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RESEARCH ARTICLE

AI-ASSISTED SURVIVAL PREDICTION IN COLORECTAL CANCER: A CLINICAL DECISION SUPPORT TOOL

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ABSTRACT

Purpose: This study was planned to determine the problems and affecting factors that children encounter Purpose: Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide. Accurate survival prediction is crucial for advanced-stage patients to optimize treatment strategies and improve clinical outcomes. This study aimed to develop an artificial intelligence-assisted clinical decision support system (CDSS) for survival prediction in CRC patients using clinical and genomic data from the Cancer Genome Atlas Colon Adenocarcinoma Collection (TCGA-COAD) dataset.
Methods: Machine learning algorithms, including C4.5 Decision Tree, Support Vector Machines (SVM), Random Forest, and Naive Bayes, were employed to create survival prediction models. Clinical parameters and genomic data from key pathways, such as glycolysis/gluconeogenesis and mTORC1, were integrated into the models. The models were evaluated based on accuracy and performance.
Results: The Random Forest algorithm achieved the highest accuracy (82.3%) when only clinical parameters were used. When clinical data were combined with gene expression data, the model's accuracy increased further. The resulting models were incorporated into a user-friendly web interface, SurvCOCA, for clinical use.
Conclusions: This study demonstrates the potential of AI-based tools to improve prognosis predictions in CRC patients. Further research is needed, with larger datasets and additional machine learning algorithms, to enhance clinical decision-making and optimize treatment strategies.

Key words: Colorectal cancer, survival prediction**,** artificial intelligence, **c**linical decision support system, machine learning

INTRODUCTION

Colorectal cancer (CRC) is one of the most common types of cancer worldwide in both men and women and ranks third in cancer-related mortality (1). The multifactorial nature of CRC indicates that genetic, environmental, and lifestyle factors play roles in the development of the disease (2). Early diagnosis and

treatment of CRC are critical for improving survival rates. However, the effectiveness of standard treatment approaches, such as surgical interventions, chemotherapy, and radiotherapy, largely depends on the stage of the disease and the biological characteristics of the tumor (3).

In cancer treatment, survival predictions have emerged as an important component in clinical decision-making processes. However, the accuracy of these predictions is often limited by traditional methods based on available clinical data. At this point, advances in genetics and molecular biology offer a powerful tool for more accurately predicting patient survival times. Specifically, technologies such as gene expression profiling allow for the identification of molecular subtypes of tumors and provide insights into how these subtypes affect survival (4, 5).

In recent years, the use of artificial intelligence (AI) and machine learning (ML) technologies in healthcare has increased, offering significant opportunities for integrating large datasets into clinical decision-making processes. ML algorithms can combine various clinical and genomic data to predict disease prognoses more accurately and personalized (6). In this context, integrating clinical and genomic data to improve survival predictions in heterogeneous tumors like CRC can contribute to identifying more suitable treatment options for patients (7).

The aim of this study is to develop a clinical decision support system (CDSS) that can predict survival outcomes in CRC patients using clinical and genomic data from the Cancer Genome Atlas Colon Adenocarcinoma Collection (TCGA-COAD) dataset (8). Survival prediction models were created using machine learning algorithms such as C4.5 Decision Tree, Support Vector Machines (SVM), Random Forest, and Naive Bayes, and the accuracy of these models was evaluated. Additionally, these models were integrated into a user-friendly web interface called SurvCOCA, making it a tool that can be used in clinical applications. The developed CDSS aims to provide accurate and reliable results for predicting survival in colon cancer, thereby contributing to clinical decision-making processes.

METHODS

Data Source and Study Material

This study, conducted as a master's thesis, was approved by the Non-Interventional Research Ethics Committee of Dokuz Eylul University (Date: 23.11.2020, Number: 2020/28-29). For this study, clinical and genomic gene expression data of colorectal cancer (CRC) patients were obtained from the Cancer Genome Atlas Colon Adenocarcinoma Collection (TCGA-COAD) project (8), accessed through the Genomic Data Commons (GDC) Data Portal (9). The clinical data included variables such as gender, race, tumor stage, T stage, N stage, M stage, previous cancer diagnosis, tissue or organ origin, body mass index (BMI), and primary diagnosis. Genomic data focused on pathways like glycolysis/gluconeogenesis, glycan degradation, pantothenate and CoA biosynthesis, apoptosis, mTORC1 signaling pathways, and the genes active in these pathways (ADH1C, AKR1A1, BCAT1, CAPN2, CASP2, MAN2B2, PFKM, TCEA1, TOMM40).

Data Collection and Processing

Data from the TCGA-COAD project was downloaded and analyzed using the TCGAbiolinks package in the R programming language (10-12). TCGAbiolinks is an R/Bioconductor package used for querying, downloading, and analyzing cancer data stored in GDC (11,13).

The following steps were applied to the downloaded data:

1. Normalization and Filtration: The data were cleaned to remove noise. Gene expression data were normalized by selecting the primary solid tumor subtype, and samples containing multiple data points were filtered out.
2. Right and Left Colon Information: To show the gene expression changes between right and left colon patients, gene expression analysis was performed, fold change was calculated, and p-values were adjusted using the False Discovery Rate (FDR) method.

Statistical Analyses

The statistical analysis of clinical data was performed using SPSS 24.0 (SPSS Inc., Armonk, NY, USA) (14). The following tests were applied: Mann-Whitney U test for comparing two independent groups, Kruskal-Wallis test for comparing two or more groups, Fisher's exact test for comparing categorical data.

The effects of factors on survival were evaluated using Kaplan-Meier and Log Rank (Mantel-Cox) tests. Parameters that were significant in the univariate analysis were further evaluated with

multivariate Cox Regression Analysis. A significance level of $p < 0.05$ was accepted.

Gene Enrichment Analysis

Gene enrichment analysis was performed for genes that showed significant changes in gene expression data. For this process, the Enrichr package was used (15-17), and the gene lists were subjected to enrichment analysis in the MSigDB (Molecular Signatures Database) (18-20) and KEGG (Kyoto Encyclopedia of Genes and Genomes) databases (21-23). The significant pathways and genes were then used as features in machine learning algorithms.

Machine Learning Algorithms

Machine learning algorithms were used to predict survival outcomes. These algorithms included C4.5 Decision Tree, Naive Bayes, Random Forest, and Support Vector Machines (SVM).

- *C4.5 Decision Tree:* This algorithm is a machine learning method that creates decision trees to classify data. Decision trees divide the data, making a decision at each node, and ultimately classify it. C4.5 is one of the most popular decision tree algorithms, often preferred for its ease of interpretation (24, 25).
- *Support Vector Machines (SVM):* SVM is a powerful algorithm used for solving classification problems. SVM finds the best hyperplane that separates the data between two classes. It is particularly effective in high-dimensional data and is widely used for classifying complex diseases like cancer (24, 26).
- *Random Forest:* This is an ensemble learning method where multiple decision trees work together. Random Forest analyzes the data with several decision trees and combines their results to offer more accurate and generalizable predictions, making it a suitable option for healthcare data analysis (24, 27).
- *Naive Bayes:* Naive Bayes is a probabilistic classification algorithm. It makes predictions based on the likelihoods of each class. Despite its simplicity, it produces effective results in areas such as text classification and disease diagnosis (24).

The performance of the algorithms was evaluated through the following steps:

- Model Training: Training sets were defined for each algorithm, and models were trained.
- Ten-Fold Cross-Validation: The ten-fold cross-validation method was used to separate the training and test data.
- Performance Evaluation: Metrics such as accuracy, sensitivity, and specificity of the algorithms were calculated, and a confusion matrix was created for each model.

Clinical Decision Support Tool: SurvCOCA

The developed machine learning algorithms were integrated into a web-based clinical decision support system using the R-Shiny package. This system, named SurvCOCA, provides an interface for users to make survival predictions. SurvCOCA runs on TCGA-COAD data and is accessible via the shinyapps.io platform (7,28).

RESULTS

Analysis of Clinical Data

This study included 454 patients from the "COAD" (Colon adenocarcinoma) project, which is part of the National Cancer Institute's Cancer Genome Atlas Program (TCGA), accessible via the GDC Data Portal. The demographic characteristics and clinical parameters of these patients, along with survival analyses, are presented below.

Of the patients, 47.14% (n: 214) were female, and 52.86% (n: 240) were male. Among the 283 patients whose race was known, 74.91% (n: 212) were White, 20.85% (n: 59) were African American, 3.89% (n: 11) were Asian, and 0.35% (n: 1) were classified as Native American or Alaska Native.

Among the 232 patients for whom body mass index (BMI) data were available, 33.19% (n: 77) had a normal BMI, while 66.81% (n: 155) had a high BMI.

A total of 86.56% (n: 393) of the patients had no prior cancer diagnosis, while 13.44% (n: 61) had a previous cancer diagnosis.

Of the 443 patients with available tumor staging data, 16.93% (n: 75) were classified as Stage 1, 39.73% (n: 176) as Stage 2, 28.89% (n: 128) as Stage 3, and 14.45% (n: 64) as Stage 4.

Kaplan-Meier Survival Analysis Results

Kaplan-Meier survival analyses were conducted based on variables such as gender, body mass index, prior cancer diagnosis, primary diagnosis, resection or biopsy site, tumor stage, T stage, N stage, and M stage.

Table 1. Gene enrichment analysis (KEGG)

KEGG	P value	Pathway	Matching Genes
1	0,001	Glycolysis/Gluconeogenesis	ADH1C; AKR1A1; PFKM (3/68)
2	0,044	Other glycan degradation	MAN2B2 (1/18)
3	0,046	Biosynthesis of pantothenate and CoA	BCAT1 (1/19)
4	0,049	Apoptosis	CAPN2; CASP2 (2/143)

Table 2. Gene enrichment analysis (KEGG) (Cancer Hallmark)

Hallmark	P value	Pathway	Matching Genes
1	0,014	mTORC1 pathway	TOMM40; TCEA1; BCAT1 (3/200)

Table 3. Performance results of clinical parameters

Evaluation / Algorithms	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)	Accuracy (ACC)	AUC
C4.5 Decision Tree	%96,6	%28,8	%83,5	%69,7	%82,3	%67,8
Support Vector Machines	%93,0	%16,3	%80,5	%38,2	%76,7	%54,6
Random Forest	%83,9	%45,0	%85,0	%42,9	%75,7	%72,2
Naive Bayes	%88,3	%41,3	%84,8	%48,5	%78,3	%73,7

Table 4. Common performance results of genes in the glycolysis-gluconeogenesis pathway with clinical parameters

Evaluation / Algorithms	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)	Accuracy (ACC)	AUC
C4.5 Decision Tree	%92,6	%28,8	%82,9	%51,1	%79,1	%66,2
Support Vector Machines	%93,0	%17,5	%80,8	%40,0	%77,0	%55,2
Random Forest	%91,6	%31,3	%83,2	%50,0	%78,8	%73,8
Naive Bayes	%88,6	%36,3	%83,8	%46,0	%77,5	%69,9

- Survival by Gender: No significant difference in survival was found between genders (Log Rank test: 0.334, p: 0.563).
- -Survival by Body Mass Index: No significant difference in survival was observed based on BMI (Log Rank test: 2.555, p: 0.110).
- Survival by Prior Cancer Diagnosis: No significant difference in survival was found between patients with and without a prior cancer diagnosis (Log Rank test: 1.164, p: 0.281).
- Survival by Tumor Stage: A significant difference in survival was found based on tumor stage (Log Rank test: 57.061, p: 0.000). Patients in Stages 1, 2, and 3 had higher survival rates compared to Stage 4 patients.

Analysis of Gene Expression Data

Gene enrichment analyses conducted in the KEGG and MSigDB databases revealed that specific genes play a significant role in survival prediction.

- KEGG Database: Genes associated with glycolysis/gluconeogenesis pathways, such as ADH1C, AKR1A1, and PFKM, showed significant matches.
- MSigDB Cancer Hallmark Gene Set: Genes involved in the mTORC1 signaling pathway, including TOMM40, TCEA1, and BCAT1, were found to be important.

Machine Learning Algorithm Results

Model evaluations using various machine learning algorithms showed that the Random Forest algorithm achieved the highest accuracy when clinical and genetic data were used together.

- Performance Results of Clinical Parameters: The Random Forest algorithm showed the
- best performance with an accuracy rate of 82.3% when evaluated using clinical parameters.
- Performance Results of Clinical Parameters Combined with Glycolysis-Gluconeogenesis Pathway Genes: When clinical parameters were combined with gene expression data, the accuracy increased to 79.1%.

Survival Prediction Clinical Decision Support Tool: SurvCOCA

The web interface of the developed SurvCOCA tool was created using the Shiny platform. This open-access tool integrates clinical and genetic data to predict the survival outcomes of colorectal cancer patients.

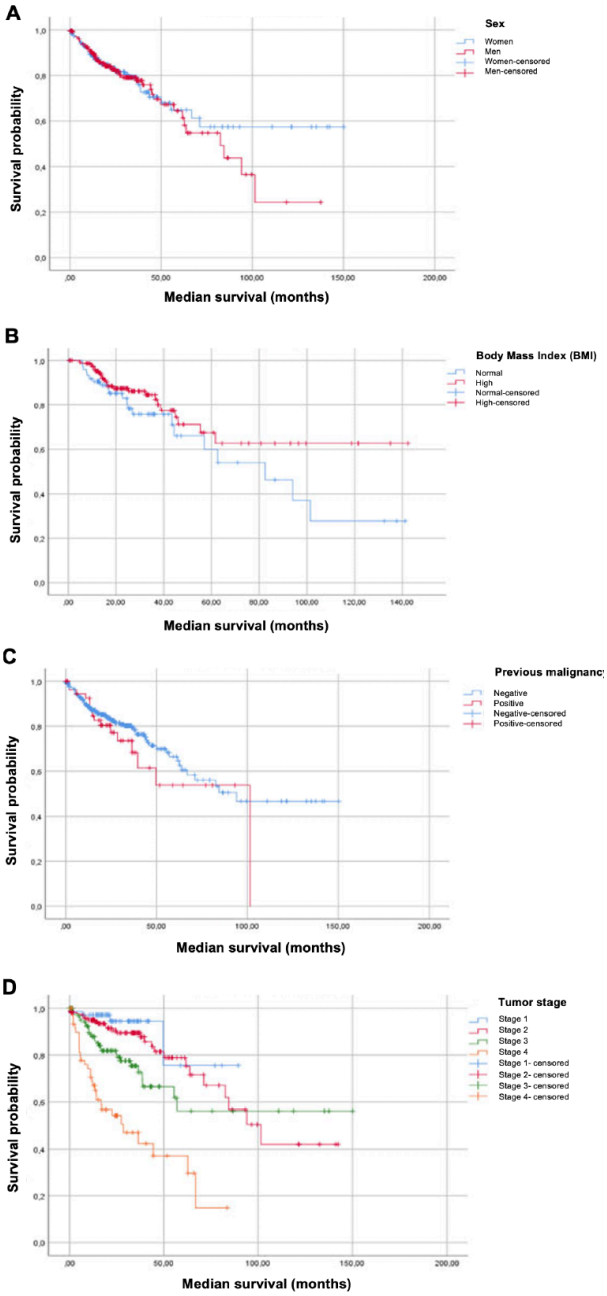

Figure 1. Survival analysis. A) Survival by gender. B) Survival by body mass index. C) Survival by previous cancer diagnosis. D) Survival by tumor stage.

DISCUSSION

This study aimed to evaluate the capacity of an artificial intelligence-assisted clinical decision support system (CDSS) to predict survival in colorectal cancer patients using machine learning techniques. Particularly, given that cancer treatments can cause side effects that may negatively impact the quality of life of patients, survival prediction is of great importance, especially for advanced-stage (Stage 4) cancer patients. It is known that physicians often tend to be more optimistic in their survival estimates compared to actual outcomes, highlighting the need for accurate prognostic models (29,30). Kaplan-Meier survival analyses in our study revealed that many demographic and clinical factors examined did not have a significant impact on survival. Factors such as

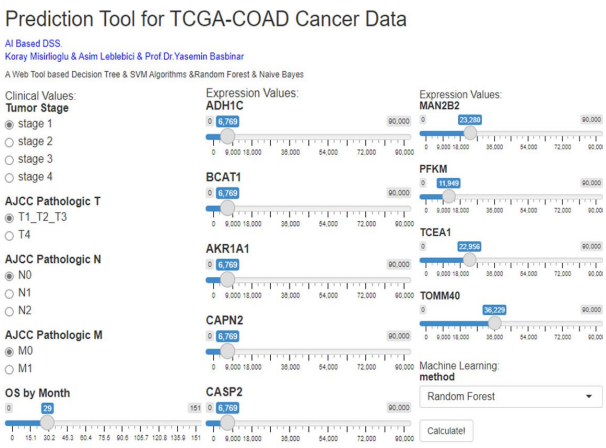

Figure 2. Clinical decision support tool for predicting survival: SurvCOCA Shiny web interface parameter setting screen

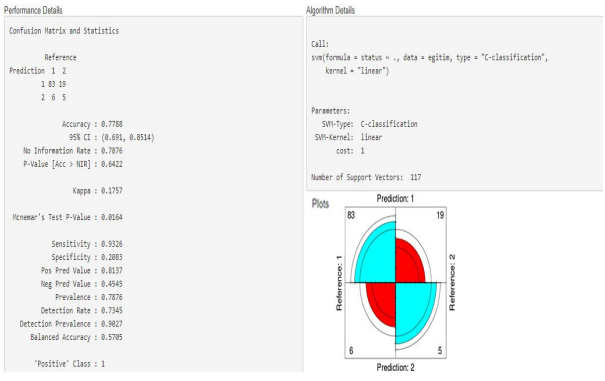

Figure 3. Clinical decision support tool for predicting survival: SurvCOCA Shiny web interface decision output screen

gender, body mass index, prior cancer diagnosis, and primary diagnosis showed no significant difference in survival (Figure 1). However, factors like tumor stage had a significant effect on survival, demonstrating that survival decreases markedly in the more advanced stages of cancer (Figure 1).

Cancer signaling pathways regulate critical biological processes involved in tumor progression and drug resistance. Gene enrichment analyses conducted in this study identified that glycolysis/gluconeogenesis, apoptosis, and mTORC1 signaling pathways play a crucial role in survival prediction (31). Specifically, the expression data of genes such as ADH1C, AKR1A1, PFKM, MAN2B2, BCAT1, CAPN2, CASP2, TOMM40, and TCEA1 showed significant associations with survival (Table 1 and Table 2). In this study, four different machine learning algorithms (C4.5 Decision Tree, Support Vector Machines, Random Forest, and Naive Bayes) were evaluated for their use in survival prediction by utilizing clinical and genomic data. The Random Forest algorithm achieved the highest accuracy, particularly in models where all data were combined (Table 3 and Table 4). As supported by the literature, this result demonstrates that more data leads to better machine learning performance (3).

A key contribution of this study is the integration of survival prediction models developed using machine learning algorithms into a clinical decision support system called SurvCOCA, which features a web interface. This system allows users to make colorectal cancer survival predictions by offering different algorithm options. It is emphasized that such clinical decision support systems should be used more frequently in prognosis and survival predictions and that further research in this area is necessary (31).

CONCLUSION

In conclusion, this study demonstrates the potential of an AI-based clinical decision support system developed for survival prediction in colorectal cancer patients. For further improvement, it is recommended to work with larger datasets and evaluate a broader range of machine learning algorithms. Additionally, enhancing the user interface of SurvCOCA and presenting survival predictions as percentage probabilities could increase the system's acceptance in clinical practice.

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Conflict of interests: The authors declare no conflict of interest.

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REFERENCES

1. Simon HA. The Sciences of the Artificial. 3rd Edition. Cambridge: The MIT Press; 1996.
2. Harrington P. Machine Learning in Action. 1stEdition. New York: Manning Publications; 2012.
3. Kartal E. Sınıflandırmaya Dayalı Makine Öğrenmesi Teknikleri ve Kardiyolojik Risk Değerlendirmesine İlişkin Bir Uygulama (Dissertation). Istanbul: Istanbul University. 2015.
4. RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL http://www.rstudio.com/.
5. Chang W, Cheng J, Allaire J, Sievert C, Schloerke B, Xie Y, Allen J, McPherson J, Dipert A, Borges B (2024). shiny: Web Application Framework for R. R package version 1.9.1.9000, https://github.com/rstudio/shiny, https://shiny.posit.co/.
6. Kuhn M. Building Predictive Models in R Using the caret Package. Journal of Statistical Software 2008;28(5):1–26.
7. team shinyapps io [İnternet]. shinyapps.io user guide [Accessed date: 1 September 2024]. Available from: https://docs.posit.co/shinyapps.io/guide/index.html
8. Kirk S, Lee Y, Sadow CA, Levine S, Roche C, Bonaccio E, Filiippini J. (2016). The Cancer Genome Atlas Colon Adenocarcinoma Collection (TCGA-COAD) (Version 3) [Data set]. The Cancer Imaging Archive.

https://doi.org/10.7937/K9/TCIA.2016.HJJHBOXZ.
9. Grossman RL, Heath AP, Ferretti V, Varmus HE, Lowy DR, Kibbe WA, Staudt LM. Toward a Shared Vision for Cancer Genomic Data. New England Journal of Medicine 2016;375(12):1109-1112
10. Colaprico A, Silva TC, Olsen C, Garofano L, Cava C, Garolini D, Sabedot T, Malta TM, Pagnotta SM, Castiglioni I, Ceccarelli M, Bontempi G, Noushmehr H. TCGAbiolinks: An R/Bioconductor package for integrative analysis of TCGA data. Nucleic Acids Research 2016;44(8):e71.
11. Silva TC, Colaprico A, Olsen C, D'Angelo F, Bontempi G, Ceccarelli M, Noushmehr H. TCGA Workflow: Analyze cancer genomics and epigenomics data using Bioconductor packages. F1000Research 2016:5;1542.
12. Mounir M, Lucchetta M, Silva TC, Olsen C, Bontempi G, Chen X, Noushmehr H, Colaprico A, Papaleo E. New functionalities in the TCGAbiolinks package for the study and integration of cancer data from GDC and GTEx. PLoS Comput Biol 2019;15(3):e1006701.
13. Colaprico A, Silva TC, Olsen C, Garofano L, Garolini D, Cava C, Sabedot T, Malta T, Pagnotta SM, Castiglioni I, Ceccarelli M, Bontempi G, Noushmehr H. TCGAbiolinks: TCGAbiolinks: An R/Bioconductor package for integrative analysis with GDC data (Version 2.32.0). Available from: URL: https://www.bioconductor.org/packages/release/bioc/manuals/TCGAbiolinks/man/TCGAbiolinks.pdf
14. IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp
15. Chen EY, Tan CM, Kou Y, Duan Q, Wang Z, Meirelles GV, Clark NR, Ma'ayan A. Enrichr: interactive and collaborative HTML5 gene list enrichment analysis tool. BMC Bioinformatics 2013;14:128.
16. Kuleshov MV, Jones MR, Rouillard AD, Fernandez NF, Duan Q, Wang Z, Koplev S, Jenkins SL, Jagodnik KM, Lachmann A, McDermott MG, Monteiro CD, Gundersen GW, Ma'ayan A. Enrichr: a comprehensive gene set enrichment analysis web server 2016 update. Nucleic Acids Research 2016;44(W1):W90-7.
17. Xie Z, Bailey A, Kuleshov MV, Clarke DJB, Evangelista JE, Jenkins SL, Lachmann A, Wojciechowicz ML, Kropiwnicki E, Jagodnik KM, Jeon M, Ma'ayan A. Gene Set Knowledge Discovery with Enrichr. Curr Protoc 2021;1(3):e90.
18. Subramanian A, Tamayo P, Mootha VK, Mukherjee S, Ebert BL, Gillette MA, Paulovich A, Pomeroy SL, Golub TR, Lander ES, Mesirov JP. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. Proc Natl Acad Sci USA 2005;102(43):15545-50.
19. Liberzon A, Subramanian A, Pinchback R, Thorvaldsdóttir H, Tamayo P, Mesirov JP. Molecular signatures database (MSigDB) 3.0. Bioinformatics 2011;27(12):1739-40.
20. Liberzon A, Birger C, Thorvaldsdóttir H, Ghandi M, Mesirov JP, Tamayo P. The Molecular Signatures Database (MSigDB) hallmark gene set collection. Cell Syst 2015;1(6):417-425.
21. Kanehisa M, Goto S. KEGG: kyoto encyclopedia of genes and genomes. Nucleic Acids Res 2000;28(1):27-30.
22. Kanehisa M. Toward understanding the origin and evolution of cellular organisms. Protein Sci 2019;28(11):1947-1951.
23. Kanehisa M, Furumichi M, Sato Y, Kawashima M, Ishiguro-Watanabe M. KEGG for taxonomy-based analysis of pathways and genomes. Nucleic Acids Res 2023;51(D1):D587-D592.
24. Awaysheh A, Wilcke J, Elvinger F, Rees L, Fan W, Zimmerman KL. Review of Medical Decision Support and Machine-Learning Methods. Vet Pathol. 2019;56(4):512-525.
25. Wiharto W, Kusnanto H, Herianto H. Interpretation of Clinical Data Based on C4.5 Algorithm for the Diagnosis of Coronary Heart Disease. Healthc Inform Res 2016;22(3):186-95.
26. Mendi B. Sağlık Bilişimi ve Güncel Uygulamalar. 1st Edition. Istanbul, Nobel Tıp Kitabevi; 2016.
27. Persidis A, Persidis A. Medical Expert Systems: An Overview. J Manag Med 1991;5(3):27-34.
28. Shiny [Internet]. [Accessed date: 31 Mayıs 2021]. Available from: https://cancerapp.shinyapps.io/shiny/
29. Glare P, Virik K, Jones M, Hudson M, Eychmuller S, Simes J, Christakis N. A systematic review of physicians' survival predictions in terminally ill cancer patients. BMJ

2003;327(7408):195-8.
30. Viganó A, Bruera E, Jhangri GS, Newman SC, Fields AL, Suarez-Almazor ME. Clinical survival predictors in patients with advanced cancer. Arch Intern Med 2000;160(6):861-8.
31. Feng J, Zhang H, Li F. Investigating the relevance of major signaling pathways in cancer survival using a biologically meaningful deep learning model. BMC Bioinformatics 2021;22(1):47.