Quality and performance of validated prognostic models for survival after resection of intrahepatic cholangiocarcinoma: a systematic review and meta-analysis

Buttner, S.; Galjart, B.; Beumer, B.R.; Vugt, J.L.A. van; Eijck, C.H.J. van; Polak, W.G.; ... ; Koerkamp, B.G.

REVIEW ARTICLE

Quality and performance of validated prognostic models for survival after resection of intrahepatic cholangiocarcinoma: a systematic review and meta-analysis

Stefan Büttner[1,*], Boris Galjart[1,*], Berend R. Beumer[1], Jeroen L.A. van Vugt[1], Casper H.J. van Eijck[1], Wojciech G. Polak[1], Jeroen de Jonge[1], Marjolein Y.V. Homs[2], Lydi M.J.W. van Driel[3], Timothy M. Pawlik[4], Ewout W. Steyerberg[5], Jan N.M. Ijzermans[1] & Bas Groot Koerkamp[1]

[1]Department of Surgery, [2]Department of Medical Oncology, [3]Department of Gastroenterology and Hepatology, Erasmus MC Cancer Institute, Rotterdam, Netherlands, [4]Department of Surgery, Ohio State Medical Center, Columbus, OH, United States of America, and [5]Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, Netherlands

Abstract

Background: The objective of this systematic review was to evaluate the performance of prognostic survival models for intrahepatic cholangiocarcinoma (iCCA) when validated in an external dataset. Furthermore, it sought to identify common prognostic factors across models, and assess methodological quality of the studies in which the models were developed.

Methods: The PRISMA guidelines were followed. External validation studies of prognostic models for patients with iCCA were searched in 5 databases. Model performance was assessed by discrimination and calibration.

Results: Thirteen external validation studies were identified, validating 18 different prognostic models. The Wang model was the sole model with good performance (C-index above 0.70) for overall survival. This model incorporated tumor size and number, lymph node metastasis, direct invasion into surrounding tissue, vascular invasion, Carbohydrate antigen (CA) 19-9, and carcinoembryonic antigen (CEA). Methodological quality was poor in 11/12 statistical models. The Wang model had the highest score with 13 out of 17 points.

Conclusion: The Wang model for prognosis after resection of iCCA has good quality and good performance at external validation, while most prognostic models for iCCA have been developed with poor methodological quality and show poor performance at external validation.

Received 2 June 2020; accepted 5 July 2020

Correspondence

Bas G. Koerkamp, Department of Surgery, Erasmus MC Cancer Institute, 's Gravendijkwal 230, Room H-809, 3015 CE Rotterdam, Netherlands. Tel: +31 10 703 1810. E-mail: b.grootkoerkamp@erasmusmc.nl

Introduction

Intrahepatic cholangiocarcinoma (iCCA) is an adenocarcinoma forming in the peripheral bile ducts. Its incidence in Europe and the United States is approximately 1–2 per 100,000.[1–3] iCCA is the second most common malignancy arising from the liver, accounting for 3% of all cases of gastro-intestinal cancer.[4,5] Only about 10% of patients with iCCA present with resectable disease.[6] To obtain negative resection margins, major hepatectomies are required, because tumors are often large and show intraductal and periductal spread.[4]

Many prognostic models have been proposed to predict survival for individual patients after resection of iCCA.[7–10] More accurate prediction of outcomes may improve shared decision-making and personalized medicine.[7–10] For example, post-operative models can be used to guide adjuvant therapy and frequency of surveillance for recurrent disease. The performance

[*] These authors contributed equally to this work.

of a prognostic model is determined by discrimination and calibration.[11] Discrimination is the ability of the model to determine which patient is at high-risk and which patient is at low-risk of adverse outcomes. Calibration is the agreement between the observed and predicted outcomes for individual patients.[11] Model performance should be judged at external validation prior to clinical use. Non-validated models are at a risk of overestimating predictive ability, a risk known as optimism.[11] This is especially important in a heterogeneous disease such as iCCA.[12]

A recent systematic review demonstrated that the majority of prognostic models in high-impact journals do not follow methodological recommendations, limiting their applicability and reliability.[13] To determine the external validity of prognostic models in patients with resected iCCA, a systematic review to identify all externally validated prognostic models for survival was performed. Furthermore, this article sought to identify common prognostic factors across models, and assess methodological quality of the studies in which the models were developed.

Methods

This study was part of the VALidated surgIcal moDels of hepATobiliary malignanciEs (VALIDATE) effort, to index and appraise all validated surgical models for survival after hepatobiliary malignancies (hepatocellular carcinoma, colorectal liver metastasis, pancreatic duct adenocarcinoma, pancreatic neuroendocrine tumors, distal, perihilar and intrahepatic cholangiocarcinoma). The PRISMA Statement was followed for the reporting of this systematic review (www.prisma-statement.org). A comprehensive search of Embase, Medline, Web of Science, the Cochrane database, and Google Scholar was performed, using the search terms provided in Appendix A1. The last search was conducted on July 18th, 2019. Eligible studies performed an external validation of one or more prognostic models for disease-free survival (DFS) or overall survival (OS) among patients who underwent a resection for iCCA. All studies written in the English language and published after 1990 were considered. Non-original articles (i.e. reviews or expert opinions) were excluded. Studies with prognostic models containing prognostic factors that are not used in clinical practice (e.g., RNA/DNA sequencing data or liquid biopsies) were also excluded. Studies were excluded if no model performance measures were reported.[14] Studies with patients treated with transplantation, ablation, or other techniques other than resection were excluded. Studies focused on recurrence of iCCA were excluded.

Validation studies

Three reviewers (SB, BGa and BB) independently assessed the abstracts of all studies identified by the search. Eligibility was determined by reviewing the full manuscript of potentially relevant studies. Disagreement among the reviewers was resolved by discussion. Descriptive, methodological, and outcome data from each validation study were extracted using a standard form by two reviewers (SB and BGa) and independently validated by a third reviewer (JV). If a validation study validated more than one prognostic model, data was extracted for each validated model.

Performance of the prognostic models at external validation was evaluated by discrimination and calibration. Discrimination was assessed using the area under the curve (AUC) of the receiver operating characteristic (ROC), Harrell's concordance index (c-index), the Brier score, or a similar measure.[11,15] Because the c-index was the most commonly reported discrimination measure, it was used as the principal measure of external validity. The c-index is the probability that for two random patients, the patient with the worst *predicted* survival had the worst *observed* survival. A c-index of 0.5 indicates no predictive discrimination and a value of 1.0 indicates perfect separation of patients with different outcomes.[15] For binary outcomes, i.e. studies in which time to event is disregarded, the AUC equals the c-index.[15] An AUC or c-index below 0.6 was considered poor quality, while a c-index between 0.6 - 0.7 was considered moderate quality, and a c-index above 0.7 was considered good quality. Calibration is the agreement between observed outcomes and predictions for individual patients. Calibration was assessed using the calibration plot, intercept and/or slope. Because most models do not provide an estimate of OS or DFS, assessment of the calibration of the models in validation studies was difficult. Survival curves were also used to grossly compare prognosis per risk group in the validation study with prognosis and model estimates in the development study.

Development studies

The included validation studies performed an external validation of one or more prognostic models. Using the reference lists of these studies, the corresponding publications describing the original studies in which the prognostic model was developed were identified. To determine the methodological quality of these models, a review by participants of the Cochrane Prognostic Studies group and the CHARMS checklist were used as a guideline.[13,16] Based on this review a quality assessment considering cohort description, statistical analysis, reporting of results, and model performance was systematically performed. For all reported characteristics one point could be earned, except for statistical selection of prognostic factors. The total score per model is the sum of the individual points.

Statistical analysis

Analyses were conducted using the *meta* package for R 3.5.1 (cran.r-project.org). Pooled hazard ratios (HR) with 95% confidence intervals (95% CI) were calculated by using the inverse variance method from the HR estimates in the final models. Random effects models were used as heterogeneity between included populations was assumed. C-indices were pooled on the probability scale using inverse variance weighting and random

effects meta-analysis.[17] In case of overlapping studies, the smallest study was excluded from pooling. Studies that reported no confidence bounds or standard error for their c-index or HR could not be included in pooled analysis.

Results

Validation studies

Electronic searches identified 10,282 results (Fig. 1). Of the full-text articles, 13 external validation studies for prognosis in iCCA met the inclusion criteria (Table 1). The median number (interquartile range (IQR)) of patients in which models were validated was 126 (82–367). Three studies included more than 500 patients.[18–20]

Included models

The 13 validation studies validated 18 different prognostic models (Table 1; listed separately Appendix A2). Ten prognostic models were validated in only one study. The 18 prognostic models were validated 23 times for DFS and 52 times for OS. Two models were only validated for OS,[21,22] two only for DFS,[23,24] and the other models for both outcomes. In twelve prognostic models,[10,21–31] statistical methods were used for model development; six models were expert opinion or consensus based.[32–37] One prognostic model was developed for mixed iCCA and hepatocellular carcinoma.[24] Ten models[21,25,27,30,32,33,35–38] could be applied in the preoperative setting; the other eight models required pathological prognostic factors that are only available after resection.

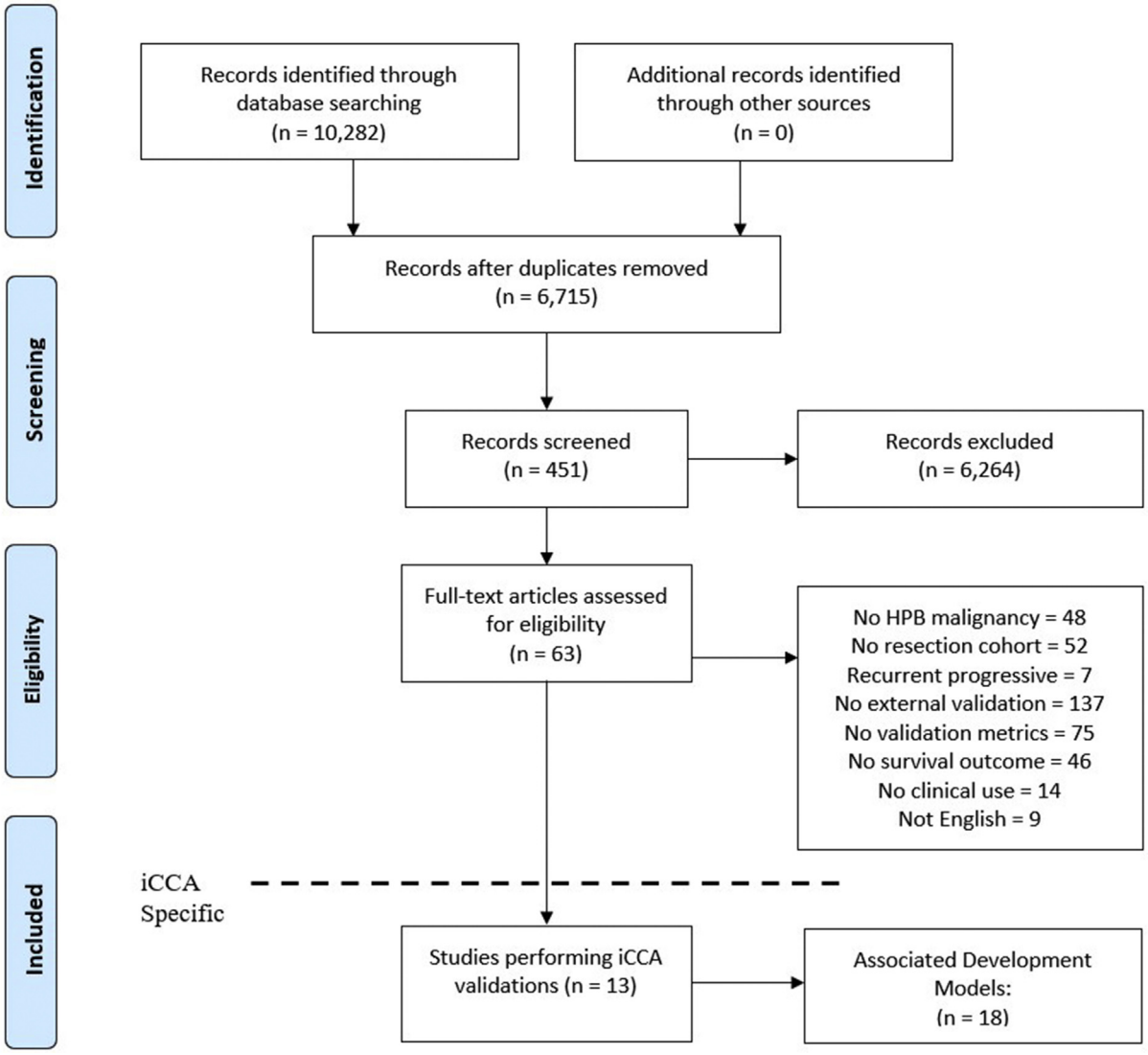

Figure 1 Prisma flow diagram of the VALIDATE effort, to find studies that validate prognostic models after resection of HPB cancer

Table 1 External validation studies of prognostic models for iCCA. Models in red have a poor performance (i.e. c-index < 0.6), in yellow a moderate performance (0.6–0.7), and in green a good performance (>0.7). The method of the PNI development study was unknown as it was not available in English. Studies that reported no confidence bounds or standard error for their c-index could not be included in pooled analysis

Outcome	Model	Validation studies	Total Patients	Pooled C-index (95%CI)	Range	I^2	Consensus or Statistical	Quality Points /17	Calibration Curve/Kaplan Meier
DFS	AJCC 6th [32]	41	54		0.68		C		None
	AJCC 7th [33]	18,23,24, 41	1528	0.58 (0.53-0.63)	0.52-0.66	74%	C		KM
	AJCC 8th [34]	41, 59	208		0.61-0.73		C		KM
	BCLC [35]	39	99		0.57		C		KM
	CLIP [25]	39	99		0.59		S	9	KM
	Hyder [26]	18	1054		0.52		S	11	KM
	LCSGJ [36]	18, 41, 59	1262	0.59 (0.52-0.66)	0.56-0.70	83%	C		KM
	mGPS [27]	39	99		0.52		S	8	KM
	Nathan [28]	18	1054		0.58		S	9	KM
	Okabayashi [29]	18	1054		0.56		S	6	KM
	Okuda [30]	39	99		0.56		S	6	KM
	PECAR score [24]	24	101		0.61		S	10	CC
	PNI [37]	39	99		0.51		N/A		KM
	Renji [23]	23	106		0.65		S	9	CC
	SHPBSJ [31]	18	1054		0.56		S	6	KM
	Wang [10]	18	1054		0.61		S	13	KM
OS	AJCC 6th [32]	10, 22, 41, 60	919	0.62 (0.58-0.67)	0.60-0.67	0%	C		KM
	AJCC 7th [33]	10, 18, 20, 22, 40, 41, 60, 61	2329	0.62 (0.59-0.64)	0.59-0.68	45%	C		KM
	AJCC 8th [34]	19, 20, 41, 59	1216	0.61 (0.51-0.72)	0.56-0.67	84%	C		KM
	BCLC [35]	39	99		0.61		C		KM
	CLIP [25]	39	99		0.58		S	9	KM
	Fudan [21]	40	188		0.55		S	8	KM
	Hyder [26]	18, 40	1242	0.61 (0.58-0.64)	0.59-0.63	0%	S	11	CC
	LCSGJ [36]	10, 18, 41, 59-61	2051	0.64 (0.61-0.66)	0.61-0.68	38%	C		KM
	mGPS [27]	39	99		0.46		S	8	KM
	Nathan [28]	10, 18, 61	1717	0.62 (0.57-0.67)	0.59-0.64	73%	S	9	KM
	Okabayashi [29]	10, 18, 60, 61	1843	0.61 (0.58-0.64)	0.59-0.67	26%	S	6	KM
	Okuda [30]	39	99		0.55		S	6	KM
	PNI [37]	39	99		0.60		N/A		KM
	SHPBSJ [31]	18	1054		0.61		S	6	KM
	Wang [10]	10, 18, 40	1243	0.70 (0.65-0.76)	0.65-0.76	51%	S	13	CC
	Yeh [22]	22	105	0.68 (0.55-0.83)	0.64-0.79	64%	S	11	CC

Consensus based models included various editions of the American Joint Committee on Cancer (AJCC) TNM staging for iCCA.[32–34] Consensus based models for HCC including the Barcelona Clinic Liver Cancer (BCLC),[35] and the prognostic nutritional index (PNI) were validated in patients with mixed iCCA and HCC tumors.[39]

Prognostic factors

The most common prognostic factors in models for iCCA are shown in Table 2. Lymph node metastases had the most severe impact on survival (pooled HR 2.20, 95% CI 1.74–2.78),[10,22] followed by multiple tumors (HR 1.63, 95% CI 1.26–2.11),[21,26] and vascular invasion (HR 1.44, 95% CI

Table 2 Model prognostic factors

	Imaging / Pathology							Clinical	Laboratory					Other
	Tumor Size	Tumor Number	Vascular Invasion	Involvement of Visceral Peritoneum	Invasion of Adjacent Organs	Regional Lymph Node Metastases	Distant Metastases	Child-Pugh	Carbohydrate Antigen 19-9	Carcino-embryonic antigen	C-reactive Protein	Lymphocyte Count	Albumin	Other factors[b]
AJCC TNM 6th Edition	a	a	a			a	a							
AJCC TNM 7th Edition		a	a	a	a	a	a							
AJCC TNM 8th Edition	a	a	a	a	a	a	a							
BCLC	a	a	a			a	a	a						
CLIP	a	a	a					a						a
FUDAN	a	a							a					a
Hyder	a	a	a			a								a
LCSGJ	a	a	a	a		a	a							
mGPS											a		a	
Nathan		a	a		a	a	a							
Okabayashi		a	a			a	a							
Okuda	a												a	a
PECAR score†			a			a								a
PNI												a	a	
Renji	a					a		a						a
SHPBSJ	a	a	a			a	a							
Wang	a	a	a		a	a			a	a				
Yeh	a		a			a				a				a
Models including factor	12	12	13	3	5	13	8	3	2	2	1	1	3	7

a Model designed for mixed hepatocellular/intrahepatic cholangiocarcinoma.
b Other prognostic factors include gender, age, symptoms, mucobilia, hepatholithiasis, tumor boundary on radiology, resection margin, growth pattern, differentiation, hepatitis B surface antigen, cirrhosis, alkaline phosphatase, gamma glutamyltransferase, bilirubin, alfa foetoprotein. Details in Appendix A3.

1.05–1.96).[10,22] The HR per centimeter tumor size increase was 1.08 in one model.[10] Two studies included demographic factors, such as age and sex.[24,26] Laboratory investigations that were used included carbohydrate antigen 19-9 (CA 19-9),[10,21] carcinoembryonic antigen (CEA),[10,22] alfa fetoprotein (AFP),[25] c-reactive protein (CRP),[27] lymphocyte count,[37] and albumin.[27,30,37] Most models used different cut-offs when categorizing prognostic factor values, limiting pooled analyses (Appendix A3).

Performance of models at validation – discrimination

The performance of 18 models was assessed in 75 external validations (Table 1). For DFS, 11 models performed poorly at pooled external validation with an AUC or c-index below 0.6 and 5 models had moderate performance with a c-index between 0.6 and 0.7, For OS, four models performed poorly and eleven models had a moderate performance. Only the Wang model reached a good performance for OS (c-index: 0.70) at pooled validation using seven prognostic factors: tumor size, tumor number, vascular invasion, invasion into adjacent organs, lymph node metastases, CA 19-9 and CEA (Fig. 2a).[10] The Wang model was validated in three external cohorts from China (n = 82; c-index: 0.75),[10] the U.S. (n = 188; c-index 0.72),[40] and Europe, China and North America (n = 1054; c-index: 0.67).[18] Yeh's model showed good discrimination (0.79) in one small validation cohort (n = 38), and comparatively low (0.64) in another (n = 67).[22] All AJCC (American Joint Committee on Cancer) staging systems had a poor or moderate performance (Fig. 2b – c). In one study, the 8th edition AJCC staging systems reached a c-index of 0.73.[41] The LCSGJ, the Japanese consensus model, performed equally modest (0.64; Fig. 2d).[36]

Performance of models at validation – calibration

Kaplan–Meier survival estimates of the different risk groups were reported in 55/75 (73%) validations. In contrast, calibration plots or tables, for comparing predicted with observed survival for individual patients were only reported in six validation studies (8%) of four prognostic models. Calibration was not reported at all in 18 (24%) validations. The Wang model demonstrated good calibration in an external validation study performed by the same authors.[10] Reasonable calibration at external validation was noted for the Wang and Hyder models.[40]

Quality assessment of development studies

The quality of six model development studies was not formally evaluated, because the prognostic models were expert or consensus based.[32–37] Quality assessment was performed for the 12 studies that used statistical modeling. The cohort was well described in all studies (Table 3; studies listed in Appendix A2). All studies were retrospective. Ten studies dichotomized or categorized continuous prognostic factors resulting in loss of information. Interaction was evaluated in two studies. Six studies had more than 15 events per variable (EPV) in the multivariable analysis, and one study had EPV <5. Handling of missing data was not adequately reported in eight studies. Statistical methods for variable selection were accurately described in only six studies. Six studies evaluated discrimination. Five studies evaluated calibration. External validation was reported in four development studies. The points score per model is appended to Table 1. The median number of points achieved was 9/17 (IQR: 8–10). The model by Wang and colleagues outperformed the other models with a score of 13/17.

Discussion

This review identified 18 validated prognostic models for survival of patients after resection of iCCA.[38,42,43] All but one of the prognostic models had a poor to moderate performance (c-statistic < 0.7) for OS on external validation and eight were

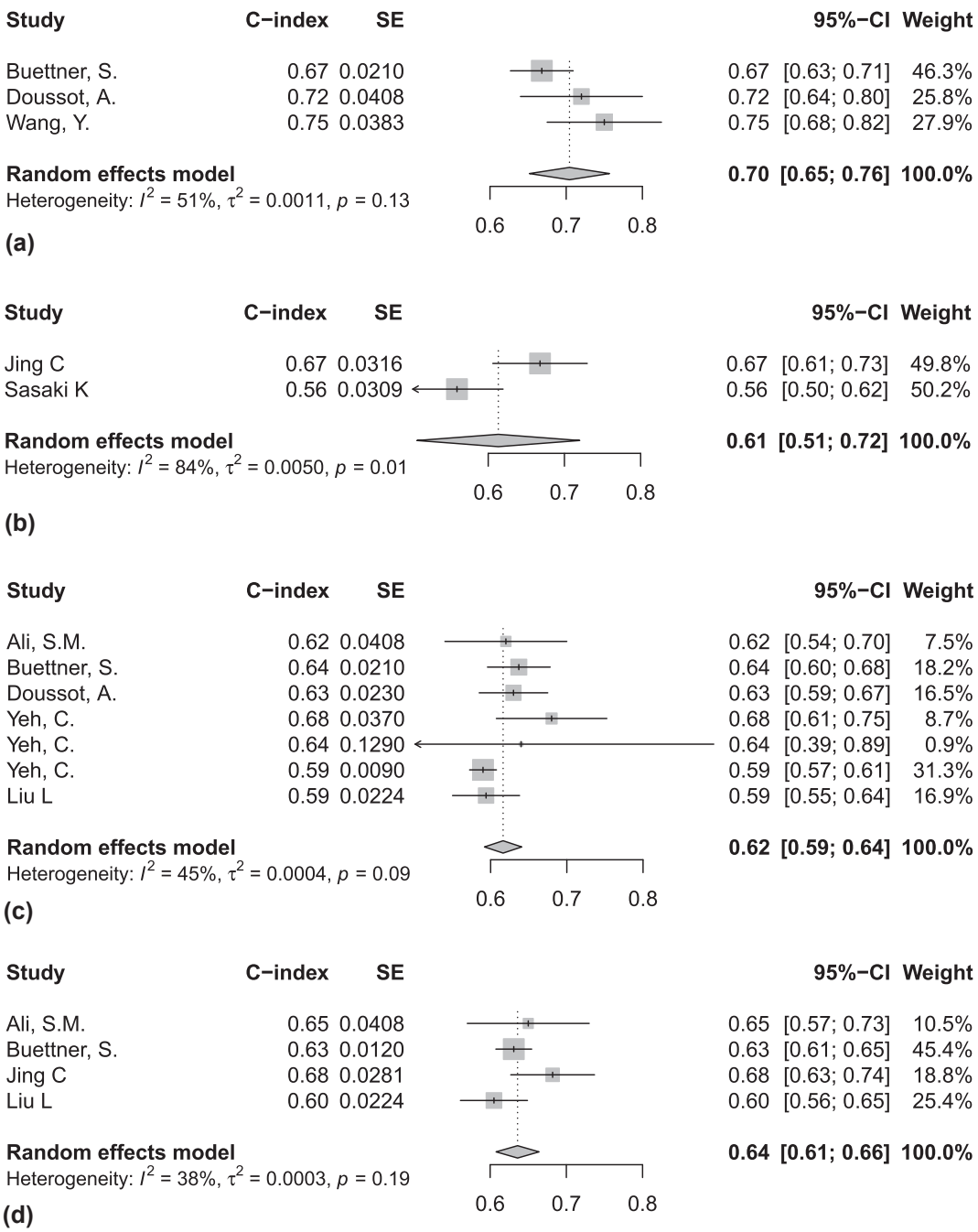

Figure 2 Forest plots of the c-index of the most relevant models for overall survival. (a) Wang model, (b) AJCC TNM 8th Edition, (c) AJCC TNM 7th Edition, (d) LCSGJ

validated only in small cohorts ($n < 500$). Only the Wang model had a good pooled performance score of 0.70 and good calibration at multiple validations.[10] The Wang model requires seven prognostic factors: tumor size, tumor number, vascular invasion, invasion into adjacent organs, lymph node metastases, CA 19-9, and CEA.[10] Performance of models predicting DFS was worse compared to models predicting OS, presumably because studies were retrospective and follow-up was not protocolized. Methodological quality of the development studies was poor, with the Wang model as one of few exceptions.

Most patients with iCCA and their treating physicians are interested in individual prognosis. Assessment of prognosis is often based on informal assessment of one or more key prognostic factors, for example, lymph node status and the number of

Table 3 Methodological quality of studies that developed prognostic models for iCCA. Quality was assessed for the cohort description, analyses, results, and performance analyses. The numbers in the table are the counts of studies that handled each quality item adequately

Cohort description	Number of Studies	iCCA (n=8)	Mixed iCCA & HCC (n=4)	Total (n=12)
	Prospective Cohort	0	0	0
	Inclusion Criteria Clear	8	4	12
	Baseline Characteristics	7	4	11
	Recruitment Dates	8	4	12
	Follow-Up Reported	7	1	8
Analyses	Outcome Definition	3	4	7
	Interaction Tested	2	0	2
	Continuous Predictors Used	2	0	2
	15 Events per variable	3	3	6
	Missing Data Reported	0	0	0
Results	Adequate Handling of Missing Data	3	1	4
	Statistical Variable Selection	8	2	10
	Clear Method for Variable Selection	3	3	6
	Univariable Results Presented	6	3	9
Performance	Multivariable Results Presented	7	2	9
	Calibration Analyzed	4	1	5
	Discrimination Analyzed	5	1	6
	Validity Assessment	5	2	7
	External Validity Assessment	3	1	4

tumors. Prognostic models are a formal method of bringing together all independent prognostic factors for the most accurate prognosis. In the era of electronic patient records, a complex equation for individual prognosis should not be a hurdle to be replaced by a simplified but inaccurate staging system or risk score. Unfortunately, individual prognosis of even the best prognostic model remains inaccurate; patients may still have an OS that is much better or worse than predicted. To some extent this leaves room for improvement of the best prognostic models, but uncertainty will always remain because of the stochastic nature of disease.[44]

Six of the 18 prognostic models for iCCA patients were based on expert opinion or consensus, rather than statistical analyses. The AJCC staging system is the best-known consensus based staging system for iCCA with three validated editions (6th, 7th, and 8th). It aims to determine prognosis for patients and physicians as well as advice on the best treatment.[34] The 8th edition continues to adhere to anatomical prognostic factors; T-stage is determined by the number of tumors, the size of the largest tumor, the presence of vascular invasion, perforation of the visceral peritoneum, and direct extrahepatic invasion; N-stage by regional lymph node involvement; and M-stage by distant metastases.[34] The performance of all three AJCC staging systems was moderate at best. Five out of seven prognostic factors in the Wang model, however, are also present in the 8th edition of the AJCC staging system. The Wang model has improved the AJCC staging by adding two nonanatomic factors (CA 19-9 and CEA) and used statistical analysis to determine the weight of each risk factor.

Poor methodological quality of the model development studies also contributed to poor performance. The four studies that described their statistical variable selection process, employed stepwise selection of prognostic factors, which leads to high variability of included prognostic factors in small studies.[11] Dichotomizing continuous prognostic factors at arbitrary cutoffs contributes to bias and less power.[45] In theory, only one definition or categorization of a risk factor is ideal per outcome and subpopulation. Furthermore, information on missing data and the way it was handled was lacking in all studies and in 8/12 studies, respectively. Commonly, regression analyses were performed with complete cases only, reducing statistical power and potentially introducing selection bias.[11,46,47] Six out of twelve studies had <15 EPV. Quality recommendations for prognostic models are available in the TRIPOD statement for transparent reporting of a multivariable prediction model for individual prognosis.[48] Organizations such as the AJCC have also developed strict guidelines for endorsement of prediction models.[49]

Performance of prognostic models was often good in small development cohorts, but poor when models were validated in a larger external dataset. This might partially be remedied by employing proper internal validation methods, most notably

bootstrapping[14,50] and internal-external cross-validation (e.g., in multicenter studies patients of each hospital are left out once in a sub analysis).[50,51] These methods were employed only in a third of the included development studies. Small cohort size is also a problem for external validation. The median validation cohort was only about 100 patients, while each year about 4000 patients are diagnosed with iCCA in the U.S. alone.[52,53] A consequence of the small sample size of validation cohorts is the observed variation in model performance between external validations. This variation resulted in a high I^2 score at pooled analyses of model performance of validation studies.

Future research should focus on collaborative development of prognostic models. The current tendency is to develop new prognostic models rather than validating existing models. This is reflected by the publication of 18 different models. Furthermore, authors should validate existing models in large cohorts from different settings, such as different hospitals in different care systems. Subsequently, models should be recalibrated if existing models have suboptimal performance (discrimination or calibration) at external validation with large cohorts. Recalibration is a simple form of model updating. It means readjusting the baseline hazard and hazard ratios of independent prognostic factors. Only in the event that validation and recalibration fail, should new models be developed.[11,42] New prognostic models for resected iCCA should explicitly report whether they are applicable in the preoperative setting or only after resection, because they require factors available after pathological exam of the resected specimen. Prognostic models with readily available patient and tumor characteristics (e.g., age and tumor stage) are important as a benchmark for novel prognostic biomarkers.[54,55] The Wang model is the current benchmark for novel prognostic biomarkers for iCCA. Expensive measurement of a novel biomarker is only useful for prognostication, if it improves on the Wang model. Novel biomarkers, however, may also aim to predict response to treatment. For example, targeted treatments for iCCA patients with genomic alterations in IDH and FGFR are currently evaluated.[56–58] The main value of such biomarkers is to determine treatment benefit rather than prognosis.

This study has several limitations. It only assessed externally validated prognostic models. Consequently, recent promising prognostic models that have not yet been validated may have been excluded. Secondly, calibration of models is difficult to quantify and summarize; consequently, only a general description of calibration was presented. Pooled hazard ratio estimates for prognostic factors are hampered by methodological quality in the published studies. Finally, all prognostic models were validated in retrospective cohorts that inherently have missing data. Validation studies rarely included all eligible consecutive patients.

Out of 18 prognostic models for iCCA, the Wang model, consisting of tumor size, tumor number, vascular invasion, invasion into adjacent organs, lymph node metastases, CA 19-9 and CEA, performed best on external validation. Most models have poor methodological quality and poor performance on external validation. Future research should focus on external validation of existing models in large cohorts from different settings, rather than developing new models in small cohorts. The best prognostic model can then be incrementally improved by adding novel biomarkers.

Acknowledgement

Wichor M. Bramer's help with constructing the search term is gratefully acknowledged.

Funding

None.

Conflict of interest

None declared.

References

1. Shin HR, Oh JK, Masuyer E, Curado MP, Bouvard V, Fang Y *et al*. (2010) Comparison of incidence of intrahepatic and extrahepatic cholangiocarcinoma–focus on East and South-Eastern Asia. *Asian Pac J Cancer Prev* 11:1159–1166.
2. Singal AK, Vauthey JN, Grady JJ, Stroehlein JR. (2011) Intra-hepatic cholangiocarcinoma–frequency and demographic patterns: thirty-year data from the M.D. Anderson Cancer Center. *J Cancer Res Clin Oncol* 137:1071–1078.
3. Everhart JE, Ruhl CE. (2009) Burden of digestive diseases in the United States Part III: liver, biliary tract, and pancreas. *Gastroenterology* 136: 1134–1144.
4. DeOliveira ML, Cunningham SC, Cameron JL, Kamangar F, Winter JM, Lillemoe KD *et al*. (2007) Cholangiocarcinoma: thirty-one-year experience with 564 patients at a single institution. *Ann Surg* 245:755–762.
5. Konstantinidis IT, Koerkamp BG, Do RK, Gonen M, Fong Y, Allen PJ *et al*. (2016 Mar 1) Unresectable intrahepatic cholangiocarcinoma: systemic plus hepatic arterial infusion chemotherapy is associated with longer survival in comparison with systemic chemotherapy alone. *Cancer* 122:758–765.
6. Spolverato G, Vitale A, Cucchetti A, Popescu I, Marques HP, Aldrighetti L *et al*. (2015) Can hepatic resection provide a long-term cure for patients with intrahepatic cholangiocarcinoma? *Cancer* 121:3998–4006.
7. Song C, Kim K, Chie EK, Kim JH, Jang JY, Kim SW *et al*. (2013) Nomogram prediction of survival and recurrence in patients with extrahepatic bile duct cancer undergoing curative resection followed by adjuvant chemoradiation therapy. *Int J Radiat Oncol Biol Phys* 87:499–504.
8. van der Gaag NA, Kloek JJ, de Bakker JK, Musters B, Geskus RB, Busch OR *et al*. (2012) Survival analysis and prognostic nomogram for patients undergoing resection of extrahepatic cholangiocarcinoma. *Ann Oncol* 23:2642–2649.
9. Wang SJ, Lemieux A, Kalpathy-Cramer J, Ord CB, Walker GV, Fuller CD *et al*. (2011) Nomogram for predicting the benefit of adjuvant chemoradiotherapy for resected gallbladder cancer. *J Clin Oncol* 29: 4627–4632.
10. Wang Y, Li J, Xia Y, Gong R, Wang K, Yan Z *et al*. (2013) Prognostic nomogram for intrahepatic cholangiocarcinoma after partial hepatectomy. *J Clin Oncol* 31:1188–1195.
11. Steyerberg EW. (2009) *Clinical prediction models: a practical approach to development, validation, and updating*. In: Gail M, Krickeberg K, Samet J, Tsiatis A, Wong W, eds. New York: Springer, p. 497.

12. Bragazzi MC, Ridola L, Safarikia S, Matteo SD, Costantini D, Nevi L *et al*. (2018) New insights into cholangiocarcinoma: multiple stems and related cell lineages of origin. *Ann Gastroenterol* 31:42–55.
13. Bouwmeester W, Zuithoff NP, Mallett S, Geerlings MI, Vergouwe Y, Steyerberg EW *et al*. (2012) Reporting and methods in clinical prediction research: a systematic review. *PLoS Med* 9:1–12.
14. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N *et al*. (2010) Assessing the performance of prediction models: a framework for some traditional and novel measures. *Epidemiology (Cambridge, Mass)* 21:128–138.
15. Harrell FE, Jr., Kerry LEE, Daniel MB. (1996) Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med* 15:361–387.
16. Moons KGM, de Groot JAH, Bouwmeester W, Vergouwe Y, Mallett S, Altman DG *et al*. (2014) Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist. *PLoS Med* 11. e1001744.
17. van Klaveren D, Steyerberg EW, Perel P, Vergouwe Y. (2014) Assessing discriminative ability of risk models in clustered data. *BMC Med Res Methodol* 14:5.
18. Buettner S, Galjart B, van Vugt JLA, Bagante F, Alexandrescu S, Marques HP *et al*. (2017) *Performance of prognostic scores and staging systems in predicting long-term survival outcomes after surgery for intrahepatic cholangiocarcinoma*.
19. Sasaki K, Margonis GA, Andreatos N, Bagante F, Weiss M, Barbon C *et al*. (2018) Preoperative risk score and prediction of long-term outcomes after hepatectomy for intrahepatic cholangiocarcinoma. *J Am Coll Surg* 226:393–403.
20. Kim Y, Moris DP, Zhang XF, Bagante F, Spolverato G, Schmidt C *et al*. (2017 Nov) Evaluation of the 8th edition American Joint Commission on Cancer (AJCC) staging system for patients with intrahepatic cholangiocarcinoma: a surveillance, epidemiology, and end results (SEER) analysis. *J Surg Oncol* 116:643–650.
21. Jiang W, Zeng ZC, Tang ZY, Fan J, Sun HC, Zhou J *et al*. (2011) A prognostic scoring system based on clinical features of intrahepatic cholangiocarcinoma: the Fudan score. *Ann Oncol* 22:1644–1652.
22. Yeh CN, Wang SY, Chen YY, Chen MH, Chiang KC, Cheng CT *et al*. (2016) A prognostic nomogram for overall survival of patients after hepatectomy for intrahepatic cholangiocarcinoma. *Anticancer Res* 36:4249–4258.
23. Jeong S, Cheng Q, Huang L, Wang J, Sha M, Tong Y *et al*. (2017) Risk stratification system to predict recurrence of intrahepatic cholangiocarcinoma after hepatic resection. *BMC Cancer* 17.
24. Tian MX, Luo LP, Liu WR, Deng W, Yin JC, Jin L *et al*. (2019) Development and validation of a prognostic score predicting recurrence in resected combined hepatocellular cholangiocarcinoma. *Cancer Manag Res* 11:5187–5195.
25. A new prognostic system for hepatocellular carcinoma: a retrospective study of 435 patients: the Cancer of the Liver Italian Program (CLIP) investigators. *Hepatology (Baltimore, Md)* 28, (1998):751–755.
26. Hyder O, Marques H, Pulitano C, Marsh JW, Alexandrescu S, Bauer TW *et al*. (2014) A nomogram to predict long-term survival after resection for intrahepatic cholangiocarcinoma: an Eastern and Western experience. *JAMA Surg* 149:432–438.
27. McMillan DC, Crozier JE, Canna K, Angerson WJ, McArdle CS. (2007) Evaluation of an inflammation-based prognostic score (GPS) in patients undergoing resection for colon and rectal cancer. *Int J Colorectal Dis* 22:881–886.
28. Nathan H, Aloia TA, Vauthey JN, Abdalla EK, Zhu AX, Schulick RD *et al*. (2009) A proposed staging system for intrahepatic cholangiocarcinoma. *Ann Surg Oncol* 16:14–22.
29. Okabayashi T, Yamamoto J, Kosuge T, Shimada K, Yamasaki S, Takayama T *et al*. (2001) A new staging system for mass-forming intrahepatic cholangiocarcinoma: analysis of preoperative and postoperative variables. *Cancer* 92:2374–2383.
30. Okuda K, Ohtsuki T, Obata H, Tomimatsu M, Okazaki N, Hasegawa H *et al*. (1985) Natural history of hepatocellular carcinoma and prognosis in relation to treatment. Study of 850 patients. *Cancer* 56:918–928.
31. Uenishi T, Ariizumi S, Aoki T, Ebata T, Ohtsuka M, Tanaka E *et al*. (2014) Proposal of a new staging system for mass-forming intrahepatic cholangiocarcinoma: a multicenter analysis by the Study Group for Hepatic Surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. *J Hepatobiliary Pancreat Sci* 21:499–508.
32. Greene F, Page D, Fleming I, Balch C, Haller D, Morrow M. (2002) *AJCC cancer staging manual*, 6th ed. Springer.
33. Edge S, Byrd D, Compton C, Fritz A, Greene F, Trotti A. (2009) *AJCC cancer staging handbook: from the AJCC cancer staging manual*, 7th ed. Springer.
34. Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK *et al*. (2017) *AJCC cancer staging manual*, 8th ed. Springer.
35. Llovet JM, Fuster J, Bruix J. (2002) Prognosis of hepatocellular carcinoma. *Hepato-gastroenterology* 49:7–11.
36. The Liver Cancer Study Group of Japan. (2003) *General rules for the clinical and pathological study of primary liver cancer*, 2nd ed. Kanehara.
37. Onodera T, Goseki N, Kosaki G. (1984) [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. *Nihon Geka Gakkai Zasshi* 85:1001–1005.
38. Altman DG, Vergouwe Y, Royston P, Moons KG. (2009) Prognosis and prognostic research: validating a prognostic model. *BMJ* 338:b605.
39. He C, Mao Y, Wang J, Song Y, Huang X, Lin X *et al*. (2018) The predictive value of staging systems and inflammation scores for patients with combined hepatocellular cholangiocarcinoma after surgical resection: a retrospective study. *J Gastrointest Surg* 22: 1239–1250.
40. Doussot A, Groot-Koerkamp B, Wiggers JK, Chou J, Gonen M, Dematteo RP *et al*. (2015) Outcomes after resection of intrahepatic cholangiocarcinoma: external validation and comparison of prognostic models. *J Am Coll Surg* 221:452–461.
41. Kim S, An C, Han K, Kim MJ. (2009 Jun 4) Gadoxetic acid enhanced magnetic resonance imaging for prediction of the postoperative prognosis of intrahepatic mass-forming cholangiocarcinoma. *Abdom Radiol* 338:b606.
42. Moons KG, Altman DG, Vergouwe Y, Royston P. (2009) Prognosis and prognostic research: application and impact of prognostic models in clinical practice. *BMJ* 338:b606.
43. Laupacis A, Sekar N, Stiell IG. (1997) Clinical prediction rules. A review and suggested modifications of methodological standards. *J Am Med Assoc* 277:488–494.
44. Coggon DI, Martyn CN. (2005) Time and chance: the stochastic nature of disease causation. *Lancet (London, England)* 365:1434–1437.
45. Royston P, Altman DG, Sauerbrei W. (2006) Dichotomizing continuous predictors in multiple regression: a bad idea. *Stat Med* 25:127–141.
46. Greenland S, Finkle WD. (1995) A critical look at methods for handling missing covariates in epidemiologic regression analyses. *Am J Epidemiol* 142:1255–1264.

47. Little RJA, Rubin DB. (2014) *Statistical analysis with missing data*. John Wiley & Sons.
48. Collins GS, Reitsma JB, Altman DG, Moons KG. (2015) Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *BMJ* 350:g7594.
49. Kattan MW, Hess KR, Amin MB, Lu Y, Moons KGM, Gershenwald JE *et al*. (2016) American Joint Committee on Cancer acceptance criteria for inclusion of risk models for individualized prognosis in the practice of precision medicine. *CA Cancer J Clin* 66:370–374.
50. Steyerberg EW, Harrell FE. (2016) Prediction models need appropriate internal, internal–external, and external validation. *J Clin Epidemiol* 69(Suppl C):245–247.
51. Steyerberg EW, Harrell FE, Jr., Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. (2001) Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol* 54:774–781.
52. Bridgewater J, Galle PR, Khan SA, Llovet JM, Park JW, Patel T *et al*. (2014) Guidelines for the diagnosis and management of intrahepatic cholangiocarcinoma. *J Hepatol* 60:1268–1289.
53. Saha SK, Zhu AX, Fuchs CS, Brooks GA. (2016) Forty-year trends in cholangiocarcinoma incidence in the U.S.: intrahepatic disease on the rise. *Oncologist* 21:594–599.
54. Margonis GA, Buettner S, Andreatos N, Sasaki K, Ijzermans JNM, van Vugt JLA *et al*. (2017) Anatomical resections improve disease-free survival in patients with KRAS-mutated colorectal liver metastases. *Ann Surg* 266:641–649.
55. Brudvik KW, Jones RP, Giuliante F, Shindoh J, Passot G, Chung MH *et al*. (2019 Jan) RAS mutation clinical risk score to predict survival after resection of colorectal liver metastases. *Ann Surg* 269:120–126.
56. Borger DR, Tanabe KK, Fan KC, Lopez HU, Fantin VR, Straley KS *et al*. (2012) Frequent mutation of isocitrate dehydrogenase (IDH) 1 and IDH2 in cholangiocarcinoma identified through broad-based tumor genotyping. *Oncologist* 17:72–79.
57. Wang P, Dong Q, Zhang C, Kuan P-F, Liu Y, Jeck WR *et al*. (2013) Mutations in isocitrate dehydrogenase 1 and 2 occur frequently in intrahepatic cholangiocarcinomas and share hypermethylation targets with glioblastomas. *Oncogene* 32:3091.
58. Banales JM, Cardinale V, Carpino G, Marzioni M, Andersen JB, Invernizzi P *et al*. (2016) Cholangiocarcinoma: current knowledge and future perspectives consensus statement from the European Network for the Study of Cholangiocarcinoma (ENS-CCA). *Nat Rev Gastroenterol Hepatol* 13:261.

Further Reading

59. Jing CY, Fu YP, Huang JL, Zhang MX, Yi Y, Gan W *et al*. (2018) Prognostic nomogram based on histological characteristics of fibrotic tumor stroma in patients who underwent curative resection for intrahepatic cholangiocarcinoma. *Oncologist* 23:1482–1493.
60. Ali SM, Clark CJ, Mounajjed T, Wu TT, Harmsen WS, Reid-Lombardo K *et al*. (2015) Model to predict survival after surgical resection of intrahepatic cholangiocarcinoma: the Mayo Clinic experience. *HPB* 17:244–250.
61. Liu LZ, Yang LX, Zheng BH, Dong PP, Liu XY, Wang ZC *et al*. (2018) CK7/CK19 index: A potential prognostic factor for postoperative intrahepatic cholangiocarcinoma patients. *J Surg Oncol* 117:1531–1539.

Appendix A1. Search terms

Embase.com

(('nomogram'/de OR (nomogram*):ab,ti) OR ((((prediction/de OR prognosis/de OR survival/exp OR mortality/exp OR 'tumor recurrence'/exp OR recurrence/de OR 'cancer prognosis'/exp OR 'predictive validity'/de) AND (model/exp OR 'proportional hazards model'/de OR 'algorithm'/de)) OR ((predict* NEAR/6 (model* OR surviv* OR mortalit* OR recurren* OR algorithm*))):ab,ti) AND (validity/exp OR 'validation study'/de OR 'validation process'/de OR 'receiver operating characteristic'/de OR 'area under the curve'/de OR 'reproducibility'/de OR (validat* OR validit* OR (discriminat* NEAR/3 (perform* OR power*)) OR roc OR rocs OR (receiver* NEAR/3 operat* NEAR/3 (characteristic* OR curve*)) OR (area* NEAR/3 curve*) OR auc OR aucs OR concordan* OR calibrat* OR reproducib*):ab,ti))) AND ('digestive system tumor'/exp OR 'intestine resection'/exp OR 'liver resection'/exp OR 'pancreas resection'/de OR ((('digestive system' OR hepat* OR intrahepat* OR gastrointestin* OR liver OR pancrea* OR hpb OR billiar*) NEAR/3 (tumor* OR tumour OR neoplas* OR cancer OR carcino* OR adenocarcino* OR resect*)) OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom* OR cholangiocarcinom*):ab,ti) AND ('surgery'/exp OR 'surgery':lnk OR (surg* OR operative* OR operation* OR resect* OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom*):ab,ti) NOT ([animals]/lim NOT [humans]/lim)

Medline ovid

(("nomograms"/OR (nomogram*).ab,ti.) OR ((((survival/OR exp mortality/OR mortality.xs. OR "recurrence"/OR "Neoplasm Recurrence, Local"/OR "prognosis"/) AND (exp "Models, Theoretical"/OR "Algorithms"/)) OR ((predict* ADJ6 (model* OR surviv* OR mortalit* OR recurren* OR algorithm*))).ab,ti.) AND ("Reproducibility of Results"/OR "Validation Studies"/OR "Validation Studies as Topic"/OR "ROC Curve"/OR "Area Under Curve"/OR (validat* OR validit* OR (discriminat* ADJ3 (perform* OR power*)) OR roc OR rocs OR (receiver* ADJ3 operat* ADJ3 (characteristic* OR curve*)) OR (area* ADJ3 curve*) OR auc OR aucs OR concordan* OR calibrat*).ab,ti.))) AND (exp "Gastrointestinal Neoplasms"/OR "Hepatectomy"/OR "Pancreatectomy"/OR ((("digestive system" OR hepat* OR intrahepat* OR gastrointestin* OR liver OR pancrea* OR hpb OR billiar*) ADJ3 (tumor* OR tumour OR neoplas* OR cancer OR carcino* OR adenocarcino* OR resect*)) OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom* OR cholangiocarcinom*).ab,ti.) AND (exp "Surgical Procedures, Operative"/OR "surgery".xs. OR (surg* OR operative* OR operation* OR resect* OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom*).ab,ti.) NOT (exp animals/NOT humans/)

Cochrane

(((nomogram*):ab,ti) OR ((((predict* NEAR/6 (model* OR surviv* OR mortalit* OR recurren* OR algorithm*))):ab,ti)

AND ((validat* OR validit* OR (discriminat* NEAR/3 (perform* OR power*)) OR roc OR rocs OR (receiver* NEAR/3 operat* NEAR/3 (characteristic* OR curve*)) OR (area* NEAR/3 curve*) OR auc OR aucs OR concordan* OR calibrat* OR reproducib*):ab,ti))) AND ((((’digestive system’ OR hepat* OR intrahepat* OR gastrointestin* OR liver OR pancrea* OR hpb OR billiar*) NEAR/3 (tumor* OR tumour OR neoplas* OR cancer OR carcino* OR adenocarcino* OR resect*)) OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom* OR cholangiocarcinom*):ab,ti) AND ((surg* OR operative* OR operation* OR resect* OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom*):ab,ti)

Web of science

TS=((((nomogram*)) OR ((((predict* NEAR/5 (model* OR surviv* OR mortalit* OR recurren* OR algorithm*)))) AND ((validat* OR validit* OR (discriminat* NEAR/2 (perform* OR power*)) OR roc OR rocs OR (receiver* NEAR/2 operat* NEAR/2 (characteristic* OR curve*)) OR (area* NEAR/2 curve*) OR auc OR aucs OR concordan* OR calibrat* OR reproducib*)))) AND ((((("digestive system" OR hepat* OR intrahepat* OR gastrointestin* OR liver OR pancrea* OR hpb OR billiar*) NEAR/2 (tumor* OR tumour OR neoplas* OR cancer OR carcino* OR adenocarcino* OR resect*)) OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom* OR cholangiocarcinom*)) AND ((surg* OR operative* OR operation* OR resect* OR hepatectom* OR pancreatectom* OR whipple OR pancreaticoduodenectom*)) NOT ((animal* OR rat OR rats OR mouse OR mice OR murine) NOT (human* OR patient*)))

PubMed publisher

(("nomograms"[mh] OR (nomogram*[tiab])) OR ((((survival [mh] OR mortality[mh] OR mortality[sh] OR "recurrence"[mh] OR "Neoplasm Recurrence, Local"[mh] OR "prognosis"[mh]) AND ("Models, Theoretical"[mh] OR "Algorithms"[mh])) OR ((predict*[tiab] AND (model*[tiab] OR surviv*[tiab] OR mortalit*[tiab] OR recurren*[tiab] OR algorithm*[tiab])))) AND ("Reproducibility of Results"[mh] OR "Validation Studies"[mh] OR "Validation Studies as Topic"[mh] OR "ROC Curve"[mh] OR "Area Under Curve"[mh] OR (validat*[tiab] OR validit*[tiab] OR (discriminat*[tiab] AND (perform*[tiab] OR power*[tiab])) OR roc OR rocs OR (receiver*[tiab] AND (operating[tiab]) AND (characteristic*[tiab] OR curve*[tiab])) OR (area*[tiab] AND curve*[tiab]) OR auc OR aucs OR concordan*[tiab] OR calibrat*[tiab])))) AND ("Gastrointestinal Neoplasms"[mh] OR "Hepatectomy"[mh] OR "Pancreatectomy"[mh] OR ((("digestive system" OR hepatic*[tiab] OR hepato*[tiab] OR hepatob*[tiab] OR hepatoc*[tiab] OR intrahepat*[tiab] OR gastrointestin*[tiab] OR liver OR pancreas*[tiab] OR pancreat*[tiab] OR hpb OR billiar*[tiab]) AND (tumor*[tiab] OR tumour OR neoplas*[tiab] OR cancer OR carcino*[tiab] OR adenocarcino*[tiab] OR resect*[tiab])) OR hepatectom*[tiab] OR pancreatectom*[tiab] OR whipple OR pancreaticoduodenectom*[tiab] OR cholangiocarcinom*[tiab])) AND ("Surgical Procedures, Operative"[mh] OR "surgery"[sh] OR (surg*[tiab] OR operation*[tiab] OR operative*[tiab] OR resect*[tiab] OR hepatectom*[tiab] OR pancreatectom*[tiab] OR whipple OR pancreaticoduodenectom*[tiab])) NOT (animals[mh] NOT humans[mh]) AND publisher[sb]

Google scholar

nomogram|nomograms "liver|pancreas|pancreatic|hepatic|hpb surgery|resection"|hepatectomy|hepatectomies|pancreatectomy|pancreaticoduodenectomy|pancreatectomies|pancreaticoduodenectomies|whipple.

Appendix A2. Included models

Based on Statistical Analysis

1. **CLIP.** A new prognostic system for hepatocellular carcinoma: a retrospective study of 435 patients: the Cancer of the Liver Italian Program (CLIP) investigators. Hepatology 1998; 28(3): 751–5.
2. **Fudan.** Jiang W, Zeng ZC, Tang ZY, et al. A prognostic scoring system based on clinical features of intrahepatic cholangiocarcinoma: the Fudan score. Ann Oncol 2011; 22(7): 1644–52.
3. **Hyder et al**. Hyder O, Marques H, Pulitano C, et al. A nomogram to predict long-term survival after resection for intrahepatic cholangiocarcinoma: an Eastern and Western experience. JAMA Surg 2014; 149(5): 432–8.
4. **mGPS.** McMillan DC, Crozier JE, Canna K, Angerson WJ, McArdle CS. Evaluation of an inflammation-based prognostic score (GPS) in patients undergoing resection for colon and rectal cancer. Int J Colorectal Dis 2007; 22(8): 881–6.
5. **Nathan.** Nathan H, Aloia TA, Vauthey JN, et al. A proposed staging system for intrahepatic cholangiocarcinoma. Ann Surg Oncol 2009; 16(1): 14–22.
6. **Okabayashi.** Okabayashi T, Yamamoto J, Kosuge T, et al. A new staging system for mass-forming intrahepatic cholangiocarcinoma: analysis of preoperative and postoperative variables. Cancer 2001; 92(9): 2374–83.
7. **Okuda.** Okuda K, Ohtsuki T, Obata H, et al. Natural history of hepatocellular carcinoma and prognosis in relation to treatment. Study of 850 patients. Cancer 1985; 56(4): 918–28.
8. **PECAR score.** Tian MX, Luo LP, Liu WR, Deng W, et al. Development and validation of a prognostic score predicting recurrence in resected combined hepatocellular cholangiocarcinoma. Cancer Manag Res. 2019 Jun 5; 11:5187–5195.
9. **Renji Nomogram.** Jeong S, Cheng Q, Huang L, et al. Risk stratification system to predict recurrence of intrahepatic cholangiocarcinoma after hepatic resection. *BMC Cancer* 2017; **17**(1).

10. **SHPBSJ.** Uenishi T, Ariizumi S, Aoki T, et al. Proposal of a new staging system for mass-forming intrahepatic cholangiocarcinoma: a multicenter analysis by the Study Group for Hepatic Surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2014; 21(7): 499–508.
11. **Wang.** Wang Y, Li J, Xia Y, et al. Prognostic nomogram for intrahepatic cholangiocarcinoma after partial hepatectomy. J Clin Oncol 2013; 31(9): 1188–95.
12. **Yeh.** Yeh CN, Wang SY, Chen YY, et al. A Prognostic Nomogram for Overall Survival of Patients After Hepatectomy for Intrahepatic Cholangiocarcinoma. *Anticancer Res* 2016; **36**(8): 4249–58.

Consensus Based Models

13. **AJCC 6th Edition.** Greene F, Page D, Fleming I, Balch C, Haller D, Morrow M. AJCC Cancer Staging Manual. 6th edition ed: Springer 2002.
14. **AJCC 7th Edition.** Edge S, Byrd D, Compton C, Fritz A, Greene F, Trotti A. AJCC cancer staging handbook: from the AJCC cancer staging manual 7th edition. New York: Springer; 2009.
15. **AJCC 8th Edition.** Amin MB, Edge S, Greene F, et al. (eds.) AJCC Cancer Staging Manual. 8th ed. New York: Springer International Publishing; 2017.
16. **BCLC.** Llovet JM, Fuster J, Bruix J. Prognosis of hepatocellular carcinoma. Hepato-gastroenterology 2002; 49(43): 7–11.
17. **LCSGJ.** The Liver Cancer Study Group of Japan. General rules for the clinical and pathological study of primary liver cancer, Second edn. Tokyo: Kanehara; 2003.
18. **PNI.** Onodera T, Goseki N, Kosaki G. [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. Nihon Geka Gakkai Zasshi 1984; 85(9): 1001–5.

Appendix A3. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2020.07.007.