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New prognostic model for liver transplantation outcomes in hepatocellular carcinoma

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Abstract

Background. *Liver transplantation remains a priority treatment option for hepatocellular carcinoma in the presence of liver cirrhosis; yet precise outcome prediction post-operation continues to be a complex challenge. Existing prognostic model often overlook patient age and donor type. Enhanced models that incorporate these parameters can improve prediction accuracy and treatment efficacy, which is critically important in the dynamically evolving field of transplantation.*

Objective. *The aim of this study is to develop a prognostic model for liver transplantation outcomes in patients with hepatocellular carcinoma and liver cirrhosis.*

Material and methods. *This retrospective study included 69 patients with hepatocellular carcinoma on the background of liver cirrhosis who*

underwent liver transplantation between May 2010 and December 2022. Of these, 42 patients (61%) received organs from living donors, and 27 (39%) from deceased donors. The study involved analysis of alpha-fetoprotein levels in blood, as well as assessment of radiological (maximum tumor nodule size, number of nodules) and histological parameters (maximum tumor nodule size, number of nodules, presence of vascular invasion). Cox regression model was used to predict recurrence-free survival, and the results for five-year recurrence-free survival, recipient age, and donor type were reused in the Cox model to predict overall survival.

Results. *Four models for predicting recurrence-free survival and overall survival based on histological and radiological data were developed, demonstrating high prognostic value with C-indexes on training/test data of 0.76/1; 0.73/1; 0.78/0.8; 0.6/0.8 respectively. All models showed recurrence-free survival prediction accuracy comparable to the Milan criteria. The model outcomes are available as a calculator on the website https://nadit.ru/calculate_HCC.*

Conclusion. *The developed prognostic models are vital tools for personalized outcome prediction after liver transplantation for hepatocellular carcinoma. To enhance the accuracy of these models, further amalgamation and validation of data from various medical centers, as well as open scientific collaboration, are necessary.*

Keywords: hepatocellular carcinoma, liver transplantation, hepatocellular carcinoma recurrence, prognostic models, transplantological criteria

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AFP, alpha-fetoprotein
RFS, recurrence-free survival
HCC, hepatocellular carcinoma
LD, living donors
IQR, interquartile range
CT, computed tomography
OS, overall survival
PD, posthumous donors

Introduction

Hepatocellular carcinoma (HCC) is one of the most aggressive types of liver cancer and one of the leading causes of death from malignant tumors. Liver transplantation is one of the priority treatment options for patients with HCC due to liver cirrhosis, but the efficacy of this approach strongly depends on the extent of the tumor process [1–5].

Existing studies highlight the importance of a comprehensive assessment of a number of factors, including tumor size, tumor number, and blood alpha-fetoprotein (AFP) levels in predicting recurrence-free survival (RFS). However, overall survival (OS) is also influenced by other factors such as age, severity of the recipient's condition (MELD score), diabetes mellitus, gender, donor type and other parameters [6, 7].

The effect of donor type on OS is described in the study by A. Humar et al. [8] . They conducted a retrospective review of all living donor (LD) (n=245) and posthumous donor (PD) (n=592) adult recipient transplants performed over a 10-year period (2009–2019). OS was analyzed, as well as other outcome characteristics, such as the hospital length of stay, frequency and structure of complications, etc. The results showed that OS of patients was higher after liver transplantation from LDs (3-year survival rate of 86% versus 80%, p=0.03). In addition, shorter hospital stays, less need for blood transfusion and post-transplant hemodialysis were observed [8] .

Meanwhile, such a parameter as the donor type was not previously taken into account in prognostic models. This aspect is of particular importance given that the choice between living and deceased donor transplantation can significantly influence treatment outcomes. Including this factor in analytical models may be useful for more detailed and accurate prediction of patient survival after surgery.

In our study, we aimed to create a predictive model that both could help clinicians to more accurately guide prognosis, and would also provide patients and their families with important information that could influence decision making, especially in cases where living donor transplantation is being considered. Thus, our study aims to improve the understanding of liver transplantation outcomes for clinicians and patients.

The objective was to develop a prognostic model for liver transplantation outcomes in patients with hepatocellular carcinoma and liver cirrhosis.

Material and methods

Study design

The study was a retrospective, single-center analysis including data from 69 patients diagnosed with HCC secondary to cirrhosis who underwent liver transplantation between May 2010 and December 2022. This sample represents 14% of the total number of transplantations performed at Burnasyan Federal Medical Biophysical Center of Federal Medical Biological Agency during this period. A.I. Burnasyan. Of these, 42 patients received transplants from LD and 27 from PD. The information on donor and recipient characteristics, cancer prevalence, and transplant outcomes was extracted from the local Liver Transplant Registry.

The following were defined as key endpoints:

1. Recurrent HCC diagnosed based on re-detection of the tumor using computed tomography (CT) of the chest and abdomen with intravenous contrast or based on autopsy results.
2. Death of the recipient.

To monitor the condition of patients after liver transplantation, a regular examination protocol was used at 6-month intervals. In some cases (4 patients), CT results were assessed remotely. Registration of outcomes was limited to March 2023, which provided a sufficient time period to monitor the dynamics of the patients' condition.

The study consisted of two stages.

At the first stage of the study, RFS was predicted by preoperative radiological and post-transplant histological parameters, for which the Cox proportional hazards model was used. The analyzed parameters included the size of the largest tumor node, the number of nodes, and the blood level of AFP; vascular invasion was assessed only based on histological data. In the second phase of the study, we used the prediction result of 5-year RFS as one of the key predictors in the Cox regression model in predicting OS, along with other important factors such as a patient age and donor type

Statistical data processing

Python programming language (version 3.8) was used in the study for data processing and analysis. To build up and evaluate prognostic models, we used the lifelines module, a specialized Python library for assessing survival, specifically, Cox Proportional Hazards model, CoxPHFitter.

The predictive ability of our developed models was assessed based on their Harrell fit index (C-index). To improve the accuracy of the C-index estimate, especially in the context of a limited sample size, we used

a 10-fold block validation method combined with a bootstrap method. The bootstrap method, which includes 1000 repetitions, allows us to take into account the internal variability of the sample, thereby increasing the reliability and stability of estimates in conditions of limited data. During each bootstrap iteration, a subsample was randomly drawn from the original data set and returned. For each such subsample, the C-index was calculated using a Cox model trained specifically on this subsample. Then, based on the calculated C-indexes, the mean C-index and its corresponding 95% confidence interval were obtained.

Quantitative variables were presented as median (Me) and interquartile range (IQR); where necessary, the minimum and maximum values (min–max) were given. For qualitative parameters, absolute frequencies and percentages were given.

The statistical significance of differences in quantitative and qualitative characteristics in two independent samples was assessed using the nonparametric two-sided Mann–Whitney test and the two-sided Fisher exact test, respectively.

Recurrence-free and overall survival rates were calculated using the Kaplan–Meier method. Differences in survival between two independent groups were assessed using the Log-rank test.

Differences were considered statistically significant at $p<0.05$.

Results

Characteristics of cases, and transplantation results

During the follow-up period, 18 tumor recurrence cases were recorded, being diagnosed within a period from 1 to 76 months (median 22, IQR: 9.5; 40.5) after transplantation. Twenty-one patients died in the period ranged from 1 to 79 months (median 17, IQR: 4;26), of which 13 had recurrent HCC; 43 patients survived without signs of recurrence.

Preoperative characteristics of patients in the study cohort and observation groups are presented in Table. 1.

Table 1. Preoperative characteristics of patients and prevalence of hepatocellular carcinoma in the study cohort and observation groups

Parameter	All cases (n=69)	LDs (n=42)	PDs (n=27)	p
Age at the time of transplantation, years Me (IQR) (min–max)	52.0 (48.0;58.0) (32-68)	51.0 (47.0;57.8) (32-68)	56.0 (49.0;59.5) (39-67)	0.104
Male gender, n (%)	44 (63.8%)	25 (59.5%)	19 (70.4%)	0.445
cirrhosis as a result of viral hepatitis, n (%)	66 (95.7%)	42 (100%)	24 (89%)	0.06
– HCV	42 (60.9%)	23 (54.8%)	19 (70.4%)	0.21
– HBV	5 (7.2%)	3 (7.1%)	2 (7.4%)	1.000
– HBV+HCV	2 (2.9%)	1 (2.4%)	1 (3.7%)	1.000
– HDV	17 (24.6%)	15 (35.7%)	2 (7.4%)	0.009
Child-Pugh Class:				
A, n (%)	16 (23.2%)	10 (23.8%)	6 (22.2%)	1.000
B, n (%)	35 (50.7%)	22 (52.4%)	13 (48.1%)	1.000
C, n (%)	18 (26.1%)	10 (23.8%)	8 (29.6%)	0.6
MELD-Na, scores, Me (IQR) (min–max)	13.0 (11.0;17.9) (6.0-42.7)	13.0 (10.8;18.2) (6.0-42.7)	13.0 (11.0;16.9) (7.7-24.3)	0.883
Number of tumor nodes (CT), Me (IQR) (min–max)*	2.0 (1.0;3.0) (0.0-10.0)	2.0 (1.0;3.0) (0.0-10.0)	2.0 (1.0;4.0) (0.0-10.0)	0.412
Diameter of the largest tumor node (CT), cm, Me (IQR) (min–max)*	3.5 (1.8;5.0) (0-11.6)	3.5 (2.1;5.2) (0-11.6)	3.5 (1.6;4.6) (0-8.3)	0.359
Vascular invasion according to CT data, n (%)	6 (8.7%)	6 (14.3%)	0 (0.0%)	0.075
Number of tumor nodes (Hist.), Me (IQR) (min–max)*	1.0 (1.0;3.0) (0-10)	1.0 (1.0;2.0) (0-10)	2.0 (1.0;3.0) (0-10)	0.641
Diameter of the largest tumor node (Hist.), cm, Me (IQR) (min–max)*	3.0 (2.0;4.8) (0-10.0)	3.2 (2.0;5.0) (0-10.0)	3.0 (1.5;4.1) (0-6.0)	0.343
Macrovascular invasion according to histology data, n (%)	5 (7.2%)	4 (9.5%)	1 (3.7%)	0.641
Microvascular invasion according to histology data, n (%)	7 (10.1%)	3 (7.1%)	4 (14.8%)	0.42
Vascular invasion according to histology data, n (%)	11 (15.9%)	6 (14.3%)	5 (18.5%)	0.74
Affected lymph nodes according to histology data, n (%)	5 (7.2%)	2 (4.8%)	3 (11.1%)	0.373
AFP, ng/mL, Me (IFR) (min-max)	40.1 (17.8;162.2) (2.4-13626.0)	39.5 (14.8;186.1) (2.6-13626.0)	41.4 (35.4;110.0) (2.4-10392.8)	0.98
Recurrence, n (%)	18 (26.1%)	10 (23.8%)	8 (29.6%)	0.589
Meeting the Milan criteria, CT, n (%)	25 (36.2%)	14 (33.3%)	11 (40.7%)	0.611
Meeting the Milan criteria, Hist., n (%)	40 (58.0%)	23 (54.8%)	17 (63.0%)	0.619
Donor age at the time of transplantation, years, Me (IQR) (min–max)	41.5 (29.0;51.0) (21.0-63.0)	36.0 (28.0;47.0) (21.0-63.0)	46.0 (39.0;57.5) (21.0-63.0)	0.01
Cold ischemia time, hours, Me (IQR) (min–max)	1.8 (1.2;8.0) (0.5-13.5)	1.2 (0.9;1.6) (0.5-2.5)	8.0 (7.3;9.8) (3.0-13.5)	<0.001
Waiting time for transplantation, months, Me (IQR) (min–max)	1.0 (1.0;6.0) (0-33)	1.0 (1.0;1.0) (0-7.0)	9 (2.5;12.5) (0-33)	<0.001

Notes: * Value 0 for non-viable tumor nodes after successful “downstaging” or “bridge therapy”. Quantitative parameters are presented as Me (IQR) (min–max); the significance level p was calculated when comparing between the groups of patients who received a liver graft from a living or posthumous donor

As can be seen from Table 1, the patients who received a liver graft from a living donor had shorter transplant waiting times, a lower donor age, and shorter cold ischemia time. Meanwhile, tumor characteristics and blood levels of alpha-fetoprotein were similar between the groups.

In our study, we found that donor type had an impact on the OS of patients after liver transplantation. However, the type of donor had no impact on RFS (Fig. 1, Table 2).

Table 2. Overall and recurrence-free survival of patients depending on the donor type

Observation group	n	Survival rate, % (95% [CI])						p (OS)	p (RFS)
		OS			RFS				
		1 year	3 years	5 years	1 year	3 years	5 years		
Living donor, HCC	42	88 [73–95]	82 [65–91]	82 [66–91]	92 [78–97]	80 [61–90]	63 [40–79]	0.04	0.58
Posthumous donor, HCC	27	85 [59–92]	63 [41–79]	49 [25–69]	84 [58–91]	69 [46–84]	62 [37–80]		

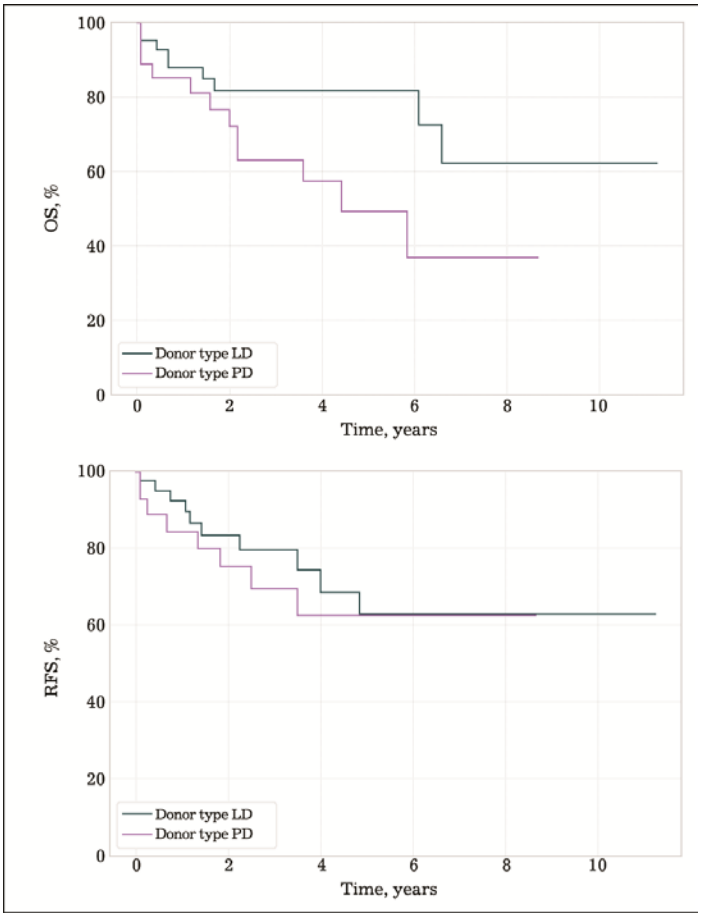

Fig. 1. Overall and recurrence-free survival of patients depending on the donor type

As can be seen from Table 2 and Fig. 1, the patients who had received liver grafts from LD have a better 5-year OS (82%, p=0.04, statistically significant) compared to patients who had received liver grafts from PD and had a 5-year OS of 49%. RFS did not show a statistically significant difference (p=0.58) between the groups, with the 5-year RFS being 63% for LD and 62% for PD. The histological data analysis revealed that 5 patients had metastases in the lymph nodes. All patients with such metastases died within 2 years after transplantation due to HCC progression. To ensure the scientific integrity and accuracy of the results, these patients were excluded from the second phase of the study, and their radiological data were retained in the first part of the analysis.

Due to the small number of cases of CT-diagnosed macrovascular invasion, we decided not to include these data in the analysis. As for histological data, the cases of macro- and microvascular invasion were combined.

There were 4 models created:

- "Rad. RFS model" trained on radiological data (diameter of the largest tumor node, number of tumor nodes) and AFP;
- "Rad. OS model" trained on the prediction results of the previous model and such parameters as the donor type and the recipient age;
- "Hist. RFS model" trained on histological data (diameter of the largest tumor node, number of tumor nodes, vascular invasion) and AFP;
- "Hist. OS model" trained on the prediction results of the previous model and such parameters as the donor type and the recipient age.

The training/testing samples for models trained on radiological and histological data were 55/14 and 51/13, respectively. The results of model development are presented in Table 3.

C-indices for models of the training and testing samples for the groups "rad. RFS", "rad. OS", "hist. RFS", "hist. OS" were 0.76/1; 0.73/1; 0.78/0.8; 0.6/0.8, respectively.

Table 3. Comparative analysis of predictors for assessing overall and recurrence-free survival rates after liver transplantation

Variable	RFS							
	Radiological data (n=55) "Rad. RFS"				Histological data (n=51) "Hist" RFS"			
	p	Coefficient (Error of the Mean) [CI]	C-index (10-fold, CV)	Mean C-index (bootstrap, [CI])	p	Coefficient (Error of the Mean) [CI]	C-index (10-fold, CV)	Average C-index (bootstrap , [CI])
Diameter of the largest tumor node	0.0009	0.39 (0.12) [0.16–0.62]	0.84	0.77 [0.63–0.9]	0.428	0.121 (0.153) [-0.178–0.42]	0.77	0.8 [0.62–0.95]
AFP	0.09	1.5×10^{-4} (8.5×10^{5}) [-2.2×10^{-5}–3×10^{-4}]			0.115	1.4×10^{-4} (8.6×10^{-5}) [-3.3×10^{-5}–3.1×10^{-4}]		
Number of tumor nodes	0.41	0.09 (0.08) [-0.1–0.24]			0.037	0.253 (0.122) [0.015–0.492]		
Vascular invasion	–	–			0.293	0.857 (0.815) [-0.74–2.455]		
Variable	**OS**							
	Radiological data (n=55) "Rad., OS"				Histological data (n=51) "Hist., OS"			
Age at time of transplant	0.01	0.09 (0.03) [0.02–0.14]	0.78	0.75 [0.63–0.88]	0.22	0.81 (0.56) [-0.28–1.89]	0.72	0.65 [0.49–0.82]
Forecast for 5 years RFS in %	0.01	-0.02 (0.009) [-0.039–0.005]			0.36	-0.01 (0.01) [-0.03–0.11]		
Donor type	0.01	1.21 (0.5) [0.27–2.2]			0.15	0.81 (0.56) [-0.28–1.89]		

Note: CV, cross-validation

Table 3 shows that almost all radiological data variables, with the exception of the number of nodes and AFP, showed the statistical significance of differences. At the same time, of the histological data, only the number of nodes turned out to be a significant predictor, which was due to the exclusion of patients with lymph node invasion from the study. These patients had higher AFP values and larger maximum tumor sizes. Since they were excluded from the histological data analysis, this resulted in the lack of statistical significance for all parameters based on the histological data. Despite this, it was possible to achieve an acceptable level of C-index based on both radiological and histological data, which confirmed the predictive value of the models. Increasing the number of

patients in future studies, in our opinion, will improve the models and increase their accuracy.

Comparison with Milan criteria

To objectively assess the predictive value of the models we developed as compared to the Milan criteria being the established standard, a ROC analysis was made. The study included patients who survived the 3-year survival threshold or had recurrence during any follow-up period, allowing us to estimate the cut-off point for predicting RFS. Thus, the threshold value was set at a level of at least 49% for “rad. RFS" for “rad. RFS", and at a level no less than 71% for " hist. RFS".

A similar analysis was performed for patients who either survived more than 3 years or died during this period to determine the OS threshold. The values were: at least 69% for “rad. OS" and at least 75% for "hist. OS". The percentage of patients meeting these new criteria compared to the Milan criteria is shown in Fig. 2.

All developed models demonstrated the significance in predicting RFS comparable to the Milan criteria ($p>0.05$). The "hist. RFS", "rad. OS", and "hist. OS" models deserved special attention, as they were highly effective in predicting overall survival ($p<0.05$), as the analysis showed, which is presented in detail in Table 4 and Fig. 3.

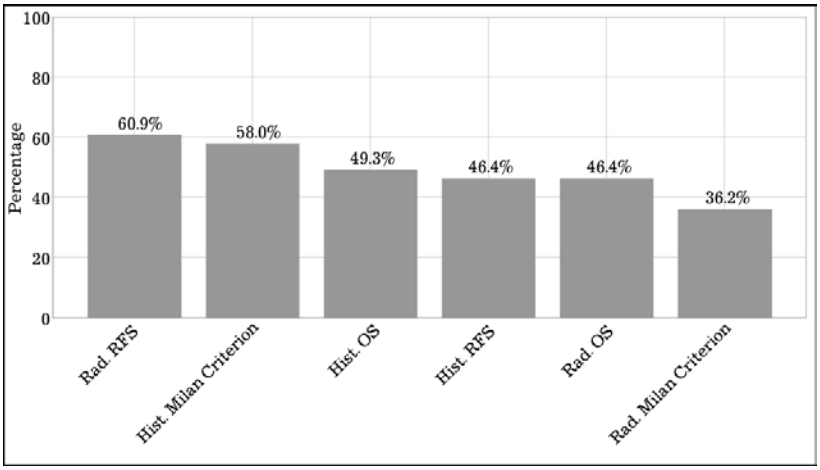

Fig. 2. Proportion of patients with hepatocellular carcinoma who met the developed criteria and the Milan criteria

As shown in Fig. 2, the lowest fit among patients meeting the Milan criteria based on radiological findings was 36.2%. The greatest fit among the new models was observed for “rad. RFS" (60.9%). For the model “rad. OS", the fit was 46.4%. According to histological data, most patients met the Milan criterion (58.0%). The fit with the new model of “hist. OS" was 49.3%, and that of "hist. RFS"was 46.4%.

Table 4. Recurrence-free and overall survival of patients depending on the criteria

Models and criteria	Consistent-with-Criterion status	Survival rate, % (95% [CI])							
		Overall				Recurrence-free			
		1 year	3 years	5 years	p	1 year	3 years	5 years	p
Rad. RFS	Consistent with the criterion	85 [70–93]	77 [60–87]	72 [54–88]	0.35	93 [78–97]	92 [78–97]	82 [59–92]	<0.005
	Inconsistent with the criterion	89 [69–96]	68 [44–84]	50 [22–75]		81 [60–92]	50 [27–69]	33 [12–56]	
Hist. RFS	Consistent with the criterion	87 [70–95]	83 [65–93]	78 [57–90]	0.04	100 [100–100]	99 [95–100]	87 [68–97]	<0.005
	Inconsistent with the criterion	86 [70–94]	65 [45–79]	58 [35–75]		78 [60–88]	55 [35–71]	40 [19–61]	
Rad. OS	Consistent with the criterion	87 [70–95]	84 [65–93]	84 [65–93]	<0.005	97 [79–100]	88 [68–96]	82 [56–93]	0.01
	Inconsistent with the criterion	86 [70–94]	65 [45–79]	50 [25–70]		80 [62–90]	64 [44–79]	45 [23–65]	
Hist. OS	Consistent with the criterion	92 [76–97]	88 [71–95]	88 [71–95]	<0.005	100 [100–100]	92 [73–98]	80 [53–92]	<0.005
	Inconsistent with the criterion	79 [60–90]	58 [38–74]	44 [21–64]		74 [53–86]	57 [36–73]	44 [23–64]	
Rad. Milan criterion	Consistent with the criterion	88 [66–96]	78 [56–90]	78 [56–90]	0,11	91 [69–98]	91 [69–98]	91 [69–98]	<0.005
	Inconsistent with the criterion	86 [72–93]	71 [58–83]	56 [31–75]		86 [71–94]	65 [46–79]	37 [15–60]	
Hist. Milan criterion	Consistent with the criterion	87 [72–95]	76 [59–87]	68 [49–81]	0.98	95 [80–99]	88 [70–95]	73 [51–87]	0.01
	Inconsistent with the criterion	86 [67–95]	70 [46–85]	70 [46–85]		79 [58–90]	58 [36–76]	47 [20–70]	

As can be seen from Table 4, in OS, the statistical significance ($p<0.05$) was noted only in the “hist RFS”, "rad. OS", and "hist. OS" groups. Meanwhile, for RFS, the statistical significance was noted in all groups.

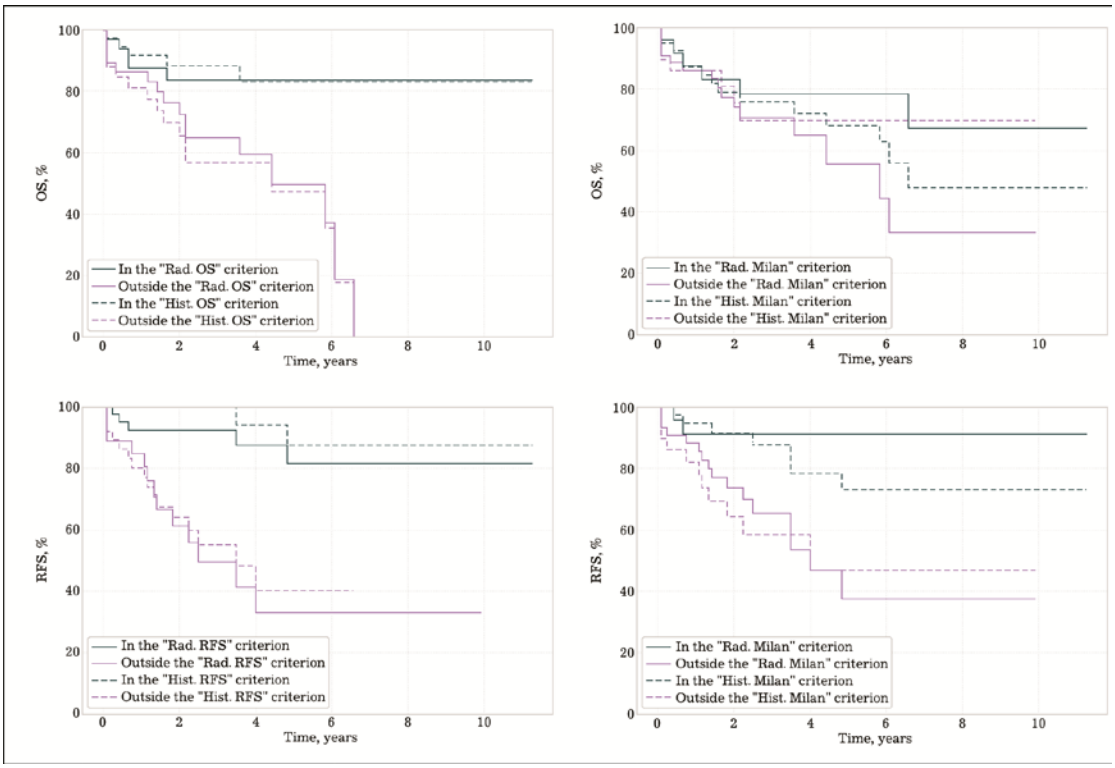

Fig. 3. Overall and recurrence-free survival rates for the developed models and Milan criteria

As can be seen from Fig. 3, in the OS, the statistical significance was noted in the “rad. OS” and "hist. OS” groups, which is confirmed by the graphs where the lines of fit to these models show better results compared to others. As for RFS, the statistical significance was noted in all groups, which is also reflected in the graphs, where there is a significant difference between the data of patients who met the criteria and the data of those who did not meet them.

Discussion

The study found that the donor type has a significant impact on the overall survival of patients after liver transplantation for HCC. However, it

should be emphasized that this relationship may be due to a number of factors, primarily the waiting period for liver transplantation, as well as the planned nature of surgery, cold ischemia time, and the tendency to provide organs from expanded criteria donors to stable recipients with expanded transplant criteria for HCC [9].

A study conducted using UNOS-OPTN data highlights the importance of waiting time in the context of liver transplantation for patients with HCC. The analysis showed that an increase in waiting time from 2 to 12 months was associated with a significant decrease in overall survival after transplantation: 5-year survival decreased by 5.07% and 10-year survival decreased by 8.33%. Median survival time reduced by 3.41 years [10]. These data highlight that prolonged waiting times may negatively impact the transplant outcomes in this patient population. In our study, we control for donor type, which is indirectly associated with waiting time: patients having LD typically wait a shorter time for a transplant (median one month), in contrast to patients waiting for an organ from a deceased donor (median nine months). This difference in waiting times emphasizes the need to integrate these parameters into predictive models to optimize approaches to transplantation and improve long-term patient outcomes.

The impact of cold ischemia time on the HCC recurrence is a relevant issue that was raised in the studies by M. Maspero et al. [11]. In our work, this is done by taking into account the donor type.

In many well-known studies, the donor type parameter was not taken into account when developing prognostic models, which is confirmed by literature data [6, 7, 12–16]. Among the various existing models, only those developed by D. Goldberg et al. and V. Mazzaferro et al. provide web-based user interfaces to facilitate their application in clinical practice. However, none of them includes analysis of donor type

as a factor influencing prognosis, which is a significant drawback. Our models fill this gap by providing a more detailed prediction and taking into account the donor type. This addition enhances the predictive power of the models, making them particularly valuable in settings where both types of donors are available, which is a significant advantage over the studies mentioned.

Unlike the model of D. Goldberg et al. [6], our method includes the ability to analyze histological data, including the presence of vascular invasion, which allows us to adjust the prognosis in the postoperative period. Our model is enriched with additional prognostic factors such as the patient age and donor type, which contributes to a more complete assessment of potential transplant outcomes, in contrast to the V. Mazzaferro et al. approach [7]. We offer a comprehensive analysis that includes assessment of both RFS and OS, relying on the analysis of radiological and histological data, providing four prognostic scenarios and thereby surpassing the capabilities of other existing models.

Thus, our proposed models provide a new tool in hands of clinicians. These models enable better-grounded clinical decisions and help optimize liver transplantation strategies for patients with HCC.

Conclusion

The developed prognostic models provide the opportunity to individualize predictions of liver transplantation outcomes for patients suffering from hepatocellular carcinoma. They effectively predict recurrence-free and overall survival, which are critical parameters in surgical planning.

Improving and validating these models through sharing and analyzing data from different medical centers will not only improve their accuracy, but also ensure their widespread clinical application. The model

is available for use on the web resource at https://nadit.ru/calculate_HCC (Fig. 4), which makes it easily accessible and convenient to use in clinical practice.

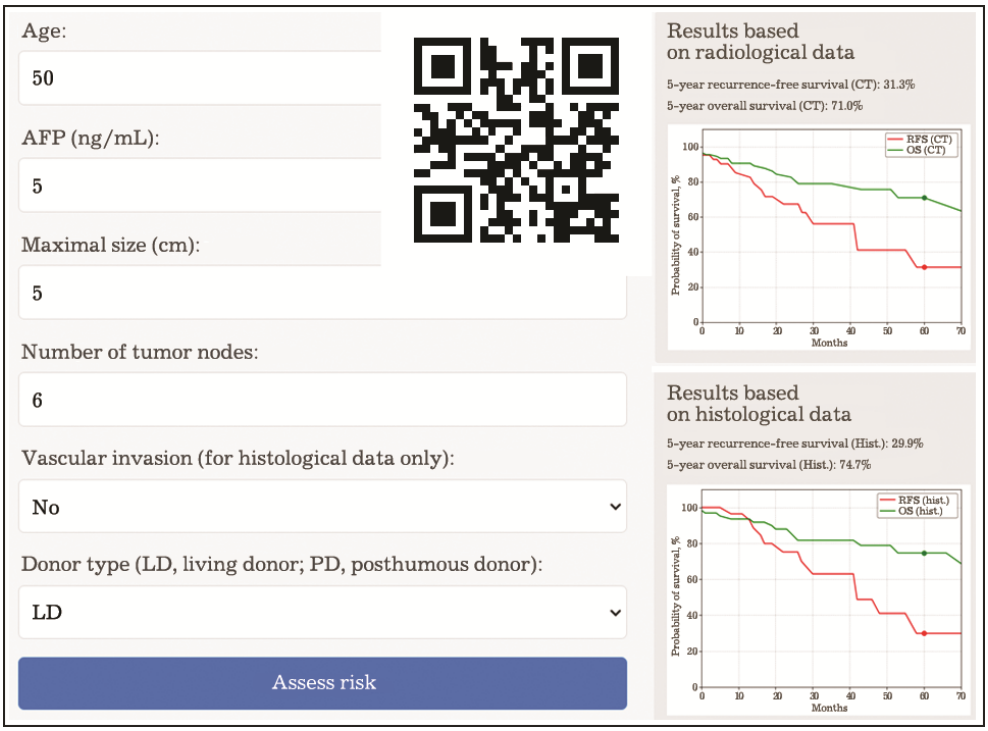

Fig. 4. Interface and QR code for access to the prognostic model (https://nadit.ru/calculate_HCC)

The tool shown in Fig. 4, allows one to quickly enter patient data and receive personalized predictions, which facilitates making well-grounded clinical decisions.

Integrating these models into routine clinical practice will allow physicians to more accurately determine the prognosis of patients undergoing liver transplantation, thereby increasing the chances of a successful treatment outcome. It is expected that the data exchange between different medical institutions will further improve these models, making them more reliable and adaptable to different clinical scenarios.

Based on our study results we have made the following conclusions:

1. The developed models demonstrate comparable efficacy to the widely used Milan criteria in predicting hepatocellular carcinoma recurrence after liver transplantation ($p>0.05$).

2. The type of donor (living or postmortem) had a statistically significant effect on the overall five-year survival of patients after liver transplantation (82% and 49%, respectively, $p=0.04$).

3. Five-year recurrence-free survival did not differ between living and deceased donor recipients (63% and 62%, respectively, $p=0.58$).

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