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ORIGINAL ARTICLE

Nomogram predicting death and heart transplantation before appropriate ICD shock in dilated cardiomyopathy

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Abstract

Aims This study aimed to develop and validate a competing risk nomogram for predicting all-cause mortality and heart transplantation (HT) before first appropriate shock in non-ischaemic dilated cardiomyopathy (DCM) patients receiving implantable cardioverter-defibrillators (ICD).

Methods and results A total of 218 consecutive DCM patients implanted with ICD between 2010 and 2019 at our institution were retrospectively enrolled. Cox proportional hazards model was primarily built to identify variables associated with death and HT. Then, a Fine–Gray model, accounting for the appropriate shock as a competing risk, was constructed using these selected variables along with implantation indication (primary vs. secondary). Finally, a nomogram based on the Fine–Gray model was established to predict 1-, 3-, and 5-year probabilities of all-cause mortality and HT before first appropriate shock. The area under the receiver operating characteristic (ROC) curve (AUC), Harrell's C-index, and calibration curves were used to evaluate and internally validate the performance of this model. The decision curve analysis was applied to assess its clinical utility. The 1-, 3-, and 5-year cumulative incidence of all-cause mortality and HT without former appropriate shock were 5.3% [95% confidence interval (CI) 2.9–9.9%], 16.6% (95% CI 11–25.0%), and 25.3% (95% CI 17.2–37.1%), respectively. Five variables including implantation indication, left ventricular end-diastolic diameter, N-terminal pro-brain natriuretic peptide, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, and amiodarone treatment were independently associated with it (all $P < 0.05$) and were used for constructing the nomogram. The 1-, 3-, and 5-year AUC of the nomogram were 0.83 (95% CI 0.73–0.94, $P < 0.001$), 0.84 (95% CI 0.75–0.93, $P < 0.001$), and 0.85 (95% CI 0.77–0.94, $P < 0.001$), respectively. The Harrell's C-index was 0.788 (95% CI 0.697–0.877, $P < 0.001$; 0.762 for the optimism-corrected C-index), showing the good discriminative ability of the model. The calibration was acceptable (optimism-corrected slope 0.896). Decision curve analysis identified our model was clinically useful within the entire range of potential treatment thresholds for ICD implantation. Three risk groups stratified by scores were significantly different between cumulative incidence curves ($P < 0.001$). The identified high-risk group composed 17.9% of our population and did not derive long-term benefit from ICD.

Conclusions The proposed nomogram is a simple, useful risk stratification tool for selecting potential ICD recipients in DCM patients. It might facilitate the shared decision-making between patients and clinicians.

Keywords Nomogram; Implantable cardioverter-defibrillators; Non-ischaemic dilated cardiomyopathy; Mortality; Heart transplantation

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Introduction

Non-ischaemic dilated cardiomyopathy (DCM) is characterized by left ventricular systolic dysfunction that cannot be explained by abnormal loading conditions or coronary artery disease.[1,2] Patients with DCM still have a high annual mortality rate of 5–7% despite optimal medical therapy, primarily occurring from pump failure and sudden cardiac death (SCD).[3–7] Implantable cardioverter-defibrillators (ICD) implantation has been recommended for primary and secondary prevention of SCD in those patients for several decades.[8] Nonetheless, it is substantially either underutilized or misused because of the unmet needs of precise risk stratification. Approximately 50–70% of ICD recipients do not receive appropriate therapy approaching device replacement.[9–12] In contrast, 5–10% patients experience inappropriate therapies each year[9,12–14] and surgery-related complications are not rare.[15,16] Most ICD recipients have to survive long enough to receive appropriate device therapy before expecting to derive benefit from the device.[8] This unsolved problem bothers clinicians consistently.

Much effort has been put into selecting the risk factors of death and appropriate therapy separately, and a variety of risk factors were identified.[17] But information gained from those predictors is hard to be integrated, impeding its further use. Recent studies have been focusing on modelling both risks simultaneously,[18–20] specifically, the risks of appropriate therapy and mortality. Those patients with low risk of appropriate therapy and high risk of mortality are unlikely to benefit from ICD implantation.[18–20] But these models are not straightforward to understand and use either. As a result, a simple algorithm for predicting death and heart transplantation (HT) before receiving appropriate shock is urgently needed prior to ICD implantation.

To fill this knowledge gap, we developed and internally validated a nomogram to predict the 1-, 3-, and 5-year risks of death and HT without former appropriate shock by competing risk regression.

Methods

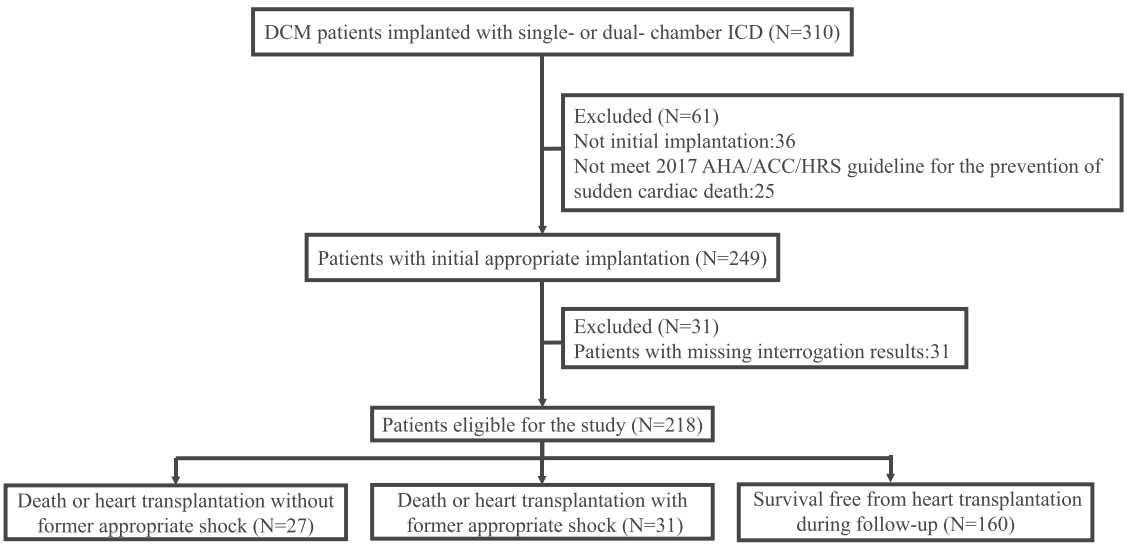
Study population

All patients who were diagnosed with DCM and received initial single- or dual-chamber ICD implantation from 1 January 2010 to 31 December 2019 at Fuwai Hospital were retrospectively enrolled (shown in *Figure 1*). DCM was defined as ventricular dilatation and systolic dysfunction in the absence of abnormal loading conditions and significant coronary artery stenosis.[1,2] Exclusion criteria include the following: patients did not meet the criteria of the 2017 AHA/ACC/HRS guideline for the prevention of SCD[8]; patients had prior ICD implantation; and patients did not have interrogation results. The study conformed to the 1975 Declaration of Helsinki and was approved by the local ethics committee, and informed consent was obtained from all participants.

Data collection and follow-up

Baseline demographic information, comorbidities, medications, implantation indication (primary vs. secondary prevention), laboratory tests, and echocardiography parameters

Figure 1 Patient flow diagram. DCM, dilated cardiomyopathy; ICD, implantable cardioverter-defibrillators.



including left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), and left ventricular ejection fraction (LVEF) were collected from electronic medical records. Patients were requested to receive routine device interrogation 6 months after implantation, then annually, and unplanned visits after ICD activation. Although the ICD programming strategy was set at the discretion of their treating physician, ICD shocks were delivered for ventricular fibrillation (VF) zone or ATP failing to terminate ventricular tachycardia (VT). Survival status was obtained by electronic medical records or phone contact with patients and their relatives.

Study endpoints

The primary composite endpoints included all-cause mortality and HT (whichever came first) without former appropriate shock. The appropriate ICD shock was chosen because it was associated with life-threatening ventricular arrhythmia events.

Statistical analysis

Categorical variables were summarized as frequencies (percentage); continuous variables were described as mean ± standard deviation or median [interquartile range (IQR), 25th to 75th percentile] as appropriate. Baseline characteristics were compared among the patients with or without all-cause mortality and HT using univariable Cox proportional hazards model. Then, a multivariable Cox regression model was developed using all variables with P-value < 0.2 from univariable analyses. This step was aimed at exploring clinical variables related to all-cause mortality and HT regardless of appropriate shocks, as the limited number of primary outcomes in our study. Subsequently, these variables along with implantation indication were used for the selection of variables related to death and HT without appropriate shock by Fine–Gray subdistribution hazard model accounting for the competing risk of appropriate shock. Finally, variables that were statistically significant in Fine–Gray model were used to build the nomogram to predict 1-, 3-, and 5-year probabilities of primary outcomes. Multivariable Cox regression was based on P-value (backward selection, $P > 0.2$ being removed and $P < 0.1$ being added), and Fine–Gray regression based on Akaike information criterion rule. N-terminal pro-brain natriuretic peptide (NT-proBNP) was dichotomized at the median (1024 pg/mL). The proportional hazard assumption and multicollinearity were tested for all covariates, and no violations were found.

The performance of this model was evaluated and internally validated by discrimination and calibration. Discrimination was measured by the receiver operating characteristic (ROC) curve (AUC) and Harrell's C-index, which equals the probability that a patient with the higher predicted survival is the one who indeed survives longer, thus higher value meaning better discrimination. To obtain the optimism-corrected C-index, bootstrapping with 1000 resamples was used. A calibration curve was plotted representing the agreement between observed outcomes and predictions, with the 45° diagonal line meaning perfect calibration. To assess its clinical usefulness, decision curve analysis (DCA) was used to identify the range of threshold probabilities in which this model was valuable. Finally, based on the scores derived from the nomogram, patients were divided into three increasing risk stratums from low (score from 0 to 4 on a scale of 10, n = 99), intermediate (5 to 6, n = 80), to high risk (7 to 10, n = 39). Cumulative incidence function for primary outcomes was calculated within each group and assessed by Fine–Gray test.

A two-sided P-value of 0.05 was regarded as statistically significant. Analyses were performed using Stata/IC 16.1 (StataCorp, Texas, USA) and package 'riskRegression', 'cmprsk', and 'rms' of R software 4.1.0 (R Core Team, Vienna, Austria).

Demographic and clinical characteristics of the patients

A total of 218 patients with a mean age of 55.3 ± 12.6 years were included. The mean LVEF was 33%. Patients were predominately male (80.7%), with secondary prevention indication (70.6%), and receiving angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB) (78.0%), beta-blockers (78.4%), spironolactone (80.3%), and loop diuretics (82.1%) treatment. Other characteristics were summarized in *Table 1*. During a median follow-up of 3.6 years (IQR, 3.0–7.1), 58 (26.6%) patients had died (n = 40) or undergone HT (n = 18), among which 27 (46.6%) had not received appropriate shock. Seventy-one (44.4%) of 160 patients who survived free from HT received appropriate shocks after a median follow-up of 1.6 years (IQR, 0.7–2.7). The 1-, 3-, and 5-year cumulative incidence of primary outcomes were 5.3% [95% confidence interval (CI) 2.9–9.9%], 16.6% (95% CI 11–25.0%), and 25.3% (95% CI 17.2–37.1%), respectively.

Prognostic variables selection

To identify the variables associated with death and HT before the first appropriate shock, we first explored variables related to death and HT. Univariable Cox analyses in *Table 1* revealed that implantation indication, New York Heart Association (NYHA) class, blood pressure (BP), LAD, LVEDD, LVEF, atrial fibrillation, hypertension, diabetes, prior stroke, NT-proBNP,

Table 1 Baseline characteristics

Characteristics	All patients (N = 218)	Survival free from heart transplantation (n = 160)	Death or heart transplantation (n = 58)	Hazard ratio (95% CI)	P-value
Age (years)	55.3 ± 12.6	55.1 ± 12.2	55.7 ± 13.7	1.01 (0.99–1.03)	0.601
Male sex	176 (80.7%)	128 (80.0%)	48 (82.8%)	1.17 (0.57–2.39)	0.662
Body mass index (kg/m^2)	25.2 ± 3.98	25.2 ± 3.89	25.3 ± 4.25	1.02 (0.95–1.08)	0.627
Current smoking	98 (45.0%)	70 (43.8%)	28 (48.3%)	1.18 (0.70–1.99)	0.525
Primary prevention	64 (29.4%)	44 (27.5%)	20 (34.5%)	1.57 (0.91–2.71)	**0.106**
Family history of DCM	8 (3.67%)	5 (3.12%)	3 (5.17%)	2.03 (0.63–6.51)	0.236
Dual-chamber ICD	66 (30.3%)	53 (33.1%)	13 (22.4%)	0.75 (0.40–1.39)	0.356
NYHA class					
I/II	101 (46.3%)	87 (54.4%)	14 (24.1%)	Ref.	Ref.
III/IV	117 (53.7%)	73 (45.6%)	44 (75.9%)	3.56 (1.91–6.64)	**<0.001**
Systolic BP (mmHg)	115 ± 14.8	117 ± 13.9	111 ± 16.6	0.97 (0.95–0.99)	**0.007**
Diastolic BP (mmHg)	73.0 ± 10.4	73.7 ± 10.0	71.2 ± 11.2	0.98 (0.96–1.00)	**0.096**
Echocardiogram					
LAD (mm)	44.9 ± 7.36	43.9 ± 7.05	47.6 ± 7.59	1.08 (1.05–1.12)	**<0.001**
LVEDD (mm)	67.2 ± 9.27	65.9 ± 8.88	70.8 ± 9.43	1.06 (1.03–1.09)	**<0.001**
LVEF (%)	33.2 ± 10.2	34.6 ± 9.78	29.6 ± 10.7	0.95 (0.92–0.98)	**<0.001**
Comorbidities					
AF/flutter	75 (34.4%)	49 (30.6%)	26 (44.8%)	1.74 (1.04–2.94)	**0.036**
Hypertension	77 (35.3%)	51 (31.9%)	26 (44.8%)	1.55 (0.92–2.60)	**0.102**
Diabetes	35 (16.1%)	22 (13.8%)	13 (22.4%)	1.80 (0.97–3.35)	**0.063**
Stroke	22 (10.1%)	11 (6.88%)	11 (19.0%)	2.20 (1.14–4.26)	**0.019**
Dyslipidaemia	66 (30.3%)	49 (30.6%)	17 (29.3%)	0.91 (0.51–1.60)	0.739
Laboratory tests					
NT-proBNP (pg/mL)	1024 (568–2267)	841 (483–1563)	2296 (1254–4346)	2.26 (1.71–2.99)[a]	**<0.001**
hs-CRP (mg/L)	1.97 (0.93–4.66)	1.81 (0.88–4.00)	2.44 (1.00–7.67)	1.07 (1.02–1.13)	**0.01**
Fasting glucose (mmol/L)	5.72 ± 1.67	5.67 ± 1.64	5.88 ± 1.73	1.03 (0.90–1.19)	0.644
HbA1c (%)	6.29 ± 1.00	6.24 ± 0.97	6.42 ± 1.07	1.16 (0.91–1.48)	0.222
Haemoglobin (g/L)	147 ± 17.0	148 ± 17.9	146 ± 14.1	1.00 (0.98–1.01)	0.616
Albumin (g/L)	42.1 ± 4.43	42.2 ± 4.23	42.0 ± 4.96	0.96 (0.90–1.02)	**0.146**
Creatinine (μmol/L)	95.6 ± 25.6	94.2 ± 25.2	99.6 ± 26.6	1.01 (1.00–1.02)	**0.061**
BUN (mmol/L)	7.89 ± 3.22	7.62 ± 3.01	8.64 ± 3.66	1.06 (0.99–1.13)	**0.072**
Sodium (mmol/L)	140 ± 2.82	140 ± 2.89	139 ± 2.53	0.93 (0.85–1.02)	**0.142**
HDL (mmol/L)	1.10 ± 0.32	1.12 ± 0.32	1.04 ± 0.30	0.49 (0.20–1.17)	**0.108**
LDL (mmol/L)	2.74 ± 0.92	2.67 ± 0.89	2.94 ± 0.97	1.22 (0.91–1.63)	**0.184**
Medications					
ACEI/ARB	170 (78.0%)	131 (81.9%)	39 (67.2%)	0.49 (0.28–0.85)	**0.012**
Beta-blockers	171 (78.4%)	127 (79.4%)	44 (75.9%)	1.04 (0.57–1.91)	0.902
Amiodarone	114 (52.3%)	89 (55.6%)	25 (43.1%)	0.60 (0.36–1.01)	**0.056**
Diuretics	179 (82.1%)	130 (81.2%)	49 (84.5%)	1.08 (0.53–2.21)	0.83
Spironolactone	175 (80.3%)	129 (80.6%)	46 (79.3%)	0.84 (0.44–1.59)	0.597
Digitalis	75 (34.4%)	51 (31.9%)	24 (41.4%)	1.25 (0.74–2.12)	0.406

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AF, atrial fibrillation; BP, blood pressure; BUN, blood urea nitrogen; CI, confidence interval; DCM, non-ischaemic dilated cardiomyopathy; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; ICD, implantable cardioverter-defibrillator; LAD, left atrial diameter; LDL, low-density lipoprotein; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association.

Values are presented as mean ± standard deviation, median (interquartile range), or frequency (%). All P-values < 0.2 were highlighted in bold type as we used this significant level for selecting variables.

[a]Hazard ratio was calculated by taking natural log transformation of variable.

high-sensitivity C-reactive protein, albumin, creatinine, blood urea nitrogen, sodium, low-density and high-density lipoprotein, ACEI/ARB, and amiodarone were potential predictors. Multivariable Cox analysis shown in *Table 2* found that NYHA III/IV functional class [hazard ratio (HR) 2.81; 95% CI 1.43–5.54], diastolic BP (HR 0.98; 95% CI 0.95–1.00), LVEDD (HR 1.04; 95% CI 1.01–1.07), prior stroke (HR 3.39; 95% CI 1.66–6.92), NT-proBNP above median (HR 2.76; 95% CI 1.43–5.31), ACEI/ARB (HR 0.54; 95% CI 0.29–0.99), and amiodarone (HR 0.54; 95% CI 0.30–0.95) were independent predictors of death and HT irrespective of appropriate shock. Then, these variables along with implantation indication were included in the Fine–Gray regression accounting for the competing risk of appropriate shock. The result shown in *Table 2* found that primary prevention [subdistribution hazard ratio (sdHR) 2.93; 95% CI 1.32–6.53], LVEDD (sdHR 1.04; 95% CI 1.01–1.08), NT-proBNP above the median (sdHR 2.93; 95% CI 1.19–7.17), ACEI/ARB (sdHR 0.37; 95% CI 0.17–0.83), and amiodarone (sdHR 0.39; 95% CI 0.16–0.92) were independent risk factors for death and HT without former appropriate shock.

Table 2 Multivariable Cox regression model analysis of all-cause mortality and heart transplantation and Fine–Gray model for composite endpoints of all-cause mortality and heart transplantation before appropriate shock

	Cox model for all-cause mortality and heart transplantation			Fine–Gray model for primary endpoints		
Predictors	HR	95% CI	*P*-value	sdHR	95% CI	*P*-value
Primary prevention	1.55	0.84–2.86	0.166	2.93	1.32–6.53	**0.008**
NYHA (III/IV vs. I/II)	2.81	1.43–5.54	**0.003**			
Diastolic BP (mmHg)	0.98	0.95–1.00	**0.038**			
LVEDD (mm)	1.04	1.01–1.07	**0.014**	1.04	1.01–1.08	**0.009**
Hypertension	1.67	0.97–2.89	0.066			
Stroke	3.39	1.66–6.92	**<0.001**			
NT-proBNP (above vs. below median)	2.76	1.43–5.31	**0.002**	2.93	1.19–7.17	**0.019**
LDL (mmol/L)	1.30	0.95–1.79	0.105			
ACEI/ARB	0.54	0.29–0.99	**0.046**	0.37	0.17–0.83	**0.015**
Amiodarone	0.54	0.30–0.95	**0.032**	0.39	0.16–0.92	**0.032**

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BP, blood pressure; CI, confidence interval; HR, hazard ratio; LDL, low-density lipoprotein; LVEDD, left ventricular end-diastolic diameter; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; sdHR, subdistribution hazard ratio.
All *P*-values < 0.05 were highlighted in bold type as we used this significant level for selecting variables.

Development and validation of the model

The five predictors (implantation indication, LVEDD, NT-proBNP, ACEI/ARB, and amiodarone) were incorporated into the competing risk nomogram (*Figure 2*). Based on the nomogram, the score of each patient can be calculated and used to estimate the 1-, 3-, and 5-year probabilities of primary outcomes. The AUC of the nomogram (*Figure 3*) of 1, 3, and 5 years were 0.83 (95% CI 0.73–0.94; $P < 0.001$), 0.84 (95% CI 0.75–0.93; $P < 0.001$), and 0.85 (95% CI 0.77–0.94; $P < 0.001$), respectively. The overall discrimination of the model was evaluated by Harrell's C-index of 0.788 (95% CI 0.697–0.877; $P < 0.001$), which demonstrated the good discriminative ability of the model. After internal validation, the optimism-corrected C-index was 0.762.

The calibration curves (*Figure 4*) for the competing risk nomogram of 1, 3, and 5 years were close to the 45° diagonal for the most part, but slightly went underneath the diagonal in high predicted risk (optimism-corrected slope 0.896). It indicated that the nomogram was well calibrated in most situation but might overestimate the risk when the risk was already high.

The DCA of the nomogram was shown in *Figure 5*. For predicting cumulative 1-, 3-, and 5-year probabilities of

Figure 2 Nomogram for predicting 1-, 3-, and 5-year probabilities of death and heart transplantation before appropriate shock. ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; LVEDD, left ventricular end-diastolic diameter; NT-proBNP, N-terminal pro-brain natriuretic peptide.

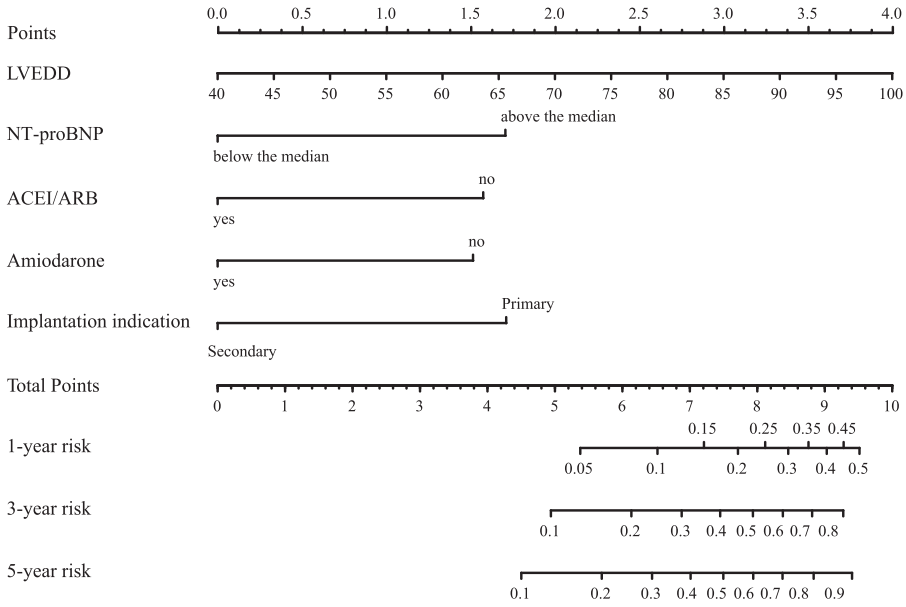


Figure 3 One-, 3-, and 5-year receiver operating characteristic curve of the model. AUC, the area under the receiver operating characteristic curve; CI, confidence interval.

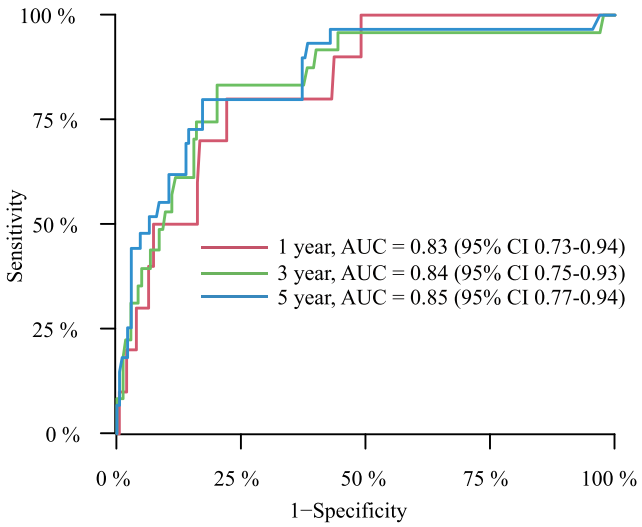
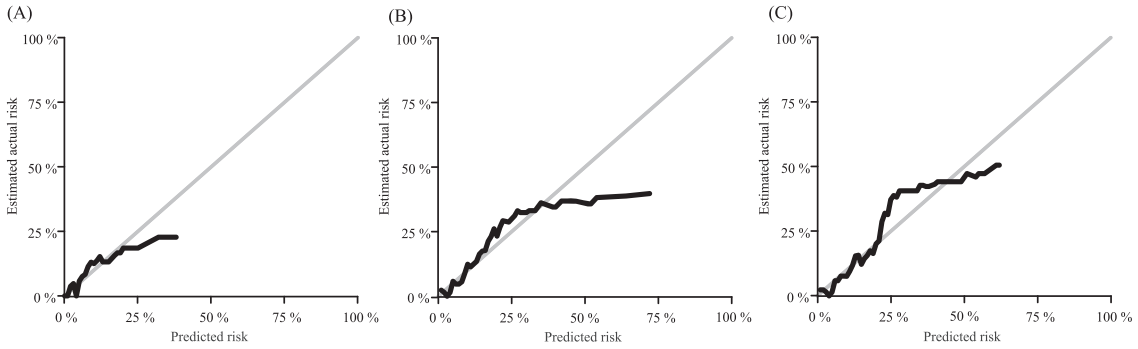


Figure 4 Calibration curves for the nomogram of (A) 1, (B) 3, and (C) 5 years in internal validation.



primary outcomes, when the threshold probabilities were within 0.01–0.31, 0.01–0.51, and 0.01–0.26, respectively, net benefit of the nomogram was higher than the situations when all or no patients were treated.

According to the overall distribution of scores, patients were categorized into low-risk, intermediate-risk, and high-risk groups. As shown in *Figure 6*, the high-risk group had the highest risk of death and HT without former appropriate shock, followed by the intermediate-risk and low-risk groups ($P < 0.001$). The high-risk group composed 17.9% of our population and did not derive long-term benefit from ICD.

Discussion

We developed and internally validated a new competing risk model for predicting death and HT without former appropriate shock in DCM patients with ICD. The model accurately distinguished approximately 18% of our patients who did not derive benefit from ICD implantation despite strictly following current guidelines. The model showed good overall calibration, except for slight overestimation of risk when actual risk was already high. Nevertheless, it is not troublesome in this condition, because high-risk patients indeed deserve further evaluation. In addition, the model illustrated great utility in clinical practice in DCA analysis by showing greater net benefit than not using the model in the entire range of threshold probability.

The evidence of primary and secondary prevention ICD in ischaemia cardiomyopathy has been well documented.[8] In contrast, clinical trials in DCM had mixed results.[5,7,21,22] The Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial showed a significant reduction in SCD and a trend towards reduced all-cause mortality in ICD group.[5] However, the recently published DANISH trial found

Figure 5 Decision curve analysis for the nomogram of (A) 1, (B) 3, and (C) 5 years in internal validation.

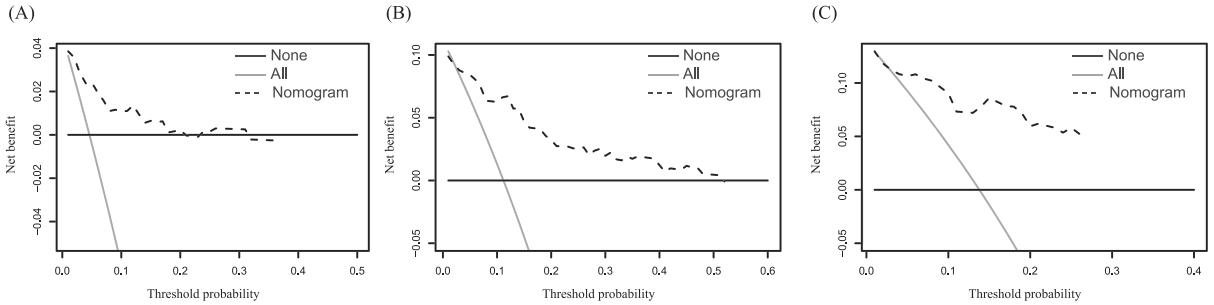
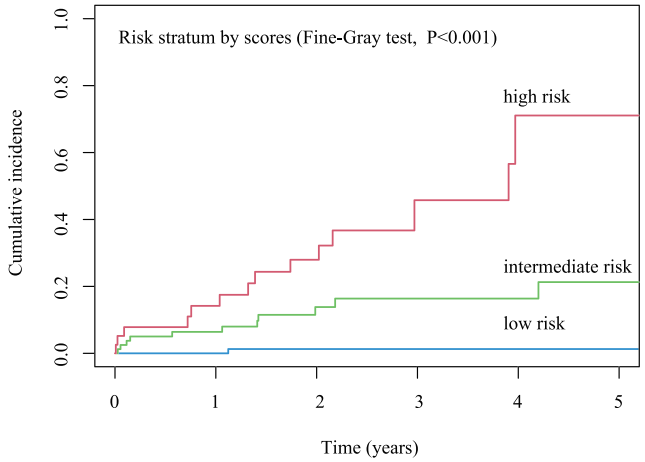


Figure 6 Cumulative incidence by risk stratum.



no reduction in overall mortality.[21] Therefore, the appropriateness of ICD in DCM patients for primary prevention has been broadly questioned.[17] On the other hand, approximately 10% of patients for secondary prevention died within 1 year since ICD implantation.[23,24] And in the long-term follow-up of 7 years, up to 28% of patients died without experiencing any appropriate ICD therapy.[25] Furthermore, the incidence of inappropriate shocks and surgery-related complications are not negligible.[9,12–16] Therefore, there is an urgent need to partition patients according to the likelihood of benefit.

Prior investigations of risk stratification for ICD recipients are either the risk of occurring ventricular arrhythmias (including VT, VF, and SCD)[26–29] or death.[6,30–32] Various methods including risk score algorithm based on multivariable regression,[28] landmark analysis,[27] and random forest[26] were applied to evaluate the risk of life-threatening ventricular arrhythmias, and all showed satisfactory performance. Among models predicting survival in heart failure, the Seattle Heart Failure Model (SHFM)[31] was widely recognized. The SHFM, first introduced in 2006 by Levy *et al.*,[31] can be used in both settings of ischaemic and non-ischaemic aetiology. Later on, the authors developed a modified SHFM (SHFM-D) to qualify the benefits from ICD.[33] They found that the risk of sudden death was inversely correlated with estimated annual mortality, and patients with a high estimated annual mortality (>19%) did not benefit from ICD therapy.[33] Subsequently, they developed the Seattle Proportional Risk Model (SPRM) to estimate the proportional risk of SCD versus non-sudden death, which showed the overall mortality benefit of ICD would be greater when a higher proportion of sudden death was predicted.[29]

Recent studies are dedicated to integrating these two dimensions of risk. Bilchick *et al.*[20] firstly found patients with SHFM-predicted annual mortality ≤ 5.7% and SPRM-predicted risk of sudden death below the median were unlikely to derive benefit from ICD. Then Kristensen *et al.*[34] also found patients with SHFM score above the median and SPRM score below the median had no ICD benefit from the DANISH trial. Other similar scores were also built, like the bimodal survival and implantable defibrillator shock risk model (BaSIS)[18] and the model developed by Bergau *et al.*[19] Among these

models, Koller *et al.*'s[35] was most similar to ours. They also used competing risk analysis to find predictors of death without prior appropriate ICD therapy. During a median follow-up of 3.6 years in their study, 11% of patients died without prior appropriate ICD therapy, and up to 23% of patients died without prior therapy for VF. Among age, LVEF, prevention indication, beta-blocker, ACEI/ARB, and diuretic use, diuretic use was the only predictor independently associated with the primary endpoint. However, DCM patients were severely underrepresented (less than one quarter, n = 105) in their study, thus precluding the identification of more potential predictors and subsequent prediction modelling. Moreover, pharmacological therapies have improved a lot since then.

In our study, factors that conferred an increased risk of death and HT without former appropriate shock included primary prevention, higher LVEDD, and NT-proBNP, not taking ACEI/ARB and amiodarone. Although the result was suited for predicting prognosis rather than addressing aetiologic inference for the nature of the subdistribution hazard function,[36] it showed similarities with other findings. As reported, primary prevention was independently associated with a reduced risk of shocks compared with secondary prevention,[12,19,35,37] but no difference in mortality was found.[35,37] It was also found that higher LVEDD and NT-proBNP were related to an increased risk of mortality,[19,26,32] and ACEI/ARB was related to a reduced risk of mortality,[18,20] but none of these was associated with disproportionately increased risk of sudden death.[38] Although our study showed amiodarone decreased the likelihood of death prior to shock, the mechanism was intriguing. A meta-analysis[39] demonstrated that amiodarone was related to reduced SCD and all-cause mortality for primary prevention, whereas related to increased SCD and all-cause mortality for secondary prevention. But the quality of evidence was low and very low, respectively. For this reason, the effect of amiodarone in our study should be interpreted with caution.

Strengths and limitations

The strength of this analysis includes the development of a visualization risk-scoring system. It is easier to interpret and use than other tools that have to manually integrate the information of survival and ICD therapy.[18–20,34] Additionally, instead of treating appropriate shock as non-informative censoring, the competing risk model could quantify prognosis more accurately than traditional survival analysis.

There are several limitations of our study. First, our study was conducted in a single centre with a small sample size. Therefore, external validation was impossible. Although internal validation by bootstrapping showed excellent internal validity, it might not be suitable to extrapolate to other populations. Second, the model showed minimal over-optimism in calibration. Indeed, it is challenging to build such a perfectly calibrated model because risk factors for death and HT are partially same regardless of experiencing appropriate shock or not. Nevertheless, patients who received appropriate shock first were treated as experiencing competing risk in the Fine–Gray model, which precluded the occurrence of death and HT before shock. This ultimately led to the overestimation of the risk of primary outcomes. Third, our nomogram did not reflect the dynamic change in medications that might happen in the long-term follow-up. However, most patients in our study already had optimal medication therapy before ICD implantation, and their medications would not be changed significantly. Most risk prediction models mentioned earlier, like the SHFM, SPRM, and BaSIS, did not include this kind of information either. Therefore, it is safe only to use the baseline medication in our model. At last, the extent to real-world benefit of our model will be hard to know because clinicians might be discouraged from using it due to existing guidelines.

Conclusions

All-cause mortality and HT before appropriate shock are approximately 5% annually in patients with DCM receiving ICD implantation. This competing risk nomogram based on five readily available clinical parameters is a hopeful tool to facilitate individualized prognostic assessment.

Conflict of interest

None declared.

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