the age on the performance of the $CHADS_2$ score as a mortality predictor.

Our data demonstrated that mortality in both age cohorts was similar in patients with no risk factors or one risk factor, and sharply increased with addition of one more risk factor in both age groups (from 4.3% and 3.4% to 10.4% in the younger age group and from 15.8% and 16.4% to 26.7% in the older age group).

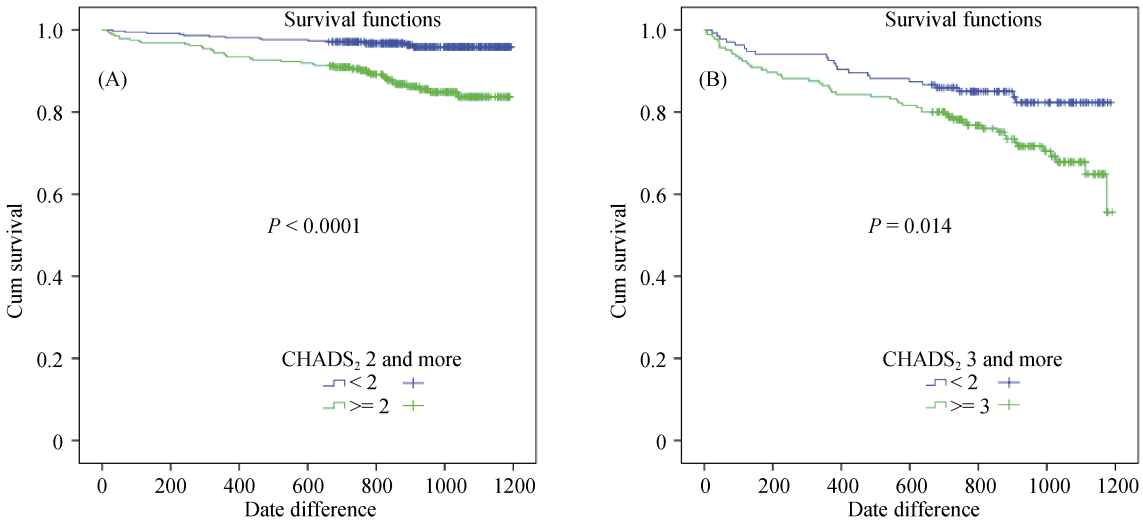


Figure 2. Kaplan Meier survival analysis according to the $CHADS_2$ score in young versus elderly groups. (A): Kaplan Meier survival analysis according to the $CHADS_2$ Score 0–1 *vs.* ≥ 2 and above in the younger age group; (B): Kaplan Meier survival analysis according to the $CHADS_2$ Score 1–2 *vs.* ≥ 3 in the older age group.

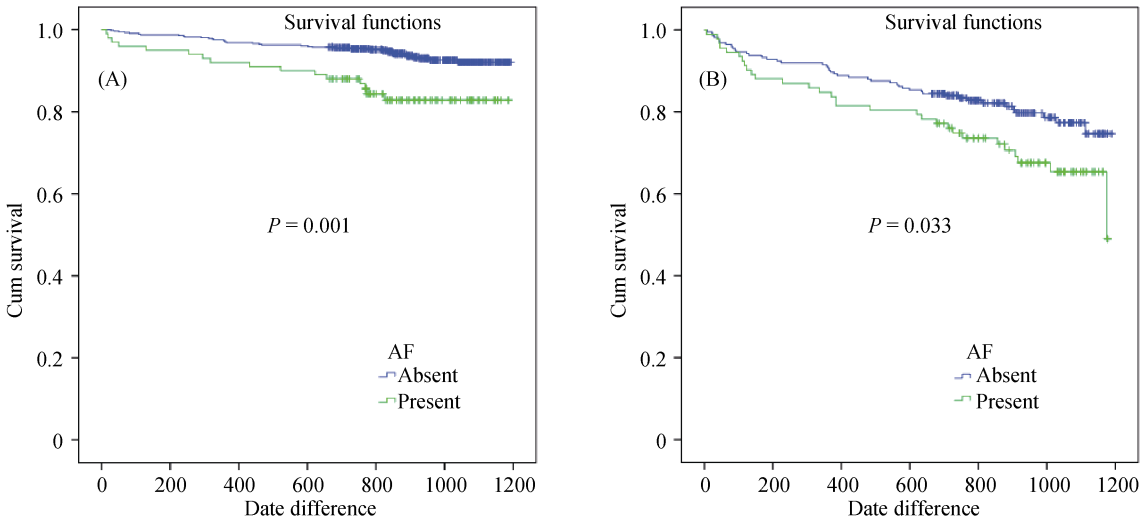


Figure 3. Kaplan Meier survival analysis according to the presence of AF in young versus elderly groups. (A): Kaplan Meier survival analysis according to the presence of the AF in the younger age group; (B): Kaplan Meier survival analysis to the presence of the atrial fibrillation in the older age group. AF: atrial fibrillation

Table 4. Cox regression multivariate analysis of effect on mortality.

Variable	Hazard ratio	95% CI	*P* Value
Young age group			
AF	2.06	1.11–3.82	0.021
CKD	2.01	1.11–3.64	0.021
HB < 13	2.07	1.15–3.73	0.03
CHADS2 ≥ 2	2.4	1.26–4.57	0.008
*The elderly group			
AF	1.76	1.09–2.82	0.021
CKD	1.92	1.20-3.09	0.007
$CHADS_2 \geq 3$	1.98	1.16–3.36	0.012

*HB < 13 g/dL was nonsignificant predictor of mortality in the multivariate analysis in the elderly group. AF: atrial fibrillation, CKD: chronic kidney disease; HB: hemoglobin.

Based on this data, we chose the $CHADS_2 \geq 2$ as a marker of high risk in younger patients and $CHADS_2 \geq 3$ in older patients. Additional analysis using C-statistics demonstrated that this cutoff was indeed optimal. Taking the cutoff lower provided less robust discrimination in both age groups and was even nonsignificant in the elderly group; while taking the cutoff value higher (i.e., three risk factors and more) did not improve the discrimination ability, but would miss a large number of patients with already increased mortality.

Kaplan Meier analysis demonstrated the ability of the pre-specified $CHADS_2$ score value to reliably predict mortality in both age groups. The multivariate analysis done with Cox regression model demonstrated that the $CHADS_2 \geq 2$ in the younger group and ≥ 3 in the elderly group is significantly associated with mortality independently of renal function, anemia and presence of AF.

Thus, our study demonstrates that absence of any, or presence of one risk factor from $CHADS_2$ score marks low risk patients in both age groups in patients undergoing coronary angiography. Presence of two risk factors, however, is associated with much higher mortality.

The performance of $CHADS_2$ and/or CHA_2DS_2VASC scores to predict cardiovascular outcomes, including mortality was studied previously.[4–15] Our study specifically demonstrated the impact of the $CHADS_2$ score to predict mortality in both young and elderly groups. Moreover, this predictive ability was demonstrated to be independent from the presence of AF, anemia and renal failure, all of which are not only significantly associated with mortality, but also much more prevalent in the elderly patients.

The ROC curve analysis also supported the predictive utility of the $CHADS_2$ score. The C-statistics in the young group was better than cited by Puurunen, *et al*.,[13] and similar to that of Chan, *et al*.[4] Elderly patients' C-statistic was also valid, but more modest. This further validates the use of $CHADS_2$score for mortality prediction in both age groups.

Several scoring systems were developed to assess risk in cardiac patients, like those undergoing coronary angiography, i.e., GRACE score. However, the calculation of the GRACE score is complex. $CHADS_2$ is a simple score with universal familiarity and ability to calculate it at the bedside. The simplicity of the $CHADS_2$ score is its main advantage.

Our study, as others,[16–18] also demonstrated the independent association between AF and mortality. We demonstrated that this is true for both young and elderly patients.

Currently, there is a controversy about the ability of rhythm control (including catheter ablation) to influence negative outcomes associated with AF. Our study suggests that geriatric population should be specifically studied in this regard.

In conclusion, we found $CHADS_2$ score can be used as a mortality predictor in patients undergoing coronary angiography. Its prediction is valid in both young and elderly patients, when presence of more than one risk factor is significantly associated with mortality.

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