Search strategies

PubMed search strategy

#1: Cardiac Surgical Procedures [mh]

#2: Cardiac Surgical Procedures or Procedure, Cardiac Surgical or Procedures, Cardiac Surgical Procedures, Cardiac or Surgical Procedures, Cardiac or Surgical Procedures, Cardiac Surgical Procedures, Cardiac or Surgical Procedures, Heart Surgical Procedures, Heart

#3: #1or #2

#4: Hyperbilirubinemia [mh]

#5: Hyperbilirubinemia or Hyperbilirubinemias or Bilirubinemia or Bilirubinemias

#6: #4 or #5

#7: #3 and #6

1,217 Search results.

Results obtained May 29, 2020.

Cochrance search strategy

#1: Cardiac Surgical Procedures or Procedure, Cardiac Surgical or Procedures, Cardiac Surgical or Surgical Procedure, Cardiac or Surgical Procedures, Cardiac or Surgical Procedures, Cardiac or Surgical Procedures, Heart Surgical Procedur

#3: #1 and #2

4 Search results.

Results obtained May 29, 2020.

Embase search strategy

#1: "heart surgery"/exp

#2: "heart surgery" or "cardiac surgery" or "cardiac surgical procedures" or "cardiosurgery" or "heart operation" or "myocardial resection" or "surgery, heart" or "extracorporeal circulation" or "cardiopulmonary bypass"

#3: #1 or #2

#4: "hyperbilirubinemia"/exp

#5: "bilirubinaemia" or "bilirubinemia" or "hyperbilirubinaemia" or "hy

#6: #4 or #5

#7: #3 and #6

357 Search results.

Results obtained May 29, 2020.

Table S1 NOS of included studies

		S	Selection							
Author	Exposed cohort	Nonexposed cohort	Ascertainment of exposure	Outcome of interest	Comparability	Assessment of outcome	Length of follow-up	Adequacy of follow-up	Total score	
Collins et al.	*	*	*	*	*	*			6	
Chu et al.	*	*	*	*	**				6	
Wang et al.	*	*	*	*	*	*			6	
Michalopoulos et al.	*	*	*	*	**	*			7	
Chandra et al.	*	*	*	*	*	*			6	
An et al.	*	*	*	*	*	*			6	
Hsu et al.	*	*	*	*	*	*	*	*	8	
Kraev et al.	*	*	*	*	*	*	*	*	8	
Nishi et al.	*	*	*	*	*	*			6	
Sharma et al.	*	*	*	*	*	*			6	

^{*,} XXXXXXXXXXX;, XXXXXXXXXXX. NOS, Newcastle-Ottawa quality assessment scale.

Table \$2 Sensitivity analyses of pooled incidence of hyperbilizabinemia

Table S2 Sensitivity analyses of pooled incidence of	hyperbilirubinemia		
Excluding studies	No. of studies	Incidence rate (95% CI)	Heterogeneity (I ²)
<100 participants	9	0.22 (0.12–0.32)	98.90%
Including off-pump surgery	9	0.22 (0.12–0.32)	98.90%
Isolated heart valve surgery	8	0.23 (0.13–0.33)	99.00%
Isolated heart transplantation	8	0.19 (0.09–0.28)	98.60%

CI, confidence interval.

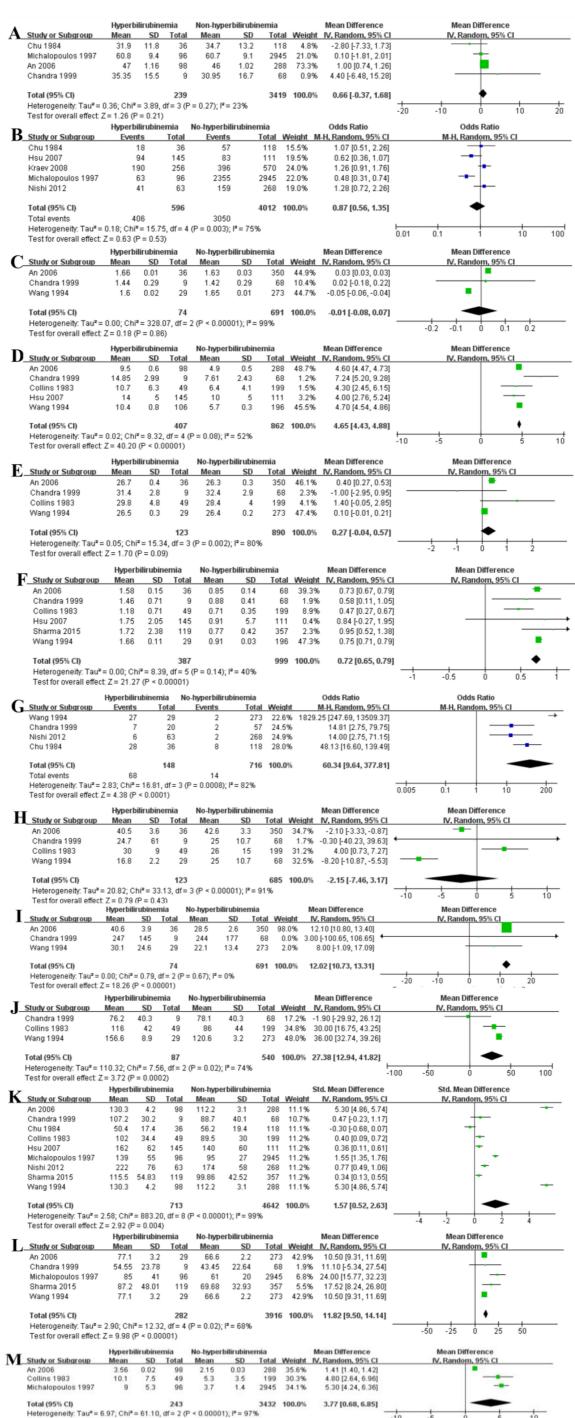


Figure S1 Forest plots of preoperative and intraoperative risk factors for postoperative hyperbilirubinemia after cardiac surgery. The included risk factors were (A) age, (B) sex, (C) body surface area, (D) right atrial pressure, (E) minimum esophageal temperature, (F) preoperative bilirubin concentration, (G) preoperative

amount of blood transfused. CPB, cardiopulmonary bypass; ACC, aortic cross-clamp; CI, confidence interval.

elevated bilirubin concentration, (H) aspartate amino transferase, (I) alanine aminotransferase, (J) alkaline phosphatase, (K) CPB time, (L) ACC time, and (M) the

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 $\textbf{Table S3} \ \ \textbf{Sensitivity analyses of pooled mortality associated with hyperbilirubinemia}$

Excluding studies	No. of studies	Incidence rate (95% CI)	Heterogeneity (I ²)
<100 participants	8	10.99 (5.62–21.49)	66%
Non-emergency surgery	8	12.30 (6.61–21.87)	46%
<100 participants and non-emergency surgery	7	13.05 (7.52–22.66)	34%
Isolated heart valve surgery	8	9.01 (4.35–18.68)	67%
Isolated heart transplantation	8	11.02 (5.00–24.28)	69%

CI, confidence interval.

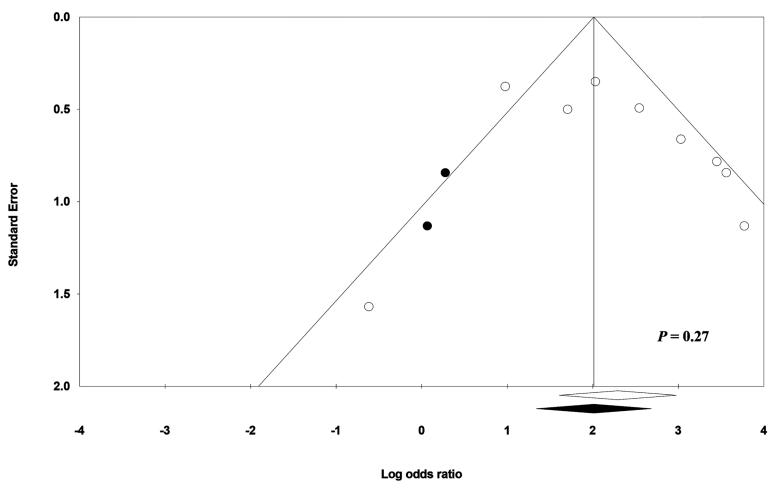
Δ	Hyperbilirubinemia			No-hyperbilirubinemia				Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ra	andom, 9	5% CI	
An 2006	1.1	0.6	98	0.7	0.4	288	33.7%	0.40 [0.27, 0.53]			•		
Michalopoulos 1997	4.3	2.1	96	0.8	0.1	2945	33.1%	3.50 [3.08, 3.92]					-
Sharma 2015	1	1.9	119	0.6	1.43	357	33.2%	0.40 [0.03, 0.77]			-		
Total (95% CI)			313			3590	100.0%	1.43 [-0.27, 3.12]			-		-
Heterogeneity: Tau ² = 1				(P < 0.000	01); I² = 9	99%		_	-4	- 2	0	2	4

lean	SD							
	Jυ	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
11.5	6.5	98	4.1	3.9	288	21.9%	7.40 [6.04, 8.76]	-
6.81	9.32	9	3.59	3.12	68	16.5%	3.22 [-2.91, 9.35]	-
12.3	7.6	96	2.3	0.9	2945	21.8%	10.00 [8.48, 11.52]	
5.14	3.32	119	4.7	3.32	357	22.2%	0.44 [-0.25, 1.13]	 -
7.3	14.5	29	3.7	4.9	273	17.7%	3.60 [-1.71, 8.91]	-
		351			3931	100.0%	5.06 [0.15, 9.97]	
1 6	5.81 2.3 5.14 7.3	3.81 9.32 12.3 7.6 5.14 3.32 7.3 14.5	5.81 9.32 9 12.3 7.6 96 5.14 3.32 119 7.3 14.5 29 351	3.81 9.32 9 3.59 12.3 7.6 96 2.3 5.14 3.32 119 4.7 7.3 14.5 29 3.7 351	3.81 9.32 9 3.59 3.12 12.3 7.6 96 2.3 0.9 5.14 3.32 119 4.7 3.32 7.3 14.5 29 3.7 4.9 351	6.81 9.32 9 3.59 3.12 68 12.3 7.6 96 2.3 0.9 2945 5.14 3.32 119 4.7 3.32 357 7.3 14.5 29 3.7 4.9 273	3.81 9.32 9 3.59 3.12 68 16.5% 12.3 7.6 96 2.3 0.9 2945 21.8% 5.14 3.32 119 4.7 3.32 357 22.2% 7.3 14.5 29 3.7 4.9 273 17.7% 3931 100.0%	3.81 9.32 9 3.59 3.12 68 16.5% 3.22 [-2.91, 9.35] 12.3 7.6 96 2.3 0.9 2945 21.8% 10.00 [8.48, 11.52] 5.14 3.32 119 4.7 3.32 357 22.2% 0.44 [-0.25, 1.13] 7.3 14.5 29 3.7 4.9 273 17.7% 3.60 [-1.71, 8.91] 351 3931 100.0% 5.06 [0.15, 9.97]

C Hyperbilirubine			mia	No-hyper	rbilirubin	emia		Mean Difference	Mean Difference	
_	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
	Chandra 1999	28.23	7.87	9	14.23	3.48	68	28.2%	14.00 [8.79, 19.21]	
	Michalopoulos 1997	15.5	9.5	96	9.2	2.3	2945	35.4%	6.30 [4.40, 8.20]	-
	Sharma 2015	9.54	5.14	119	8.75	5.05	357	36.4%	0.79 [-0.27, 1.85]	-
	Total (95% CI)			224			3370	100.0%	6.46 [0.78, 12.14]	-
	Heterogeneity: Tau² = 2	22.79; Chi		-20 -10 0 10 20						
	Test for overall effect: Z	= 2.23 (P)	' = 0.03)							-20 -10 0 10 20

Figure S2 Forest plots of the associations of duration of mechanical ventilation (A), ICU stay (B), and hospital stay (C) with postoperative hyperbilirubinemia. CI, confidence interval.

Funnel Plot of Standard Error by Log odds ratio



 $\textbf{Figure S3} \ \text{Funnel plots of studies to evaluate publication bias in in-hospital mortality risks.} \\$