



Clinical Outcome Predictions for the VICTORIA Trial

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On behalf of the VICTORIA Study Group



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Background

- Prediction of outcomes in patients with HF may inform prognosis, clinical decisions regarding treatment selection, and new trial planning
- VICTORIA included high-risk patients with HF and reduced EF and a recent worsening HF event (WHFE) despite contemporary therapies
 - Well-phenotyped with limited missing data
- To provide generalizable predictive data for a broad population with a recent WHFE, we focused on risk prognostication in the placebo group

Armstrong PW, *et al. NEJM* 2020



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Methods

- Data from 2524 participants randomized to placebo with chronic HF (NYHA II–IV) and EF <45% were studied
- Backward variable selection was used to create Cox proportional hazards models for clinical endpoints, selecting from 66 candidate predictors
 - Primary: CV death or HF Hosp. All-cause Mortality or HF Hosp; CVD
- Final model results were produced, accounting for missing data and non-linearities
- Optimism-corrected c-indices were calculated using 200 bootstrap samples



Results: Predictive Model for CV Death + HF Hosp

- During a median follow-up of 10.4 months, 972 (38.5%) patients with an event

Variable	Chi-Square	P-value	HR (95% CI)
NT-proBNP (per doubling of pg/mL)	73.36	<.001	1.25 (1.18–1.31)
Chloride (per 5 mmol/L increase)	42.40	<.001	0.79 (0.74–0.85)
NYHA class III/IV (ref: Class I/II)	25.55	<.001	1.39 (1.23–1.59)
Albumin (per 1 g/dL increase)	14.04	<.001	0.74 (0.64–0.87)
History of MI	17.55	<.001	1.31 (1.16–1.49)
Urate (per 1 mg/dL increase)	14.92	<.001	1.05 (1.03–1.08)
Bilirubin (per 0.5 mg/dL increase)	14.41	<.001	1.10 (1.05–1.15)
Time from first HF diagnosis to randomization (per doubling of years)	19.20	<.001	1.08 (1.04–1.12)
Index event (ref: HF hospitalization within 3 months)			
HF hospitalization 3-6 months	4.47	0.035	0.83 (0.69–0.99)
IV diuretic for HF (without hospitalization) within 3 months	9.81	0.002	0.73 (0.60–0.89)

Optimism-corrected C-Index = 0.68

Results: Summary of Endpoint Models



Endpoint	Trial Details	HF Details	PMH	Exam/ECG	Devices	Labs	C-Index
CV Death or HF hospitalization		HF duration NYHA class Index HF event	MI			NT-proBNP Chloride Bilirubin Albumin Urate	0.68
All-cause mortality or HF hospitalization		HF duration NYHA class Index HF event	MI	Pulse	ICD	NT-proBNP Chloride Bilirubin Albumin Urate eGFR	0.68
CV Death	Enrolling Region	HF duration NYHA class Index HF event	MI	Sys BP QTc		NT-proBNP Chloride Bilirubin Albumin Urate	0.72

BOLD indicates presence in all models; **Red**, not included in model; **Green**, added to model.



Summary/Conclusions



- NTproBNP remains a powerful predictor of outcomes
 - Accounts for the majority of discrimination
- Different outcomes have a different pattern of risk-predictive clinical characteristics
- Novel or overlooked risk predictors including clinical and laboratory values
- Discrimination of VICTORIA models (c-indices from 0.68-0.72) is similar to earlier models but extends to the high-risk population of HFrEF with recent WHFE

Data are now published online in the *Journal of Cardiac Failure*



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