Original Article Liver dysfunction as an important predicting risk factor in patients undergoing cardiac surgery: a systematic review and meta-analysis

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Abstract: Liver function is not considered as a risk factor by current risk scores, such as EUROSCORE II or STS-Score for cardiac surgery. The aim of this study was to review the role of liver dysfunction, classified by the Child-Turcotte-Pugh classification or model for end-stage liver disease scores, as a risk factor for mortality and morbidity of patients following cardiac surgery. The Pubmed referencing library was searched. The rates of mortality and morbidity were calculated using SPSS software. The mortality rates in patients of Child class A, Child class B, and Child class C were pairwise compared respectively. A total of 22 reports including 939 patients from eight countries were reviewed. The mortality rate of patients increased in accordance with increased CTP classification. The lowest mortality rate was recorded in Child class A patients, followed by Child class B patients and the highest mortality rate was observed in Child class C patients. The mean complication rate ranged from 3.82% to 22.15%. Child class C patients should be considered unacceptable for cardiovascular surgery. As two studies revealed, patients with a higher MELD score had significantly higher mortality rates. Liver function should be viewed as an important risk factor for cardiovascular surgery, based on its strong association with mortality and morbidity.

Keywords: Liver dysfunction, cardiac surgery, risk model, mortality rate, meta analysis

Introduction

Liver disease has been reported as a risk factor for mortality and complications following cardiac surgery [1-5]. Advanced liver dysfunction has been shown to increase perioperative mortality as a result of coagulation disorders, haemostatic disorders and bacterial infection [5-7]. Studies have also shown that the risk of complications including infections and impairment of various organs is increased in patients with liver disease undergoing cardiovascular operations [8]. Some current risk scores have been employed to evaluate the risk of operative mortality in cardiac surgery. However, they do not account for liver dysfunction in these surgical risk models [1-5]. For example, two well established cardiac surgical risk prediction models, the Society of Thoracic Surgeons (STS) system and the European System for Cardiac Operative Risk Evaluation (EuroSCORE) model, do not consider liver dysfunction as a surgical risk factor [7]. Consequently, for those patients with poor liver function, such as liver cirrhosis, operative mortality needs to be assessed by specific surgical risk scores.

In clinical practice, it is problematic to distinguish patients who may benefit from cardiac surgery from those whose perioperative risk exceeds benefit. Assessing individual surgical risk for each patient suffering from liver disease preoperatively, and separating patients who may benefit from cardiac surgery from those whose perioperative risk exceeds surgical benefits, using specific risk assessment systems, is vital [6, 9]. The Child-Turcotte-Pugh (CTP) classifications and the model for end-stage liver disease (MELD) scoresare the risk models widely used to determine surgical prognosis in patients with liver disease and can be used to predict operative mortality in these patients [4, 6, 9-12]. Therefore, this study reviews the role of liver dysfunction (classified by CTP or MELD) as

a risk factor for mortality and morbidity in cardiac surgery patients.

Methods

Literature search

The Pubmedreference library was searched from inception to June 1, 2013. The search terms were divided into two parts: disease (heart surgery, cardiac surgery, cardiac operation* and heart operation*) and exposure (liver dysfunction, liver function, and liver disease*). Cardiac surgerylisted under disease included mitral valve replacement, coronary artery bypass, peri-cardiectomy, aortic valve replacement, patch repair, ascending aorta replacement, pseudo lumen closure, tricuspid annuloplasty, aortic root replacement and liver disease listed under exposure included liver transplantation, liver cirrhosis. Two risk assessment systems, Child-Turcotte-Pugh (CTP) scores and the model for end-stage liver disease (MELD) score, were also used as search terms in the exposure search. No restrictions in terms of publication date, language and status were implemented.

Inclusion and exclusion criteria

Published cohort studies, case-reports and case series investigating the role ofliver dysfunctionas a risk factor for mortality and morbidity of cardiac surgery were included. The exclusion criteria included letters, comments and editorials. The reference lists of included studies were analyzed to uncover missing studies. Mortality and morbidity outcomes of the reviewed studies were analyzed.

Study selection and data extraction

Two independent reviewers selected studies to be included in this review according to the predetermined inclusion criteria. Data was analyzed including the basic information of the studies, patient demographics, the duration of follow-up, data about CTP classification and MELD score, and patient mortality and morbidity outcomes.

Data analysis and description

The influence of various degrees of liver dysfunction, as determined by CTP classification on mortality rates after cardiac surgery wasanalyzed. The mortality rate in patients of Child class A was compared with that in patients of Child class B, the mortality rate in patients of Child class A was compared with that in patients of Child class C, and the mortality rate in patients of Child class B was compared with that in patients of Child class C using Revman Software 5.0. Odd ratio (OR) with a 95% confidence interval (95% CI) was calculated. The heterogeneity across the studies were tested using an l^2 test and the difference was deemed significant when a score of $l^2 > 50\%$ or a p value of ≤0.05 was obtained. Begg's rank correlation method and Egger's weighted regression method were also used to statistically assess the publication bias (P<0.05 was considered to be representative of statistically significant publication bias).

As postoperative complications in the included studies were not classified by CTP, an analysis of the influences of various degrees of liver dysfunction on patient morbidity could not be conducted. Only the mean postoperative complication rates could be calculated and analyzed. The combined mean rates of mortality including hospital mortality and late mortality (dying after hospital discharge) and morbidity rates were analyzed using SPSS software version 17.00.

Results

Search results and characteristics of included studies

A total of 144 citations were recovered, however only 22 studies [1-4, 6, 8-24] (939 patients) and 20 reports [1-3, 6, 8-12, 14-24] (599 patients, from eight countries) included CTP classification and were therefore analyzed in this review as these studies represented the most suitable source to evaluate the association between liver dysfunction and the outcomes of cardiac surgery. The MELD score was used inanothertworeports [4, 13] (340 patients).

Mortality and morbidity

Clinical outcomes after cardiac surgery in patients with liver dysfunction are summarized in **Tables 1** and **2**.

Study ID	Country	NO. of	Disease	Surgery	Age	Gender	Patientin CTP clas- sification (Number)			De sifio	eath in CTP clas- fication (Number)			Follow-up
		patient				(IVI:F)	А	В	С	А	В	С	Overall	
Arif 2012	Germany	109	Cirrhosis	СРВ	64.0 years	82:27	74	29	6	14	12	2	28/109	Hospital deaths
										55	27	6	81/109	5 years
Bacha 2004	USA	4	Alagille's syndrome	Repair of ventricular septal defect and tricuspid regurgitation, Atrioven- tricular canal, subaortic stenosis, or supravalvular aortic stenosis	10 week-2 year	-	1	3	0	0	2	0	2/4	4 years
Bizouarn 1999	France	12	Cirrhosis	СРВ	25-74 years	8:4	10	2	0	2	1	0	3/12	26 months
Filsoufi 2007	USA	27	Cirrhosis	CABG, valve replacement, Aortic procedure, Pericardiectomy	58±10 years	20:7	10	11	6	1	2	4	7/27	1052±654 days
Hayashida 2004	Japan	18	Cirrhosis	CPB, CABG	44-81 years	11:7	10	7	1	0	2	1	3/18	Hospital deaths
Kaplan 2002	Turkey	10	Chronic Liver Disease	AVR, CABG, CPB, MVR	57.1±6.85 years	6:4	4	6	0	0	3	0	3/10	30.85±12.21 months
Klemperer 1998	USA	13	Cirrhosis	CABG; valve operations	53-79 years	11:2	8	5	0	0	4	0	4/13	Hospital deaths
Kur 2009	Germany	1	Hepatitis C	Aortic valve and ascending aorta replacement	43 years	1:0	0	0	0	0	0	0	0	Hospital deaths
Lin 2005	China	18	Cirrhosis	Valve replacement, CABG, CPB,	35-76 years	14:4	13	4	1	1	0	0	1/13	Hospital deaths
				mitral valvuloplasty						2	1	0	3/13	3-101 months
Lopez-Delgado 2013	Spain	58	Cirrhosis	Valve replacement, CABG	64.9±11.6 years	40:18	34	21	3	0	5	2	7/34	120 months
Marrocco-Trischitta 2011	Italy	24	Cirrhosis	Repair of infrarenal aortic aneurysm	68±7 years	23:1	22	2		3	2		5/24	30.7±22.1 months
Morimoto 2013	Japan	18	Cirrhosis	СРВ	70.6 years	14:4	0	14	4	0	3	0	3/18	Hospital deaths
							0	14	4	0	5	3	8/18	5.9 years (range 1.3-10.1)
Morisaki 2010	Japan	42	Cirrhosis	CABG, valve surgery	68.7±8.5 years	31:11	30	12	0	0	4	0	4/42	Hospital deaths
Murashita 2009	Japan	12	Cirrhosis	CABG, valve surgery	57-83 years	5:7	6	6	0	3	1	0	4/12	Hospital deaths
										4	1	0	5/12	23.9±13.5 months
Ota 2012	USA	61	Liver transplant	CABG, valve surgery, aortic root	61.5±8.2 years	45:16	33	28	0	2	2	0	4/61	Hospital deaths
			recipients	replacement						14	17	0	31/61	3.1±2.6 years
Sugimura 2012	Japan	13	Cirrhosis	CABG, valve replacement, patch	41-78 years	10:3	7	5	1	0	1	0	1/13	Hospital deaths
				repair, pericardiectomy						0	2	0	2/13	2 years
Suman 2004	USA	44	Cirrhosis	СРВ	15-74 years	27:17	31	12	1	1	5	1	7/44	3 months
Thielmann 2010	Germany	57	Cirrhosis	СРВ	62±10 years	38:19	39	14	4	6	4	4	14/57	1528±256 days
Vanhuyse 2012	France	34	Cirrhosis	Cardiac surgery with or without extracorporeal circulation	64.8±12.8 years	26:8	22	10	2	4	3	2	9/34	Hospital deaths
An 2006	China	24	Cirrhosis	AVR, MVR, TVR, CABG, pericardiec- tomy, Ascending aorta replacement	53±13 years	10:14	17	6	1	1	4	1	6/24	Hospital deaths

Table 1. Characteristics and mortality of included studies classified by CTP

AVR: aortic valve replacement; CABG: coronary artery bypass graft; CPB: cardiopulmonary bypass; MVR: mitral valve replacement; TVR: tricuspid valve repair.

Study ID	No. Of patient	Country	Dise	ase	Sur	gery		Age	Ger (Male:F	nder Female)	Meld score cutoff	Patient in each group	Death in each group	Follow-up duration
Ailawadi 2009	168	USA	Cirrh	osis .	Tricuspid va	alve sur	gery	61±14 years	96	:72	15	37:131	7:8	30 day
Tsuda 2013	172	Japan	Cirrh	osis -	Tricuspid va	alve sur	gery (63.8±10.3 years	66/	106	7	54:114	8:2	-
Study or Sub	group	Ev	Child ents	A Total	Child Events	B Total	Weig	Odds Ra ht M-H, Fixed	ntio 1, 95% CI		M-1	Odds Ra H, Fixed, S	tio 95% Cl	
1.1.1 hospita	l mortali	y												
An 2006			1	17	4	6	5.9	% 0.03 [0.0	00, 0.44]		1			
Arif 2012			14	73	12	30	14.5	% 0.36 [0.1	14,0.91]					
Hayashida 20	004		0	10	2	7	2.9	% 0.10 [0.0	00, 2.59]	_	11. A.			
Klemperer 19	398		0	8	4	5	5.4	% 0.02 [0.0	00, 0.59]	•				
Lin 2005			1	13	0	4	0.7	% 1.08 [0.04	4,31.63]					
Morisaki 201	0		0	30	4	12	6.6	% 0.03 [0.0	00, 0.63]		- 1 C			
Murashita 20	09		3	6	1	6	0.5	% 5.00 [0.34	4,72.77]				1.1	
Ota 2012			2	33	2	28	2.1	% 0.84 [0.1	11,6.37]					
Sugimura 20	12		0	7	1	5	1.7	% 0.20 [0.0	01,6.04]	_		1 A		
Vanhuyse 20	12		4	22	3	10	3.6	% 0.52 [0.0	09, 2.93]		-		-	
Subtotal (95%	% CI)			219		113	43.8	% 0.30 [0.1	17, 0.54]			•		
l otal events	- 01-17	i i o i de	25		33									
Test for overa	y: Chi== all effect: .	Z = 4.09	= 9 (P (P < 0.	= 0.1 0001)	1), 1= 37 %	0								
1.1.2 late mo	rtality											*- 12. ¹		
Arif 2012			55	73	27	30	9.9	% 0.34 [0.0	09, 1.25]		-	-		
Bacha 2004			0	1	2	3	1.3	% 0.20 [0.0	00, 8.82]			10		
Bizouarn 199	9		2	10	1	2	1.4	% 0.25 [0.0	01, 5.98]			1997 - 19		
Filsoufi 2007			1	10	2	11	1.8	% 0.50 [0.0	04, 6.55]					
Kaplan 2002			0	4	3	6	2.8	% 0.11 [0.0	00, 2.94]			12		
Lin 2005			2	13	1	4	1.4	% U.55 [U.I	04, 8.27]		4.6	2 10		
Lopez-Delga	ao 2013		0	34	5	21	7.0	% U.U4 [U.I	00, 0.83]		- 25			
Marrocco-Tris	schitta Zu	11	3	22	2	2	3.9	% 0.04 [0.0 % 22 40 00 00	64.2.001					
Murasriila 20	09		4	22	17	20	11.1	% 23.40 [0.89, % 0.40 [0.	17 1 221			<u> 1 6 6 </u>		
Sugimura 20	12		14		2	20	2.0	% 0.48[0. % 0.00[0]	00 2 511			<u></u>		
Suman 2004	12		1	31	5	12	2.0	% 0.05[0.0 % 0.05[0.0	00, 2.31	_				
Thielmann 2004	010		6	30	4	14	5.2	% 0.4510	11 1 941					
Subtotal (95%	% CI)		Ŭ	283	4	144	56.2	% 0.34 [0.2	20. 0.571			•		
Total events	,		88		71									
Heterogeneit	v: Chi ² =	14.95. df	= 12 (P = 0.	24); I ² = 20)%								
Test for overa	all effect:	Z= 4.14	(P < 0.	0001)										
Total (95% CI)			502		257	100.0	% 0.32 [0.2	22, 0.47]			•		
Total events			113		104									
Heterogeneit	y: Chi² =	29.11, df	= 22 (P = 0.	14); I ^z = 24	%				0.002	0.	1 1	10	500
Test for overa Test for subg	in eπect: . roup diffe	∠= 5.79 erences:	(P < 0. Chi ² =	0.08.	df=1 (P=	0.78).	l ² = 09	6	F	avours (experim	iental] Fa	avours (co	ontrol]

Table 2. Characteristics of included studies classified by MELD

Figure 1. The mortality rate in patients of Child A versus the mortality rate in patients of Child B.

Mortality: In the 19 studies (the study conducted by Kur was not analyzed asitwas a case report and did not report any useful information in terms of mortality), there were 354 patients (61.57%) in Child class A, 205 in Child class B (35.65%) and 33 in Child class C (5.74%). The mean in-hospital mortality rates for patients in Child class A, B, and C were 8.92%, 31.38%, and 47.62% respectively and the mean late mortality rates were 20.58%, 43.58%, 56.48% for patients in Child class A, B and C respectively.

Compared topatients in Child class B, patients in Child class A had lower hospital mortality rates (OR 0.30, 95% CI 0.17 0.54, I²=37%) and lower late mortality rates (OR 0.34, 95% CI 0.20 0.57, *I*²=20%). A meta-analysis of all data showed that patients in Child class A have lower mortality rate (OR 0.32, 95% CI 0.22 0.47, I²=24%) than patients in Child class B (Figure 1; Table 3).

Compared topatients in Child class C, patients in Child class A have lower hospital mortality

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				OR (95% C)	Но	mogene	Publication Bias		
Comparisons	subgroups	n	OR	CI	P value	Q	Ph	l² (%)	$P_{_{Begg}}$	$P_{_{Egger}}$
Child A	Hospital mortality	10	0.37	0.17-0.54	<0.01	14.21	0.11	37	0.441	0.316
VS.	Late mortality	13	0.34	0.20-0.57	<0.01	14.95	0.24	20	0.741	0.825
Child B	Total mortality	23	0.32	0.22-0.47	<0.01	29.11	0.14	24	0.411	0.325
Child A	Hospital mortality	5	0.16	0.05-0.49	<0.01	4.03	0.40	1	0.348	0.561
VS.	Late mortality	6	0.07	0.02-0.27	<0.01	4.85	0.43	0	0.829	0.891
Child C	Total mortality	11	0.10	0.05-0.24	<0.01	10.11	0.43	1	0.145	0.158
Child B	Hospital mortality	7	0.79	0.29-2.12	0.63	3.77	0.71	0	0.348	0.216
VS.	Late mortality	7	0.20	0.07-0.56	<0.01	2.88	0.82	0	0.151	0.231
Child C	Total mortality	14	0.39	0.20-0.77	<0.01	9.90	0.70	0	0.521	0.821

Table 3. Comparison of the mortality rates in patients of Child A, Child B and Child C



Figure 2. The mortality rate in patients of Child A versus the mortality rate in patients of Child C.

rate (OR 0.16, 95% CI 0.05 0.49, $I^2=1\%$) and lower late mortality rate (OR 0.07, 95% CI 0.02 0.27, $I^2=0\%$). A meta-analysis of all combined data showed that patients in Child class A have lower mortality rate (OR 0.10, 95% CI 0.05 0.24, $l^2=1\%$) than patients in Child class C (Figure 2; Table 3).

Hospital mortality rate of Child class B patients was not significantly different to that of Child

	Child B		Child C		Odds Ratio		Odds Ratio					
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl					
3.1.1 hospital mortality												
An 2006	4	6	1	1	3.2%	0.60 [0.02, 20.98]						
Arif 2012	12	29	2	6	7.4%	1.41 [0.22, 8.99]						
Hayashida 2004	2	7	1	1	6.3%	0.15 [0.00, 5.18]						
Lin 2005	0	4	0	1		Not estimable	5.0					
Morimoto 2013	3	14	0	4	2.2%	2.74 [0.12, 64.39]						
Sugimura 2012	2	5	0	1	1.7%	2.14 [0.06, 77.54]						
Sugimura 2012	1	5	0	1	2.1%	1.00 [0.02, 40.28]						
Vanhuyse 2012	3	10	2	2	10.2%	0.09 [0.00, 2.51]						
Subtotal (95% CI)		80		17	33.1%	0.79 [0.29, 2.12]	-					
Total events	27		6									
Heterogeneity: Chi ² = 3.	77, df = 6	(P = 0	.71); I² = ()%								
Test for overall effect: Z	= 0.48 (P	= 0.63)									
3.1.2 late mortality							1.11					
Arif 2012	27	29	6	6	3.4%	0.85 [0.04, 19.83]						
Filsoufi 2007	2	11	4	6	16.2%	0.11 [0.01, 1.09]						
Lin 2005	1	4	0	1	1.9%	1.29 [0.03, 53.51]						
Lopez-Delgado 2013	5	21	2	3	10.2%	0.16 [0.01, 2.11]						
Morimoto 2013	5	14	3	4	11.5%	0.19 [0.01, 2.29]						
Suman 2004	5	12	1	1	5.7%	0.24 [0.01, 7.21]						
Thielmann 2010	4	14	4	4	18.0%	0.05 [0.00, 1.08]						
Subtotal (95% CI)		105		25	66.9%	0.20 [0.07, 0.56]	-					
Total events	49		20									
Heterogeneity: Chi ² = 2.	88, df = 6	(P = 0	.82); I² = ()%								
Test for overall effect: Z	= 3.06 (P	= 0.00	2)									
Total (95% CI)		185		42	100.0%	0.39 [0.20, 0.77]						
Total events	76		26									
Heterogeneity: Chi ² = 9.	90, df = 1	3 (P =	0.70); l² =	0%								
Test for overall effect: Z	= 2.69 (P	= 0.00	7)				avours [experimental] Eavours [control]					
Test for subaroup differ	ences: C	$hi^2 = 3$	58 df=1	(P = 0)	$06) I^2 = 7$	′21% [′]	avours (experimental) Favours (control)					

Figure 3. The mortality rate in patients of Child B versus the mortality rate in patients of Child C.

class C patients (*OR* 0.79, 95% *CI* 0.29 2.12, $l^2=0\%$), however Child class B patients had a lower late mortality rate (*OR* 0.20, 95% *CI* 0.07 0.56, $l^2=0\%$) compared to Child class C. A meta-analysis of combined data showed that Child class B patients have a lower mortality rate following cardiac surgery (*OR* 0.39, 95% *CI* 0.20 0.77, $l^2=0\%$) compared with Child class C patients (**Figure 3; Table 3**).

One study included in this review reported significantly higher mortality rates in patients with a history of liver disease or MELD scores of 15 or greater (18.9% [7 of 37] vs 6.1% [8 of 131], P=0.024) compared to patients with no history of liver disease or MELD scores of less than 15 (168 patients that underwent tricuspid repair or replacement) [13]. One other study reported that hospital mortality rates increased in accordance with increased simplified MELD scores based on 172 patients that underwent tricuspid replacement or repair and that a higher simplified MELD score was an independent risk factor for increased in-hospital mortality [4].

Morbidity: A total of 22 studies [1-4, 6, 8-24] reported postoperative complications however the reported postoperative complications were not classified by CTP and could therefore not be analysed in this review in terms ofvarious degrees of liver dysfunction postoperative morbidity. Only the mean postoperative complication rates could be calculated and analyzed in this review.

The details of the morbidity if each study analyzed are presented in **Table 4**. The mean reexploration rate was 4.37%, the mean neurological complication rate 3.83%, the mean cardiovascular complication rate 2.67%, the mean

Study ID	NO. Of patient	Reexplo- ration	Neurolo- gical	Cardio- vascular	Pulmo- nary	Renal	Hepatic	Gastroin- testinal	Sepsis + MOF	Bleeding + Cardiac Tamponade	Infec- tious
Arif 2012	109	0	11	0	10	84	0	20	21	0	44
Bacha 2004	4	0	0	2	1	0	0	0	0	1	0
Bizouarn 1999	12	0	0	2	1	0	4	0	1	2	3
Filsoufi 2007	27	0	0	0	6	4	0	4	3	2	2
Hayashida 2004	18	0	0	0	5	5	0	3	0	3	6
Kaplan 2002	10	0	0	0	5	0	2	0	0	3	0
Klemperer 1998	13	4	3	0	4	3	0	3	0	0	4
Kur 2009	1	0	0	0	0	0	0	0	0	0	0
Lin 2005	18	0	1	0	1	1	2	1	0	4	4
Lopez-Delgado 2013	58	11	0	22	0	5	0	0	0	1	0
Marrocco-Trischitta 2011	24	0	0	2	1	0	1	0	0	0	0
Morimoto 2013	18	0	0	0	2	1	3	0	0	5	0
Morisaki 2010	42	0	1	2	7	6	2	2	0	4	3
Murashita 2009	12	4	0	0	0	1	3	1	2	2	2
Ota 2012	61	0	4	22	14	11	25	0	0	4	6
Sugimura 2012	13	2	1	0	3	2	0	7	0	0	1
Suman 2004	44	0	0	0	0	6	12	0	5	0	0
Thielmann 2010	57	14	2	11	0	25	0	0	0	16	0
Vanhuyse 2012	34	0	0	0	3	7	0	5	3	1	3
An 2006	24	6	0	3	17	7	0	12	2	4	8
Ailawadi 2009	168	0	4	0	49	32	0	8	7	0	0
Tsuda 2013	172	0	9	53	26	8	0	10	9	0	0
Total	939	41	36	119	155	208	54	76	53	52	86
Mean rate (%)		4.37	3.83	12.67	16.51	22.15	5.75	8.09	5.64	5.54	9.16

Table 4. Complications

MOF: multiple organ failure.

pulmonary complication rate 16.51%, the mean renal complication rate was 22.15%, the mean hepatic complication rate was 5.75%, the mean gastrointestinal complication rate was 8.09%, the mean sepsis and multi organ failure complication rate was 5.64%, the bleeding and cardiac tamponade complication rate was 5.54% and the mean infectious complication rate was 9.16%.

Heterogeneity

Heterogeneity among all studies was calculated using the Q statistic (Q>0.10) and the l^2 statistic (l=0.0%). Heterogeneity was found in some groups, and the random effects model was used. An l^2 value for heterogeneity exceeding 80.0% was not found.

Sensitivity analysis

An influence analysis and a trim and filled analysis were both conducted to investigate the sensitivity of the pooled ORs and the test results. These analyses indicated that the pooled *OR*s were statistically robust.

Publication bias

This meta-analysis found no evidence for literature publication bias based on a *Begg's* funnel plot and *Egger's* test (**Table 3**).

Discussion

Summary of finding

As a result of the findings of this systematic review and meta-analysis, both in-hospital and late mortality rates, increase in accordance with increased CTP classification with the lowest mortality rates observed in Child class A patients. These findings are consistent with several studies and suggest that cardiac surgery can be safely conducted in Child class A patients [6, 11]. The highest in-hospital and late mortality rates were observed in Child class C patients, These findings were confirmed by previous studies reporting increased mortalities following cardiac intervention in Child class C patients [1-6]. For Child class C patients, that require cardiac surgery, it is suggested that they accept additional treatments

to achieve optimal liver functions. For patients in Child class B, the in-hospital and late mortality rates were between those of the patients in Child class A, and C. Further longitudinal studies are required to determine if it is safe to conduct cardiac surgery Child class B patients Studies have shown that an MELD score may be of assistance as the MELD score relies entirely on objective parameters for its calculation without requiring subjective evaluations of the degree of ascites and encephalopathy [6]. In addition, studies have shown that the MELD score has an ample range of potential numeric values and mayfacilitate enhanced discrimination among patients with varying degrees of hepatic dysfunction [6, 25].

In this systematic review, the mean rate for the morbidity, and the morbidity rate following cardiac surgery varied from 3.83% (neurological complication) to 22.15% (renal complications). The primary three complications included renal complications (21.15%), pulmonary complications (16.51%) and cardiovascular complications (12.67%). As a result of this systematic review, it can be concluded that liver dysfunction could significantly affects the incidence of morbidity following cardiac surgery.

This review found that the mortality rate is lowest in Child class A patients and highest in Child class C patients, with a mean complication rate range from 3.83% to 22.15%. A reason for such high mortality and morbidity following cardiac surgery in patients suffering from liver disease includes increased vulnerability to bacterial infection. It has been reported that increased vulnerability to bacterial infection is related to the severity of liver dysfunction and may lead to abnormalities of the defense mechanisms [7]. Another reason may be coagulation disorders. As the liver plays an important role in the clotting process, coagulation disorders may be commonly linked with acute and chronic liver diseases. A final reason may be haemostatic disorders. Portal hypertension may lead to congestive splenomegaly with the trapping of platelets and thrombocytopenia, resulting in further postoperative bleeding [5, 6].

Strength and limitations

This study systematically reviewed the role of liver dysfunction as classified by CTP or MELD as a risk factor for increased mortality and mor-

bidity in patients after cardiac surgery. A comprehensive and rigorous search of the Pubmedreference library and other sources including reference lists was conducted, a meta-analysis method was used to compare the mortality rate among patients classified as Child class A, B and C. The meta-analysis was not without its limitations. First, all studies included used CTP to classify liver function whilst only two studies used MELD scores. The study conducted by Thielmann et al [9] showed that MELD was the most superior predictive risk model in predicting in-hospital mortality and long-term survival. Second, the diseases of this review varied significantly. The majority of the reviewed studies focused on cirrhosis indicating that the conclusions of this review are only relevant to liver cirrhosis patients undergoing cardiac surgery. Thirdly, this systematic review only included several caseseries or case reports, thus limiting the evidence level. Finally, a comparison between the morbidity rates, Child classes A, B and C was not conducted.

Implications for future studies and practice

Future cardiac surgical risk assessment models need to include liver function as a risk factor, as classified by CTP or MELD. In addition, comparative or controlled studies comparing cardiac surgical risk assessment systems with liver function and cardiac surgical risk assessment systems minus liver function need to be conducted. Furthermore, whilst MELD is the most predictive risk model, and is clearly superior to CTP in predicting in-hospital mortality and long-term survival, few studies utilize MELD to classify liver function, indicating that in the future, MELD should be utilized to classify liver function as the superior cutoff point.

Conclusion

Child class A patients have an acceptable mortality rate following cardiac surgery indicating that cardiac surgery can be safely carried out in these patients. Child class B patients however have a higher mortality rate following cardiac surgery and should seek further consultation and evaluation before surgery. The mortality in patients with Child class C is extremely high. These patients should be considered unacceptable for cardiovascular surgery. Patients with a higher MELD score havea significantly higher mortalityrate. Liver function must be viewed as an important risk factor for cardiovascular surgery, based on the strong association of this disease with mortality and morbidity.

Disclosure of conflict of interest

None.

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