Systematic review

Models for Predicting Risk of Acute Kidney Injury after Liver Surgery

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Abstract:

Background & Aims: Acute kidney injury (AKI) is a serious complication of liver surgery and associated with significant morbidity and mortality. The incidence of AKI following hepatic surgery can be as high as 94%, with highest rates seen following orthotopic liver transplantation, particularly when extended criteria grafts are used. Strategies to identify patients at risk of AKI may enable early interventions to prevent or minimise AKI.

Methods: A systematic review was conducted using PubMed, Medline, Cochrane and Google Scholar databases for literature reporting models predicting risk of AKI following liver surgery. All were scrutinised for model variables, performance of the models, and validation strategies in order to identify key factors associated with increased risk.

Results: From an initial pool of 1432 results, seven articles were identified which reported risk prediction models for AKI. These included articles using either an equation-based model or point-based system for risk prediction and two studies were clinically validated. Whilst predictive variables varied from study to study, factors relating to liver function (MELD), cardiovascular integrity and extent of surgical blood loss were important for determining risk.

Conclusions: This study has identified key discriminating variables that show promise in predicting risk of AKI in patients undergoing hepatic surgery. However it is important to note that a robust risk prediction model derived from a large prospective cohort study, recruiting

patients from multiple centres who experience specific types of hepatobiliary intervention is currently lacking. Thus further studies are required to develop a robust model that can be applicable across multiple patient populations with different underlying aetiologies.

Keywords
Hepatic; renal; acute injury; prediction; model

1. Introduction

Acute kidney injury (AKI), is characterised by a rapid (hours to days) decrease in renal function and is associated with poor estimated Glomerular Filtration rate (eGFR), longer hospital stay, development of chronic kidney disease (CKD) and increase in short- and long-term mortality in hospitalised patients [1, 2]. Recent data reveals that up to 40% of AKI cases in acutely hospitalised patients occur in perioperative settings, and are a significant contributing factor to high morbidity and mortality [3]. Since overall perioperative mortality in the AKI group may be over seven times greater than the adjusted non-AKI cohort undergoing cardiac surgery [4] much effort has been given to predicting risks of AKI following cardiac surgery. Indeed, Huen and Chirag [5] identified seven different risk stratification models for AKI following cardiac surgery in their recent systematic review of which four of the models have been independently validated in individual cohorts. However, AKI is also an important factor in non-cardiac and general surgical patients [6] with the incidence of AKI reported to be up to 22% depending on the type of surgical procedure [7]. One study of 457,656 patients who underwent non-cardiac and non-vascular abdominal surgery revealed a 30 day mortality of 31% in patients developing AKI compared to 1.9% in the non-AKI cohort after being adjusted for confounding factors [8]. A systematic review of the risk prediction models for AKI following major non-cardiac surgery (including general abdominal surgery and liver surgery) identified seven models based upon both preoperative and interoperative factors [6]. However, none of the prediction models have been validated in independent cohorts and to date there are no studies reporting clinical implementation or analyses of clinical impact. Importantly data on AKI incidence and outcomes following hepatobiliary surgery is scarce, with no robust study including outcomes following both transplant and non-transplant procedures.

Some studies suggest that incidence of AKI following specific hepatobiliary surgery types is comparable to cardiac surgery and can be as high as 94% [9]. Of note, variation in incidence is influenced by type of hepatobiliary surgery performed and the diagnostic criteria used to characterise AKI, although increase in baseline serum creatine values by above 50% is commonly used. Highest incidences of AKI are seen following orthotopic liver transplantation, and in common with cardiac surgery, this is associated with increased length of hospital stay, mortality and increased costs [10]. With the current growing burden of liver disease [11] driving increases in liver transplantation [12] and resection surgery [13], the number of patients undergoing liver surgery is increasing annually. Despite this, prediction of AKI in patients undergoing specific hepatic or biliary interventions has not received as much attention. Although risk factors for AKI following hepatobiliary surgery are reported, [14-16] the risks vary dependent on the nature of

the surgical intervention, as well as diagnostic criteria used and few authors have proposed risk prediction models to aid with management of patients. Therefore, this review endeavours to collate the literature available on AKI prediction models to consolidate current understanding of risk of AKI following all types of liver surgery. Our aim was to develop a scheme to identify high-risk patients, with a view to proposing potential preventative or early management interventions that could be undertaken to improve patient outcomes.

Ethics Statement

This work constitutes a systematic review of evidence carried out at the University of Birmingham. This article in part presents independent research funded by the NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

2. Materials and Methods

A comprehensive literature search of four databases was conducted followed by a three stage review process to identify the pertinent literature in accordance with the PRISMA standard [17]. The search was conducted with strict adherence to our pre-specified criteria to exclude irrelevant titles and ensure consistency. Pubmed, Medline, Cochrane and Google Scholar databases were searched using four search themes: 'acute kidney injury', 'surgery', 'prediction' and 'risk score', and all variations to identify studies which reported prediction models for the risk of AKI in post-operative patients (Table 1).

2.1 Study Selection Criteria

The first stage of the review was an exclusion based on article titles. Exclusion criteria included; all foreign language articles, studies reporting data from non-human subjects, duplicate articles, articles reporting non-primary data (e.g. review articles) and studies which obtained data from paediatric patients or those under 18 years of age. The second stage of the review was exclusion based on the abstract, and additional exclusion criteria were imposed. Here studies which contained qualitative data, measured primary outcome as mortality, utilised previously published datasets, reported patients with pre-existing renal disease, reported cardiac and/or vascular surgery, reported only the incidence of AKI without risk factors or reported occurrence of renal injury greater than 30 days post-operation were excluded. Articles which reported risk factors of AKI in non-surgically managed patients were excluded regardless of whether they were considered or listed for surgery. Articles were included if they contained a model stratifying risk factors for AKI after major liver surgery, including but not limited to recipients of whole liver grafts, recipients of split grafts, live liver donors and patients undergoing liver resections for both neoplastic and non-neoplastic lesions.

2.2 Data Extraction

All studies were scrutinised for the model variables applied, validation strategies and predictive performance of model (area under curve (AUC)).

Table 1 Database search terms.

| MeSH search terms		
'acute kidney injury'	**OR**	'acute kidney failure', 'acute renal failure', 'acute renal injury', 'renal insufficiency', 'acute kidney damage', 'renal replacement therapy'
AND		
'surgery'	**OR**	'surgical procedure', 'operation', 'preoperative', 'postoperative', 'perioperative'
AND		
'prediction'	**OR**	'predict', 'predictive', 'prognosis', 'prognostic'
AND		
'risk score'	**OR**	'risk model', 'risk stratification', 'risk algorithm', 'risk equation', 'risk index', 'predictive index'

Table summarising the key words and terms used for identification of relevant articles

3. Results

3.1 Studies Considered

The search yielded 1432 articles from the four databases of which 1194 results were excluded by title in the first stage of screening. The abstracts of the remaining 238 results were reviewed and 199 were excluded as they included data from patients undergoing cardiac surgery, did not measure outcome in terms of acute renal injury, included paediatric patients or used secondary data. The remaining 39 articles were included for full text review (Figure 1). Overall, the search yielded a total of seven articles proposing ten different models for predicting risk of AKI following liver surgery. Collectively, the seven articles include data from 1989 patients recruited from seven centres across six countries (USA, China, Germany, Switzerland, Japan and Korea). The results are summarised in Table 2. Six [18-23] of the seven remaining articles included cohorts of patients undergoing liver transplantation, of which two articles (Utsumi *et al*., [21] and Park *et al*., [22]) exclusively included patients receiving transplantation from living donors. The seventh study (Slankamenac *et al.,* [24]) was the only one to include patients who underwent any form of liver surgery (including liver transplantation) in their cohort. Interestingly, two of the studies [20, 22], proposed more than one risk prediction model. The number of patients included in the studies, including derivation cohort and validation cohort, ranged from 866 [18] to 71 [19] with the median being 200 [21]. Importantly, all included studies contained retrospectively collected cohort data from single centres (Table 2).

Figure 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart for study selection.
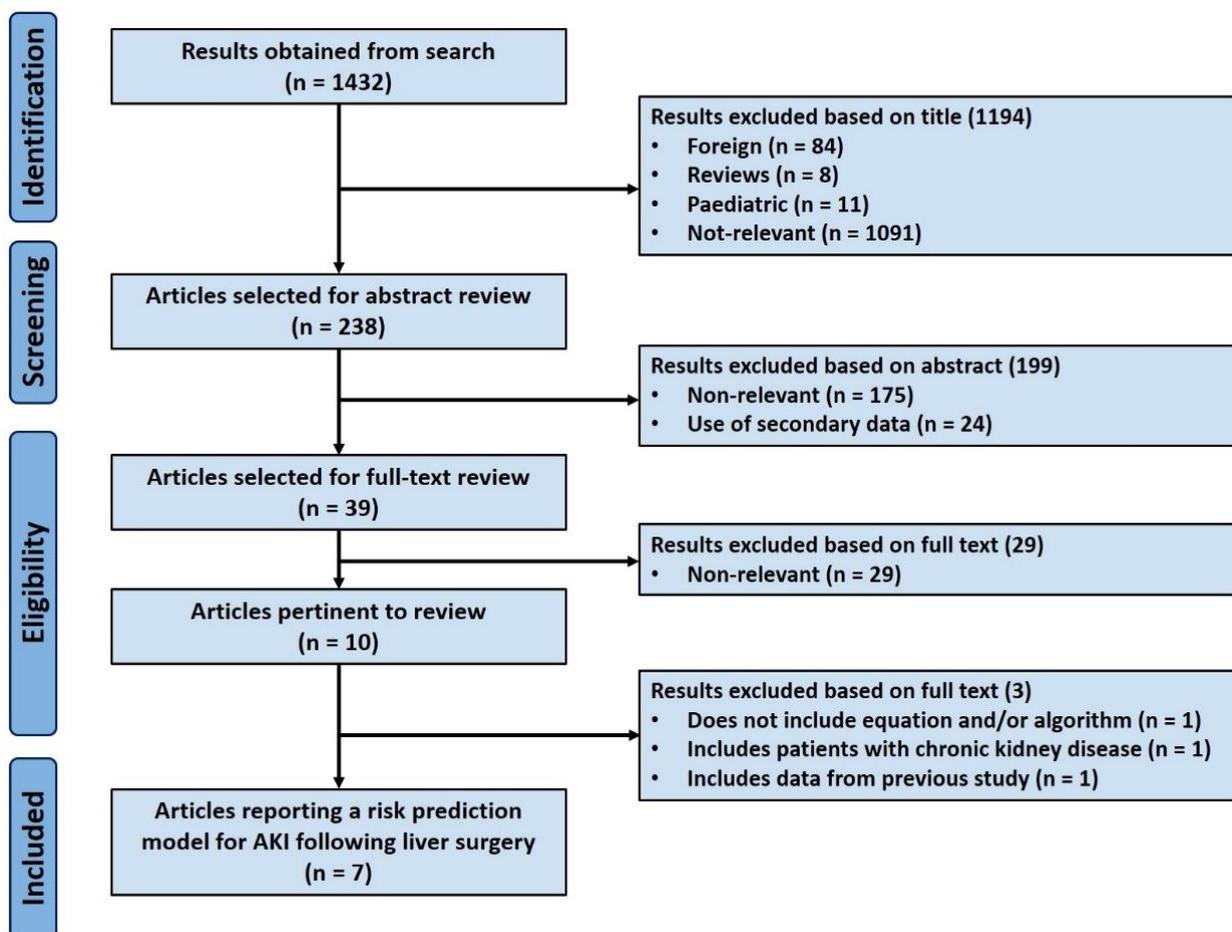
The flow chart summarises the steps taken to choose relevant articles and the number of articles included/excluded at each stage in our review process

3.2 Defining AKI and Prediction Variables

The definition of AKI and outcome measures used, varied between the studies. Two studies [18, 23] opted to define AKI as the need for renal replacement therapy (RRT). Rueggeberg *et al.* [19] also defined AKI in their study based on need for RRT, but also combined this with an increase in serum creatinine (SCr). Xu *et al.* [20] and Slankamenac *et al.* [24] defined AKI using the Acute Kidney Injury Network (AKIN) classification also based on an increase in SCr above the preoperative baseline [25]. In contrast, Utsumi *et al.* [21] and Park *et al.* [22] opted to define AKI using the Risk, Injury, Failure, Loss, End-stage Renal Disease (RIFLE) criteria [26] categorising their AKI groups into further sub-categories.

Variables that predict risk of AKI also differed between the studies and the four variables with the highest odds ratio are summarised in Table 3. These include factors such as Model for End-stage Liver Disease (MELD) score and other hepatic parameters, extended ITU stays, concurrent disease and amount of blood products needed during the procedure. Park *et al.* [22] factored in the greatest number of variables at 20 for their primary model reducing that number to 14 and 10 for their secondary and tertiary models, respectively. In contrast Xu *et al.* [20] considered the

fewest variables for their secondary model factoring only SCr and serum sodium concentrations. However, for their primary prediction score they include four factors, joint fewest with Sanchez *et al*. [18]. Four of the studies [18-20, 23] stratified the risks of AKI by using the values of the predictive variables in a model to calculate a risk score. Three studies [18-20] developed a threshold where a superthreshold score indicates risk of AKI or need for RRT. Hence Kim *et al*. [23] developed a nomogram which calculates risk of AKI using an equation score based on a hepatic encephalopathy score, use of deceased donor liver, MELD, intraoperative blood loss and cancer as the underlying cause of surgery. In contrast, other investigators [21, 22, 24] developed a points-based system where each predictive variable is attributed a certain number of points, the total of which correlates with a percentage risk of AKI. The four variables with the highest predictive values (Table 3, measured as either odds ratio or regression coefficient) from each of the primary prediction models differed between studies (greater than 3 days of intensive care unit (ICU) stay [18], diagnosis of hypertension [19], intraoperative oliguria [20], serum alanine transferase (ALT) above 35 IU [24], intraoperative blood loss of more than 55ml/kg [21], presence of hepatic encephalopathy [23] and transfusion of more than six units of cryoprecipitate [22]) with no single variable appearing in the top four of all prediction models proposed (Table 3). However as noted above, MELD score, was the most frequent variable appearing in the top four predictive variables of four studies [18, 21-23], and similarly factors relating to blood loss or replacement and cardiovascular parameters were common in most models.

3.3 Validation

Development of a predictive model that is robust when applied to an external cohort, suggests it is likely to be prognostic across a range of patient populations. Hence, previous studies using prediction models developed to identify risks of AKI following cardiac surgery [27, 28] incorporate external validation to assess their predictive power. In contrast only half of the risk prediction models in the context of liver surgery considered here [18-20] underwent clinical validation. Models from three other studies [22-24] were only validated statistically, and interestingly one of the studies [21] did not carry out any internal validation at all.

In summary, the evidence shows that the most significant variables for predicting risk of AKI in hepatobiliary surgery are greater than three-day stay in ICU, intraoperative oliguria, major intraoperative blood loss and pre-operative diagnosis of hypertension. The MELD score is also highly relevant as it is a contributing element in the majority of the models. The available evidence suggests that the best model to accurately predict risk is that proposed by Sanchez et al. [18].

Table 2 Summary of articles proposing risk prediction models.

	Sanchez et al. (2004) [18]	Rueggeberg et al. (2008) [19]	Xu et al. (2010) [20]	Slankamenac et al. (2013) [24]	Utsumi et al. (2013) [21]	Kim et al. (2014) [23]	Park et al. (2015) [22]
Prediction model							
Patient population	Patients undergoing cadaveric liver transplant	Patients undergoing live donor (17) and cadaveric (54) liver transplant	Patients undergoing cadaveric liver transplant for benign end stage liver disease	Patients undergoing any liver surgery	Patients undergoing live donor liver transplants	Patients undergoing live donor (110) and cadaveric (47) liver transplant	Patients undergoing live donor liver transplants
No. of patients (Centers)	866 (1)	71 (1)	146 (1)	549 (1)	200 (1)	157 (1)	538 (1)
Design of study	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort
Measured outcome	RRT	SCr $\geq$132 µmol/l and RRT	SCr >1.5mg/dl with increase of >50% above baseline	SCr >0.3mg/dl above baseline or >50% above baseline	RIFLE criteria	RRT	RIFLE criteria
Derivation cohort	n = 724	n = 71	n = 102	n = 549	n = 200	n = 157	n = 538
Derivation period	1996 - 2001	Aug 2000 – Jun 2001	Jan 2004 - Sep 2005	Jul 2002 – Oct 2007	Aug 1996 - Jan 2011	Jan 2008 – Dec 2011	2007 - 2013
Incidence of AKI (%)	N/A	N/A	33 (32.4%)	82 (14.9%)	121 (60.5%)	N/A	147 (27.3%)
Median outcome time		5 days	2 days				

No. needing RRT (%)	87 (12.0%)	13 (18.3%)	10 (9.8%)	23 (0.04%)	30 (15%)	42 (27.3%)	34 (6.3%)
1yr mortality AKI (no AKI)	50.9% (9.0%)	39.1% (5.6%)	29.9% (7.7%)	23% (0.8%)	15.8% (3.2%)	50% (0.1%)	19.7 % (13.7%)
Predictor selection	Logistic regression (p < 0.05)	Logistic regression (p ≤ 0.15)	Logistic regression (p < 0.05	Logistic regression (p ≤ 0.15)	Logistic regression (p < 0.05)	Logistic regression (p < 0.05)	Logistic regression (p <0.05)
Internal Validation							
Validation	Temporal cohort (142)	Latter cohort (167)	Random split 30.0% (44) of derivation cohort	Cross validation (5-fold)		Bootstrap validation 200 repetitions	Cross validation (10-fold)
Validation period	2002	Jul 2001 – Dec 2003	Nov 2005 - Jul 2006	Jul 2002 – Oct 2007		Jan 2006 – Dec 2011	2007 - 2013
Performance							
Outcome incidence (%)	20 (14%)	23 (14%)	12 (27.3%)			42 (27.0%)	
Performance statistic	AUC 0.905	AUC 0.91	AUC Model 1= 0.908; 2= 0.765	AUC 0.79 [95% CI (0.73-0.84)]		AUC 0.90	AUC Model: 1= 0.85; 2= 0.86; 3=0.86
No. of variables	4	6	Model 1= 2; 2= 4	10	5	5	Model 1= 20; 2= 14; 3= 10
Prediction tool details	Equation, threshold score predicts need for RRT	Equation, threshold score predicts risk of AKI	Equation, threshold score predicts risk of AKI	Points system, with total correlating with percentage risk of AKI	Points system, with total correlating with percentage risk of AKI	Equation, with results used to interpret nomogram	Points system, with total correlating with percentage risk of AKI

Detail of the studies used for assessment of risk prediction models. Data includes indication of study size, and validation/performance assessment used. SCr- Serum creatinine, AUC- Area under curve, RRT- Renal replacement therapy, RIFLE- Risk Injury Failure Loss End-stage renal disease

Table 3 Summary of the four predictive variables with the highest odds ratio in each study.

	Sanchez et al. (2004) [18]	Rueggeberg et al. (2008) [19]	Xu et al. (2010) [20]	Slankamenac et al. (2013) [24]	Utsumi et al. (2013) [21]	Kim et al. (2014) [23]	Park et al. (2015) [22]
Predictive Variable 1	>3 day ICU stay (OR= 10.23)	Hypertension (β= 6.82)	Intraoperative oliguria ≤60ml/hr (OR= 9.42)	ALT >35IU/L (β= 1.21)	Intraoperative Blood loss ≥55ml/kg (OR= 3.70)	Hepatic encephalopathy (OR= 5.47)	Cryoprecipitate transfusion > units (OR= 7.42)
Predictive Variable 2	SCr >1.3mg/dL (OR= 3.57)	Intraoperative MAP <50mmHg (β= 5.42)	Intraoperative hypotension (OR= 4.67)	Cardiovascular Disease (β= 1.19)	Diabetes mellitus (OR= 3.23)	Cadaveric graft (OR= 3.47)	Blood loss >60ml/kg (OR= 6.95)
Predictive Variable 3	BUN >27mg/dL (or= 2.68)	Hepatitis B/C (β= 4.96)	SCr >1.2mg/dL (OR= 3.03	Hepaticojejun-ostomy (β= 0.93)	GW/RBW, % <0.7 (OR= 3.10)	Blood loss >1000ml (OR= 1.16)	Platelet transfusion >6 units (OR= 5.80)
Predictive Variable 4	MELD score > 21 (OR= 2.50)	Units of RBC required (β= 0.60)	Intraoperative noradrenaline (OR= 0.09)	Oliguria <400ml/24hr (β0.92)	MELD score ≥20 (OR= 2.96)	MELD score ≥15 (OR= 1.09)	MELD score >20 (OR= 2.97)

Detail from the final seven studies examined illustrating which predictive variables were considered most important by the authors. SCr- Serum creatinine, BUN- Blood urea nitrogen, MELD- Model for end-stage liver disease, MAP- Mean arterial pressure, ALT- Alanine transferase, GW/RBW- Graft weight/recipient body weight percentage

4. Discussion

Incidence of AKI following liver surgery can range from 12-94% in the post-operative period [9, 29-31] and has a significant impact on mortality, length of hospital stay and cost to healthcare providers [9, 10]. Furthermore, the severity of post-operative AKI correlates with increased mortality [32]. Thus reducing the risk of AKI or indeed, minimising severity of AKI must be the aim for healthcare providers. Identification of a robust prediction score applicable to a wide surgical population demographic is necessary to permit interventions to be undertaken preoperatively, intraoperatively or postoperatively to minimise the risks of AKI and thus improve patient outcomes. Preoperatively, concurrent chronic illnesses such as diabetes, hypertension and cardiovascular disease should be managed to ensure blood sugars, blood pressures and cardiac output are strictly regulated to maximise perioperative fitness and chance of survival. Factors such as intraoperative blood pressure, use of noradrenaline and urine output can be optimised therapeutically to ensure they are within ideal parameters during the operation and strategies should be undertaken to minimise perioperative blood loss. Postoperatively, strategies such as one to one nursing and presence of hepatobiliary surgeons on site throughout recovery would assist with maintenance of fluid status and hemodynamic stability. However such measures can only be implemented once the risk of AKI is identified to avoid under-managing those at high risk and over managing low risk patients. Patients who are not at high risk of AKI following liver surgery may be managed more conservatively to ensure minimum iatrogenic harm is caused and management is cost-effective.

For any risk prediction model to be successful, it should be applicable to a general population. Consequently, articles including data from paediatric patients were excluded from our analysis, as critically ill children tend to be more responsive to haemodynamic and nephrotoxic insults that usually follow paediatric liver surgery [33, 34] and their risk of AKI is not representative of the adult population. Study population size is also important, with variability between cohorts making comparison of currently available predictive models difficult. Studies appraised here had patient numbers ranging from 866 [18] to less than 100 [19] patients, but these are eclipsed by the vast cohort sizes used by studies comparing risk prediction models for non-liver surgery [35, 36]. Ideally data derived from multiple centres and different patient ethnicities would be used in a risk-prediction model to be considered as representative of a wider population. All seven studies critiqued in this systematic review included patients from single centres and none of the models were externally validated. Thus, models should be tested further to ensure for example, that predications based on the US-based studies of Sanchez et al. are as effective as predicting risk of AKI in Korean patients [22].

Similarly the indication for liver surgery for patients from six [18-23] of the seven studies included here was liver transplantation, a major procedure which has direct effects on renal function [37], as would the presence of cirrhosis and portal hypertension prior to surgery [38]. The mortality of patients undergoing liver transplant can be up to eight-fold greater if AKI develops [39] so early prediction and optimised management of AKI could have profound effects. Nevertheless, this suggests caution when predicting risk of AKI in patients undergoing non-transplant liver surgery. Causes for non-transplant liver surgery will include resection of primary and secondary tumours [40, 41], and a significant proportion of these patients may require systemic chemotherapy [42] with anti-cancer agents, some of which are nephrotoxic [43, 44]. These

patients may have an increased predisposition to suffering AKI and this should be factored in when developing specific risk prediction models.

Even mild post-operative AKI can have a significant effect on mortality and morbidity [45]. Outcome measures vary between studies of risk-prediction with some authors [18, 23] considering need for renal replacement therapy (RRT) and others [19-22, 24] varying degrees of AKI. AKI was classified using the Risk, Injury, Failure, Loss and End stage renal disease (RIFLE) classification system [26], the Acute Kidney Injury Network (AKIN) [25] classification and other measures. The RIFLE classification is based on measuring serum creatinine (SCr) or urine output. SCr is universally used for assessing renal excretory functions as part of the widely used Cockcroft-Gault equation [46]. Urine output is used in the acute, post-operative and ICU settings, and is more sensitive to renal haemodynamic changes [47]. The AKIN classification is based on a modified version of the RIFLE criteria where an absolute increase in SCr is a criterion for AKI [25]. In contrast to need for RRT, both RIFLE and AKIN criteria enable AKI to be classified across a spectrum of severity. This means that models derived from cohorts with severe AKI (needing RRT) may need adapting before they can be applied to patients who suffer mild or moderate AKI. Hence a standardised endpoint is needed to determine the severity of AKI for future model-development and ideally this would incorporate either RIFLE- or AKIN-classified AKI as an endpoint to ensure patients at risk of mild AKI are identified.

The selection of predictive factors used to derive risk models is very important. The aim should be to include only relevant factors with a high predictive power. Only one of the studies [24] used bootstrap resampling to select their predictor variables, with other studies [18-23] using step-wise regression techniques, and there was inconsistency between studies that have used preoperative, intraoperative and postoperative variables. Model for End-stage Liver Disease (MELD) was most consistently used across the studies. This is widely used to predict prognosis of patients with liver disease and to prioritise patients for liver transplants [48, 49], but as SCr concentration, bilirubin and international normalised ratio (INR) are incorporated, it is plausible that MELD score would also correlate with risk of AKI [50]. Studies predicting risk of AKI following cardiac surgery have used more novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) and inflammatory regulators such as interleukin-18 (IL-18) [51] which showed some predictive value. Neither marker is cardiac specific, but NGAL levels have been associated with higher risk colorectal cancers in a pilot surgical study [52], suggesting there may also be utility in predicting risk following hepatobiliary surgery. Further innovative imaging strategies to identify AKI and predict risk have been summarised by Hobson et al. [53] which include computational tomography (CT), magnetic resonance imaging (MRI), Doppler ultrasound and contrast enhanced ultrasound among other techniques, which may have value in the future.

All studies were scrutinised for model variables applied, presence of validation strategies and predictive performance of model (area under curve [AUC]). While AUC, sensitivity, specificity and predictive values are important in development of prediction models, caution must be taken when comparing model performances as these values are sensitive to the size of cohorts and incidence of the predicted outcome [54]. Using only two variables, the 'preoperative model' [20] achieved an AUC of 0.765 suggesting it was a reasonable test. The 'post-operative' model from the same authors [20] achieved an AUC of 0.908 using four (one pre-operative and three intraoperative) variables; suggesting use of a greater number of factors improves predictive power. However, Park et al. [22] suggest no improvement in discriminative power using a greater number of variables.

They attained an AUC of 0.85 using 20 variables (eight preoperative, 11 intraoperative and one postoperative) in their primary model and an AUC of 0.86 using 14 and 10 variables for their secondary and tertiary models, respectively [22]. Similarly Rueggeberg et al. [19] achieved an AUC of 0.91 using just six variables (three pre-operative and three intraoperative) further suggesting that increasing the variables does not equate to greater discriminative power. There was no identifiable correlation between the proportion of variables that are preoperative, intraoperative or postoperative with the performance of the model.

Four of the studies [18-20, 23] used predictive variables to form an equation from which a score was obtained. Of those four, three studies [18-20] identified a risk threshold above, which a patient is at risk of AKI (or RRT). Dichotomising the results of the prediction model into 'at risk' and 'not at risk' has obvious benefits as it is likely to be quicker to calculate, doesn't require expert judgement (making it easier for use by supporting healthcare professionals) and makes justification for clinical decisions more straightforward. In reality however, assessment it is not black and white and patients with identical model scores will have variations in the actual risk of AKI. Indeed, those who develop AKI will have different outcomes. Thus to make the dichotomous model effective, there has to be a precipitous increase in risk of AKI at the threshold score. As an alternative, the points based system used by the remaining three studies relies on the judgement of clinicians to decide where risk is deemed significant and where an intervention is indicated.

5. Conclusion

Our analysis has shown that whilst predictive variables vary from study to study, factors relating to liver function (MELD), cardiovascular integrity and extent of surgical blood loss are significant (Table 3). Ten articles could potentially have met the review criteria however one [55] did not include an equation, algorithm or scoring method and another [56] presented a robust study but included patients with pre-existing chronic kidney disease (CKD) and so was excluded. Seven articles proposed models which fit our criteria, but all had individual limitations and improvements could be made. Taking into consideration cohort size, the model design, statistical performance and ease of applicability, the most appropriate models are those proposed by Sanchez et al. [18] and Park et al. [22] although the Park study remains to be externally validated, and no single ideal model was identified. To address the need to identify those at highest risk of AKI post-operatively in the ever growing pool of patients experiencing hepatatic surgery, further evaluation is required. Ideally a prospective cohort study, recruiting patients from multiple centres, including risk factors with high predictive power, and which measures both onset of AKI and mortality is required. Furthermore, external validation should be carried out in multiple independent cohorts if findings are to be included as part of clinical guidelines for managing patients undergoing major hepatobiliary surgery.

Author Contributions

Rahman H.P. conducted the literature search and data summarisation. Rahman H.P. and Lalor P.F. contributed equally to writing the manuscript and reviewing data. Bhogal R contributed to the writing of the manuscript.

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Competing interests

The authors have no competing interest to declare.

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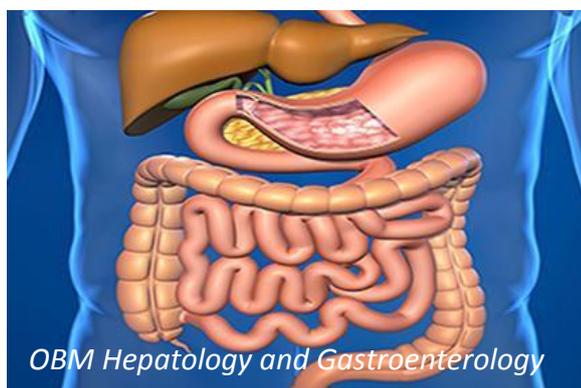
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