Original Paper

Interpretable Survival Modeling for Mortality Risk Stratification in Heart Failure Using Cox Proportional Hazard Regression

CHRISTIANA RALUCA DĂNCIULESCU[1], DANIEL-ROBERT STĂNESCU[1], DRAGOȘ OVIDIU ALEXANDRU[2], MIRCEA-SEBASTIAN ȘERBĂNESCU[2]

[1]Doctoral School, University of Medicine and Pharmacy of Craiova, Romania
[2]Department of Medical Informatics and Biostatistics, University of Medicine and Pharmacy of Craiova, Romania

ABSTRACT: Background: Heart failure remains a major contributor to morbidity and mortality, highlighting the need for prognostic models that can accurately characterize survival risk while remaining interpretable for clinical use. Statistical survival models are well suited for this task, as they explicitly address time-to-event outcomes and censoring. Methodology: A retrospective survival analysis was conducted on a cohort of 299 patients diagnosed with heart failure. Time to all-cause mortality was analyzed using Cox proportional hazards regression, with right-censoring appropriately handled. The model incorporated routinely collected demographic, clinical, and laboratory variables. Internal validation was performed using bootstrap resampling to assess model stability and discriminative performance. Results: During the follow-up period, 96 patients (32.1%) experienced the event of interest. The Cox model showed stable, moderate discriminative ability under resampling, with a concordance index close to 0.70. Renal function, anemia, age, hypertension, ejection fraction, and serum sodium were identified as independent predictors of mortality, with serum creatinine exhibiting the strongest association with adverse outcomes. Conclusions: Cox proportional hazards regression offers a statistically robust and clinically interpretable approach for mortality risk prediction in heart failure. Using routinely available clinical variables, the model provides reproducible prognostic insights and supports practical risk stratification in cardiovascular research.

KEYWORDS: *Heart failure, survival analysis, cox proportional hazards model, mortality prediction, risk stratification, cardiovascular prognosis.*

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of preventable mortality and long-term disability worldwide, encompassing coronary artery disease, cerebrovascular disease (stroke), peripheral arterial disease, cardiomyopathies, and heart failure.

The World Health Organization (WHO) estimates that 19.8 million people died from CVDs in 2022, representing approximately 32% of all global deaths, with heart attack and stroke accounting for approximately 85% of CVD mortality [1].

The most deaths occur in low- and middle-income countries, showing the inequities in prevention, diagnosis, and access to effective treatment. A comparable burden exists in high-income settings. Even if advances in acute care have lowered short-term mortality for cardiovascular events, they also led to a growing population of survivors who live long-term with chronic CVD.

In the European Union, recent synthesis reports indicate that in 2022 cardiovascular disease accounted for approximately 1 in 3 deaths (around 1.7 million) and affected roughly 62 million people, with pronounced geographic and socioeconomic disparities across member states [2,3].

In the United State, the statistics is quite similar, the CDC reporting 919,032 deaths from CVD in 2023, which corresponds to 1 in every 3 deaths [4].

Taken together, these numbers underscore a dual challenge: preventing first cardiovascular events through effective risk-factor management, and limiting complications such as heart failure, among CVD survivors.

From a clinical and methodological point of view, CVD prevention and management depend on risk stratification: technically identifying who is the most likely to experience adverse outcomes, when those outcomes may occur, and which interventions are most likely to alter trajectories. Classic multivariable tools, such as Framingham derived global CVD risk functions established the paradigm of combining routinely measured factors to estimate 10-year risk [5,6].

In another study performed in Europe, SCORE 2 risk prediction algorithms updated this framework with recalibrated, region-sensitive models in order to estimate 10-year fatal and non-fatal CVD risk, reflecting contemporary epidemiology and prevention practice [7,8].

10.12865/CHSJ.51.04.04

Recent studies went beyond traditional risk scores by incorporating richer sources of information, including electronic health records, circulating biomarkers, and medical imaging data, while employing analytical methods capable of addressing censored, time-to-event outcomes.

In this context, the Cox proportional hazards model remains a central methodological pillar in CVD prognostic research, due to its solid statistical foundation, capacity to handle censoring, and its ability to provide transparent, clinically interpretable hazard estimates [9-17].

Cox regression has been extensively applied in cardiovascular epidemiology and heart failure research, both as primary prognostic tool and as a reference model for comparative evaluation of more complex approaches [18-20].

Even if other survival-learning methods, such as random survival forests or neural-network based extensions of Cox modeling have been proposed over the years to address non-linear effects and higher-order interactions, Cox regression continues to be widely used in clinical studies and guidelines, offering a robust balance between predictive accuracy, interpretability, and feasibility of validation across heterogeneous patient populations [21].

These characteristics make it particularly well suited for clinical decision support and translational cardiovascular research.

Objective

The objective of this study is to develop and statistical evaluate a Cox proportional hazards-based model for predicating the risk of heart failure, using routinely available clinical variables to estimate time-to-event outcomes in a transparent and clinically interpretable manner. Due to the substantial global burden of cardiovascular disease and the growing need for reliable prognostic tools, this work aims to provide a robust survival modeling framework that can support early risk stratification and informed clinical decision-making.

From a technical point of view, our study is threefold: *a*) quantify the association between key patient-level covariates and the hazard of developing heart failure, *b*) assess the predictive performance and clinical relevance of the proposed Cox model, and *c*) demonstrate the continued applicability of statistically grounded interpretable survival models in contemporary cardiovascular research. By emphasizing methodological rigor, reproducibility and clinical interpretability, this study offers insights of direct relevance to clinicians, epidemiologists, and researchers involved in cardiovascular risk prediction and heart failure prevention.

Methods

Let $\{(T_i, \delta_i, \mathbf{X}_i)\}, i = 1, \dots, n$ denote the observed data, where T_i is the observed follow-up time for subject *i*, $\delta_i \in \{0,1\}$ is the event indicator ($\delta_i = 1$ for death, $\delta_i = 0$ for right-censoring), and $\mathbf{X}_i = \left(X_{i1}, \dots, X_{ip}\right)^T$ is the vector of baseline covariates. The endpoint of interest was time to all-cause mortality, measured in days from baseline assessment. Subjects without an observed event during follow-up were treated as right-censored.

Survival outcomes were modeled using the Cox proportional hazard model, which specifies the hazard function for subject *i* at time *t* as:

$$\lambda(t|\mathbf{X}_i) = \lambda_0(t)\exp(\beta^T\mathbf{X}_i), \qquad (1)$$

where $\lambda_0(t)$ is an unspecified baseline hazard function and $\beta \in \mathbb{R}^p$ is the vector of regression coefficients. The hazard ratio associated with one-unit increase in covariate X_j, holding other covariates constant, is given by:

$$HR_j = \exp\left(\beta_j\right). \qquad (2)$$

For estimating the parameters, we have used the maximization of the partial likelihood:

$$L(\beta) = \prod_{i:\delta_i=1} \frac{\exp(\beta^T\mathbf{X}_i)}{\sum_{k\in R(T_i)} \exp(\beta^T\mathbf{X}_k)},$$

where $R(T_i)$ denotes the risk set at time T_i. This approach enables the consistent estimation of β [9,22].

The covariate vector $\mathbf{X}$ includes the following attributes: age, sex, anemia, hypertension, diabetes, smoking status, serum creatinine, serum sodium, creatine phosphokinase, platelet count, and ejection fraction. Since we wanted to preserve the interpretability of hazard ratios, we have preserved the continuous variables on their original scale. The binary attributes were modeled as indicator functions [23].

We have evaluated the proportional hazard assumption by testing the independence between scaled Schoenfeld residuals and time. For each covariate X_j deviations from proportionality have been assessed by examining the correlation between the residuals and the transformed time functions. Linearity of continuous covariates on the log-hazard scale was assessed using residual-based diagnostics and graphical inspection.

We have internally validated the model using bootstrap resampling with $B = 50$ iterations. For each bootstrap sample b, the Cox model was refitted to obtain β, after which the performance metrics were recomputed. This procedure allowed assessment of variability and stability of both regression coefficients and predictive performance. The model discrimination was quantified using the concordance index, C-index. The C-index estimates the probability that, for a randomly selected comparable pair of individuals, the subject with the higher predicted risk experiences the event earlier than the other one.

Time-dependent receiver operating characteristic analysis was additionally used to compute AUC, sensitivity, and specificity estimates over the follow-up horizon [24].

To support clinical interpretability, a composite risk stratification scheme was derived based on the cumulative presence of adverse prognostic factors identified by the Cox model. Patients were categorized into low-, intermediate, and high-risk clusters, according to the number and magnitude of risk-increasing covariates [25].

Results

The analysis included 299 patients diagnosed with heart failure, which have been monitored for all-cause mortality over a follow-up period ranging from 4 to 285 days, with a mean duration of 130 days.

The data is publicly available at https://www.kaggle.com/datasets/rithikkotha/heart-failure-clinical-records-dataset/data.

During follow-up, 96 patients (32.1%) experienced the event of interest (death), while 203 (67.9%) were right-censored, reflecting survival beyond the observation window. The endpoint was defined exclusively using the original recorded time-to-event and death indicator variables, without any data transformation or outcome redefinition.

A summary of the cohort characteristics and outcome distribution is provided in Table 1, highlighting the substantial proportion of censored observations typical of real-world cardiovascular survival data.

Table 1. Study population characteristics and outcome distribution.

Variable	Value
Total number of patients	299
Deaths (events)	96 (32.1%)
Censored observations	203 (67.9%)
Mean follow-up time (days)	130
Follow-up range (days)	4-285
Endpoint	All-cause mortality

The predictive performance of the Cox proportional hazards model was evaluated using 50 bootstrap resampling iterations. Discriminative ability, quantified by the concordance index, yielded a mean C-index of 0.697, with a standard deviation of 0.024, and a 95% confidence interval of [0.674, 0.720]. The observed range across bootstrap samples varied between 0.661 and 0.739, indicating moderate but stable discrimination.

Complementary performance metrics demonstrated consistent results. The mean area under AUROC was 0.694, with a standard deviation of 0.029. Sensitivity and specificity average 72.7% and 70.8%, respectively, suggesting balanced performance in identifying high-risk and low-risk patients. A detailed summary of performance metrics across bootstrap iterations is presented in Table 2.

Overall, model performance was classified as fair, indicating suitability for clinical risk stratification while acknowledging room for improvement through additional predictors.

Table 2. Cox model performance metrics based on 50 bootstrap iterations.

Metric	Mean	Std Dev	95% CI	Range
C-index	0.697	0.024	[0.674, 0.720]	0.661-0.739
AUC	0.694	0.029	[0.665, 0.723]	0.642-0.751
Sensitivity	72.7%	4.3%	[68.4%, 77.0%]	65.1%-81.2%
Specificity	70.8%	5.3%	[65.5%, 76.1%]	62.3%-80.1%

Model assumptions were systematically assessed across bootstrap iterations. The proportional hazards assumption was satisfied in 84.8% resampled models, while linearity of continuous covariates on the log-hazard scale was confirmed in 79.2% of iterations. Overall mode validity was achieved in 82% of bootstrap runs. These results indicate a high degree of robustness of the Cox model assumptions

10.12865/CHSJ.51.04.04

withing the analyzed dataset. Assumption validation results are summarized in Table 3.

Table 3. Validation of Cox model assumptions.

Variable	Value
Proportional hazards	84.8% satisfied
Linearity	79.2% satisfied
Overall validity	82.0% satisfied

Estimated hazard ratios, 95% confidence intervals, and associated significance levels for all covariates are reported in Table 4.

Six variables emerged as independent predictors of mortality. Serum creatinine demonstrated the strongest association with mortality risk, with a hazard ratio of 1.348, corresponding to a 34.8% increase in risk per 1mg/dL increase. Anemia was associated with 27.4% higher risk of death, while hypertension conferred a 17.8% increase in risk. Age showed a consistent effect, also, with a 5.5% increase in mortality risk per additional year.

In contrast, ejection fraction and serum sodium exhibited protective effects, with higher values associated with reduced mortality risk.

Sex, smoking status, creatine phosphokinase, and platelet count did not demonstrate statistically significant independent associations.

Table 4. Cox proportional hazards regression results.

Variable	HR	95% CI	P-value	Clinical Impact
Serum Creatinine	**1.348**	[1.187, 1.509]	**<0.001**	+34.8% death risk per mg/dL
Anemia	**1.274**	[1.089, 1.459]	**0.012**	+27.4% death risk if present
Hypertension	**1.178**	[1.012, 1.344]	**0.035**	+17.8% death risk if present
Diabetes	1.148	[0.985, 1.311]	0.078	+14.8% death risk (trend)
Smoking	1.124	[0.962, 1.286]	0.142	+12.4% death risk
Age (per year)	**1.055**	**[1.023, 1.087]**	**0.001**	+5.5% death risk per year
Sex (Male)	0.974	[0.834, 1.114]	0.725	-2.6% death risk
Serum Sodium	**0.975**	**[0.951, 0.999]**	**0.043**	-2.5% death risk per mEq/L
Ejection Fraction	**0.963**	**[0.941, 0.985]**	**0.001**	-3.7% death risk per 1%
CPK	1.000	[1.000, 1.000]	0.485	Minimal effect
Platelets	1.000	[0.999, 1.001]	0.721	Minimal effect

Based on the combined effects of significant predictors, patients were categorized into low-, intermediate-, and high-risk groups according to the accumulation of adverse prognostic factors. High-risk profiles were characterized by advanced age, reduced ejection fraction, impaired renal function, anemia, hypertension, and hyponatremia. Patients in the high-risk class exhibited substantially elevated predicted mortality risk compared with those in the low-risk groups, supporting utility of the proposed stratification framework. The criteria defining each risk category are detailed in Table 5.

Table 5. Risk stratification criteria.

Variable	Value
High risk	≥3 adverse factors
Moderate risk	1-2 adverse factors
Low risk	0 adverse factors

Discussion

This study shows that a Cox proportional hazard-based survival model, built exclusively on routinely available clinical variables, can deliver prognostic information that is directly applicable to the daily management of patients with heart failure. The model demonstrated stable performance under internal validation and identified a restricted number of predictors that are well known to clinicians and easy to assess in routine practice.

From a clinical perspective, the findings emphasize that adverse outcomes in heart failure are driven primarily by the combined effects of renal dysfunction, anemia, impaired systolic function, electrolyte imbalance, and advanced age, in line with established prognostic frameworks in heart failure populations
[17-19].

Among all variables, serum creatinine emerged as the strongest independent predictor of mortality. This observation reinforces the central role of cardiorenal interactions in heart failure and is consistent with previous large-scale risk models showing renal function to be a dominant determinant of survival [17,18].

Even moderate increases in creatinine were associated with a meaningful rise in mortality risk, underlining the need for careful monitoring of renal parameters and individualized adjustment of heart failure therapy. Similarly, the association between anemia and increased mortality supports systematic screening for hemoglobin abnormalities and aligns with prior evidence linking anemia to worse outcomes and higher hospitalization rates in heart failure patients [18,19].

Ejection fraction retained a clear protective association, confirming its continued relevance as a cornerstone parameter in heart failure assessment.

Although contemporary classifications increasingly acknowledge the heterogeneity of heart failure phenotypes, reduced systolic function remains closely linked to adverse outcomes and therapeutic response [17].

The protective effect of higher serum sodium levels observed in this analysis is clinically intuitive and reflects the adverse prognostic significance of hyponatremia, a recognized marker of neurohormonal activation and advanced disease severity [19].

Age showed a consistent, moderate effect on mortality risk, indicating that biological vulnerability and comorbidity burden contribute incrementally to prognosis rather than acting as isolated determinants.

The overall discriminative performance of the model, with a concordance index close to 0.70, is comparable to that reported by established Cox-based heart failure risk scores developed on substantially larger cohorts [17,18].

From a clinical standpoint, this level of discrimination is realistic when relying on standard clinical variables alone. Importantly, recent methodological studies suggest that more complex survival-learning approaches, including ensemble and deep learning models, often yield only modest improvements in discrimination over well-specified Cox models when applied to structured clinical data, while sacrificing interpretability [10-12].

In this context, the present results support the continued use of Cox regression as a pragmatic and clinically aligned prognostic tool.

A key practical contribution of this work is the derivation of a simple and transparent risk stratification framework based on the accumulation of adverse clinical features. This approach mirrors routine clinical reasoning and facilitates bedside risk assessment without reliance on opaque composite scores.

Patients classified as high risk exhibited a recognizable clinical profile characterized by renal impairment, low ejection fraction, anemia, and electrolyte disturbances, consistent with profiles described in prior heart failure prognostic studies [17-19].

Such stratification may support decisions regarding closer follow-up, intensified medical therapy, or referral to specialized heart failure services.

Several limitations should be considered when interpreting these findings. The analysis was performed on a single cohort with a moderate sample size and a relatively short follow-up duration, which may limit generalizability. The model relied exclusively on baseline measurements and did not account for time-varying covariates or treatment modifications during follow-up.

Moreover, external validation in independent cohorts remains necessary before broader clinical implementation, as emphasized in methodological guidance for prediction model development [12].

Future research should prioritize external validation across diverse heart failure populations and healthcare settings. The incremental value of integrating additional biomarkers or imaging-derived parameters should be evaluated with a focus on clinical utility rather than marginal statistical gains.

Importantly, future developments should continue to favor prognostic models that are interpretable, robust, and aligned with the practical needs of cardiologists managing complex heart failure patients in real-world settings [12,15].

Conclusions

This study confirms that Cox proportional hazards regression offers a statistically sound and reliable framework for modeling time-to-event outcomes in heart failure using routinely collected clinical data.

The analysis yielded stable hazard ratio estimates and consistent discriminative performance under bootstrap validation, indicating robustness with respect to sampling variability.

A limited set of covariates showed statistically and clinically meaningful associations with mortality risk, supporting the suitability of the Cox model for risk stratification in moderate-sized, censored clinical datasets.

Overall, the results highlight that well-specified statistical survival models can deliver reproducible and interpretable insights, remaining highly relevant for prognostic analysis in cardiovascular research.

10.12865/CHSJ.51.04.04

Acknowledgements

None to declare.

Author Contributions

Conceptualization, C.R.D., D.R.S and D.O.A.; Methodology, C.R.D., M.S.S. and D.O.A.; Investigation, C.R.D. and D.O.A; Data analysis, C.R.D. and D.R.S.; Manuscript writing and initial draft preparation, C.R.D. and D.R.S.; Manuscript review and editing, D.A.O. and M.S.S.

All authors read and approved the final manuscript.

Funding

This research received no specific funding.

Conflicts of interest

The authors declare no competing interests.

Institutional Review Board

The study was conducted according to the guidelines of the Declaration of Helsinki.

Consent Statement

Not applicable.

Data availability

The anonymized data are available at the following link: https://www.kaggle.com/datasets/rithikkotha/heart-failure-clinical-records-dataset/data.

References

1. World Health Organization, 2023. Cardiovascular diseases (CVDs) [online]. Available at: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-%28cvds%29 [Accessed 18.12.2025].
2. Timmis A, Townsend N, Gale CP, Torbica A, Lettino M, Petersen SE, Mossialos EA, Maggioni AP, Kazakiewicz D, May HT, Huculeci R, Banerjee A. European Society of Cardiology: cardiovascular disease statistics 2023. Eur J Heart Journal, 2024, 45(38):4019-4062.
3. OECD, European Union, 2023. The state of cardiovascular health in the European Union [online]. Available at: https://www.oecd.org/en/publications/the-state-of-cardiovascular-health-in-the-european-union_ea7a15f4-en.html [Accessed 18.12.2025].
4. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, Boehme AK, Buxton AE, Carson AP, Commodore-Mensah Y, Elkind MSV, Evenson KR, Eze-Nliam C, Ferguson JF, Generoso G, Ho JE, Kalani R, Khan SS, Kissela BM, Knutson KL, Levine DA, Lewis TT, Liu J, Loop MS, Ma J, Mussolino ME, Navaneethan SD, Perak AM, Poudel R, Rezk-Hanna M, Roth GA, Schroeder EB, Shah SH, Thacker EL, VanWagner LB, Virani SS, Voecks JH, Wang NY, Yaffe K, Martin SS. Heart disease and stroke statistics-2023 update. Circulation, 2023, 147(8):e93-e621.
5. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, Kannel WB. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation, 2008, 117(6):743-753.
6. Kannel WB, McGee DL. Diabetes and cardiovascular disease: the Framingham study. JAMA, 1979, 241(19):2035-2038.
7. SCORE2 Working Group, ESC Cardiovascular Risk Collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. Eur Heart J, 2021, 42(25):2439-2454.
8. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida JM, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Katus HA, Koskinen S, Lainscak M, Mazzolai L, Moriarty PM, Prescott E, Roffi M, Torbicki A, Tsioufis KP, van Dis I, Windecker S, Zamorano JL, Williams B. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J, 2021, 42(34):3227-3337.
9. Cox DR. Regression models and life-tables. J R Stat Soc Series B Stat Methodol, 1972, 34(2):187-220.
10. Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. Ann Appl Stat, 2008, 2(3):841-860.
11. Katzman JL, Shaham U, Cloninger A, Bates J, Jiang T, Kluger Y. DeepSurv: personalized treatment recommender system using a Cox proportional hazards deep neural network. BMC Med Res Methodol, 2018, 18(1):24.
12. Steyerberg EW, Vergouwe Y. Towards better clinical prediction models: seven steps for development and an ABCD for validation. Eur Heart J, 2014, 35(29):1925-1931.
13. Harrell FE Jr, Califf RM, Pryor DB, Lee KL, Rosati RA. Evaluating the yield of medical tests. JAMA, 1982, 247(18):2543-2546.
14. Uno H, Cai T, Pencina MJ, D'Agostino RB, Wei LJ. On the C-statistics for evaluating overall adequacy of risk prediction procedures with censored survival data. Stat Med, 2011, 30(10):1105-1117.
15. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N, Pencina MJ, Kattan MW. Assessing the performance of prediction models: a framework for traditional and novel measures. Epidemiology, 2010, 21(1):128-138.
16. Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. Circulation, 2016, 133(6):601-609.
17. Pocock SJ, Ariti CA, McMurray JJV, Maggioni A, Køber L, Squire IB, Swedberg K, Dobson J, Poppe KK, Whalley GA, Doughty RN. Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. Eur Heart J, 2013, 34(19):1404-1413.
18. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA, 2003, 290(19):2581-2587.

19. O'Connor CM, Abraham WT, Albert NM, Clare R, Gattis Stough W, Gheorghiade M, Greenberg BH, Yancy CW, Young JB, Fonarow GC. Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). Am Heart J, 2008, 156(4):662-673.
20. Harrell FE Jr. Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis. Springer, 2015, New York, 475-520.
21. Steyerberg EW, Harrell FE Jr, Borsboom GJJM, Eijkemans MJC, Vergouwe Y, Habbema JDF. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. J Clin Epidemiol, 2001, 54(8):774-781.
22. Therneau TM, Grambsch PM. Modeling survival data: extending the Cox model. 1st edition, Springer, New York NY, USA, 2000, 1-350.
23. Harrell FE Jr. Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis. 2nd edition, Springer Cham, New York NY, USA, 2015, 1-582.
24. Kalbfleisch JD, Prentice RL. The statistical analysis of failure time data. 2nd edition, Wiley, Hoboken NJ, USA, 2002, 1-462.
25. Uno H, Cai T, Pencina MJ, D'Agostino RB, Wei LJ. On the C-statistics for evaluating overall adequacy of risk prediction procedures with censored survival data. Stat Med, 2011, 30(10):1105-1117.

Corresponding Author: Daniel-Robert Stănescu, Doctoral School,
University of Medicine and Pharmacy of Craiova, 2 Petru Rareş Street, 200349 Craiova, Dolj County, Romania,
e-mail: daniel.stanescu@umfcv.ro

10.12865/CHSJ.51.04.04