

APPENDIX 1 TABLES AND FIGURES

		Supplemental	Table 1 List of literatures included in our study						
ID	Title of article	Publication year	Journal	Impact factor 2018	Country of 1 st author	Study setting	Study type	Data source	Bioartificial Liver Support System
1	A Bioartificial Liver to Treat Severe Acute Liver Failure	1994	<i>Ann Surg</i>	9.203	USA	USA	Clinical trial	Full-text	HepatAssist
2	Clinical Experience With a Bioartificial Liver in the Treatment of Severe Liver Failure: A Phase I Clinical Trial	1997	<i>Ann Surg</i>	9.203	USA	USA, France	Clinical trial	Full-text	HepatAssist
3	Treatment of Severe Liver Failure with a Bioartificial Liver	2010	<i>Ann N Y Acad Sci</i>	4.277	USA	USA	Clinical trial	Full-text	HepatAssist
4	Neurological improvement during bioartificial liver sessions in patients with acute liver failure awaiting transplantation	2002	<i>Transplantation</i>	3.960	France	France	Clinical trial	Full-text	HepatAssit
5	The Hepatix Extracorporeal Liver Assist Device: Initial Clinical Experience	1994	<i>Artif Organs</i>	2.111	USA	USA	Clinical trial -pilot study	Full-text	ELAD
6	Initial experience with the modified extracorporeal liver-assist device for patients with fulminant hepatic failure: system modifications and clinical impact	2002	<i>Transplantation</i>	3.960	USA.	USA	Clinical trial	Full-text	ELAD

ID	Title of article	Publication year	Journal	Impact factor 2018	Country of 1 st author	Study setting	Study type	Data source	Bioartificial Liver Support System
7	Phase I clinical trial with the AMC-bioartificial liver	2002	<i>Int J Artif Organs</i>	1.133	The Netherlands	The Netherlands	Clinical trial -Phase I	Full-text	AMC-BAL
8	Bridging a Patient With Acute Liver Failure to Liver Transplantation by the AMC-Bioartificial Liver	2003	<i>Cell Transplant</i>	2.885	The Netherlands	The Netherlands	Case report	Full-text	AMC-BAL
9	Clinical experience with a porcine hepatocyte-based liver support system	1996	<i>Int J Artif Organs</i>	1.133	USA	USA	Clinical trial	Full-text	NA
10	Clinical extracorporeal hybrid liver support -phase I study with primary porcine liver cells	2003	<i>Xenotransplantation</i>	4.717	Germany	Germany	Clinical trial -Phase I	Full-text	MELS
11	Extracorporeal liver support based on primary human liver cells and albumin dialysis--treatment of a patient with primary graft non-function	2003	<i>J Hepatol</i>	14.911	Germany	Germany	Case report	Full-text	MELS
12	First Clinical Use of a Novel Bioartificial Liver Support System (BLSS)	2002	<i>Am J Transplant</i>	6.493	USA	USA	Case report	Full-text	BLSS
13	Early experiences with a porcine hepatocyte-based bioartificial liver in acute hepatic failure patients	2002	<i>Int J Artif Organs</i>	1.133	Italy	Italy	Clinical trial	Full-text	RFB-BAL
14	The development of a new bioartificial liver and its application in 12 acute	2003	<i>World J Gastroenterol</i>	3.300	China	China	Clinical trial	Full-text	HBAL

ID	Title of article	Publication year	Journal	Impact factor 2018	Country of 1 st author	Study setting	Study type	Data source	Bioartificial Liver Support System
	liver failure patients								
15	Clinical use of a bioartificial liver in the treatment of acetaminophen-induced fulminant hepatic failure	1999	<i>Am Surg</i>	0.607	USA	USA	Clinical trial	Full-text	HepatAssist
16	Phase 1/2a Trial of a Bioartificial Liver Support System (LifeLiver) for Acute Liver Failure Patients	2018	NR	NR	NR	Korea	Clinical trial -Phase 1/2a	Abstract	LifeLiver BAL
17	Pilot-Controlled Trial of the Extracorporeal Liver Assist Device in Acute Liver Failure	1996	<i>Hepatology</i>	14.079	England	England	RCT-Pilot study	Full-text	ELAD
18	Prospective, Randomized, Multicenter, Controlled Trial of a Bioartificial Liver in Treating Acute Liver Failure	2004	<i>Ann Surg</i>	9.203	USA	11 US and 9 European sites	RCT	Full-text	HepatAssist
19	Bioartificial liver system based on choanoid fluidized bed bioreactor improve the survival time of fulminant hepatic failure pigs	2011	<i>Biotechnol Bioeng</i>	3.952	China	China	Preclinical experiment	Full-text	FBBAL
20	Evaluation of a novel hybrid bioartificial liver based on a multi-layer flat-plate bioreactor	2012	<i>World J Gastroenterol</i>	3.300	China	China	Preclinical experiment	Full-text	HBAL

ID	Title of article	Publication year	Journal	Impact factor 2018	Country of 1 st author	Study setting	Study type	Data source	Bioartificial Liver Support System
21	Evaluation of encapsulated liver cell spheroids in a fluidised-bed bioartificial liver for treatment of ischaemic acute liver failure in pigs in a translational setting.	2013	<i>PLoS One</i>	2.766	London	London	Preclinical experiment	Full-text	NA
22	Hybrid bioartificial liver support in cynomolgus monkeys with D-galactosamine-induced acute liver failure	2014	<i>World J Gastroenterol</i>	3.300	China	China	Preclinical experiment	Full-text	HBALSS
23	No transmission of porcine endogenous retrovirus in an acute liver failure model treated by a novel hybrid bioartificial liver containing porcine hepatocytes.	2015	<i>Hepatobiliary Pancreat Dis Int</i>	1.500	China	China	Preclinical experiment	Full-text	HBAL
24	Pivotal Preclinical Trial of the Spheroid Reservoir Bioartificial Liver	2015	<i>J Hepatol</i>	14.911	USA	USA	Preclinical experiment	Full-text	SRBAL
25	Efficacy of Fluidized Bed Bioartificial Liver in Treating Fulminant Hepatic Failure in Pigs: A Metabolomics Study	2016	<i>Sci Rep</i>	4.122	China	China	Preclinical experiment	Full-text	FBBAL
26	Improved survival of porcine acute liver failure by a bioartificial liver device implanted with induced human functional hepatocytes	2016	<i>Cell Res</i>	15.393	China	China	Preclinical experiment	Full-text	hiHep-BAL

ID	Title of article	Publication year	Journal	Impact factor 2018	Country of 1 st author	Study setting	Study type	Data source	Bioartificial Liver Support System
27	A clinical-scale BioArtificial Liver developed for GMP improved clinical parameters of liver function in porcine liver failure	2017	<i>Sci Rep</i>	4.122	UK	UK	Preclinical experiment	Full-text	UCLBAL
28	Functional Evaluation of a Bioartificial Liver Support System Using Immobilized Hepatocyte Spheroids in a Porcine Model of Acute Liver Failure	2017	<i>Sci Rep</i>	4.122	Korea	Korea	Preclinical experiment	Full-text	NR
29	Novel spheroid reservoir bioartificial liver improves survival of nonhuman primates in a toxin-induced model of acute liver failure	2018	<i>Theranostics</i>	8.537	China	China	Preclinical experiment	Full-text	SRBAL
30	Randomized Trial of Spheroid Reservoir Bioartificial Liver in Porcine Model of Posthepatectomy Liver Failure	2019	<i>Hepatology</i>	14.079	USA	USA	Preclinical experiment	Full-text	SRBAL

Note: NR: not reported; ELAD: Extracorporeal Liver Assist Device; AMC-BAL: Academic Medical Center Bioartificial Liver; MELS: Modular Extracorporeal Liver Support; BLSS: Novel Bioartificial Liver Support System; RFB-BAL: Radial-flow Bioreactor Bioartificial Liver; HBAL: Hybrid Bioartificial Liver; FBBAL: Fluidized Bed Bioartificial Liver; HBALSS: Hybrid Bioartificial Liver Support System; SRBAL: Spheroid Reservoir Bioartificial Liver; hiHep-BAL: Human-induced Hepatocytes Bioreactor Bioartificial Liver.

Supplemental Table 2 Bias risk assessment of Randomized Controlled Trials in systematic review⁷

ID	Publication year	Journal	Study type	Generation of Random Sequences	Allocation concealment	Blinding Subject & Intervener	Blinding Outcome Evaluation	Results with Incomplete Data	Selective Results Reporting	Other Sources of Bias	Proportion of Low-risk
17	1996	<i>Hepatology</i>	RCT-Pilot study	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
18	2004	<i>Ann Surg</i>	RCT	Low-risk	High-risk	Low-risk	Low-risk	Low-risk	Low-risk	Low-risk	6/7
20	2012	<i>World J Gastroenterol</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
22	2014	<i>World J Gastroenterol</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
24	2015	<i>J Hepatol</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
26	2016	<i>Cell Res</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
27	2017	<i>Sci Rep</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
29	2018	<i>Theranostics</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7
30	2019	<i>Hepatology</i>	Preclinical experiment	Unclear	High-risk	Low-risk	Unclear	Low-risk	Low-risk	Low-risk	4/7

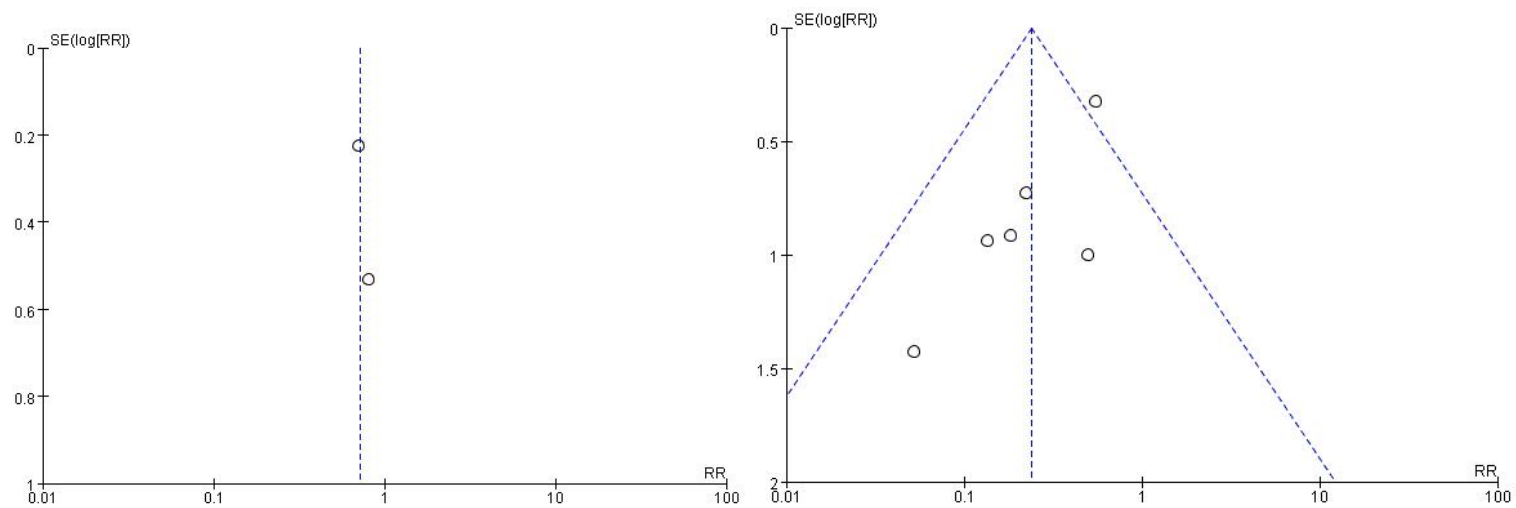
⁷The risk of bias was assessed into high-risk, low-risk, or unclear according to the Cochrane assessment standard for Randomized Controlled Trials.

Table 3 Bias risk assessment of non-Randomized Controlled Trials for systematic review⁸

ID	Publication year	Journal	Study type	Selection					Outcomes			Total score (0-9)
				Intervention group representativeness	Controls selection	Ascertainment of intervention	Outcome not present at start	Comparability of groups	Outcome assessment	Follow-up long enough	Follow-up adequacy	
1	1994	<i>Ann Surg</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6
2	1997	<i>Ann Surg</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6
3	2010	<i>Ann N Y Acad Sci</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6
4	2002	<i>Transplantation</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6
5	1994	<i>Artif Organs</i>	Clinical trial -pilot study	1	NA	1	1	NA	1	1	1	6
6	2002	<i>Transplantation</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6
7	2002	<i>Int J Artif Organs</i>	Clinical trial -Phase I	1	NA	1	1	NA	1	1	1	6
8	2003	<i>Cell Transplant</i>	Case report	1	NA	1	1	NA	1	1	1	6
9	1996	<i>Int J Artif Organs</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6
10	2003	<i>Xenotransplantation</i>	Clinical trial -Phase I	1	NA	1	1	NA	1	1	1	6
11	2003	<i>J Hepatol</i>	Case report	0	NA	1	1	NA	1	1	1	5
12	2002	<i>Am J Transplant</i>	Case report	0	NA	1	1	NA	1	1	1	5
13	2002	<i>Int J Artif Organs</i>	Clinical trial	1	NA	1	1	NA	1	1	1	6

ID	Publicati	Journal	Study type	Selection				Comparability	Outcomes			Total
14	2003	<i>World J Gastroenterol</i>	Clinical trial	0	NA	1	1	NA	1	1	1	5
15	1999	<i>Am Surg</i>	Clinical trial	0	NA	1	1	NA	1	1	1	5
16	2018	NR	Clinical trial -Phase 1/2a	NR	NA	1	1	NA	1	1	1	5
19	2011	<i>Biotechnol Bioeng</i>	Preclinical experiment	0	1	1	1	2	1	1	1	8
21	2013	<i>PLoS One</i>	Preclinical experiment	0	1	1	1	1	1	1	1	7
23	2015	<i>Hepatobiliary Pancreat Dis Int</i>	Preclinical experiment	0	1	1	1	NA	1	1	1	6
25	2016	<i>Sci Rep</i>	Preclinical experiment	0	1	1	1	2	1	1	1	8
28	2017	<i>Sci Rep</i>	Preclinical experiment	0	1	1	1	2	1	1	1	8

⁸The bias of each study was assessed by giving a maximum one star for each numbered item within the Selection and Outcome categories; and a maximum of two stars for Comparability, according to the Newcastle-Ottawa Quality Assessment Scale for cohort studies. NR: not reported. NA: not applicable.



Supplemental **Figure 1 Begg's funnel plot of publication bias in selected studies for meta-analysis of 2 clinical trials and 6 preclinical experiments.** Note: each point represents a separate study for the indicated correlation. Log [RR], natural logarithm of relative risk (RR). Horizontal line, mean magnitude of the effect.

APPENDIX 2 KEY WORDS USED IN LITERATURE SEARCH

Category	Cochrane Library	EMbase	PubMed
Patients	Acute liver failure [MeSH Terms]	exp Acute liver failure/	Acute Liver Failure[MeSH Terms] OR Failure, Acute Liver OR Fulminating Hepatic Failure OR Fulminating Hepatic Failures OR Hepatic Failure, Fulminating OR Hepatic Failures, Fulminating OR Liver Failure, Fulminant OR Fulminant Liver Failure OR Fulminant Liver Failures OR Liver Failures, Fulminant OR Hepatic Failure, Acute OR Acute Hepatic Failure OR Failure, Acute Hepatic OR Hepatic Failure, Fulminant OR Fulminant Hepatic Failure OR Fulminant Hepatic Failures OR Hepatic Failures, Fulminant OR Acute Liver Failure OR Fulminating Liver Failure OR Fulminating Liver Failures OR Liver Failure, Fulminating OR Liver Failures, Fulminating
Intervention	Liver, Artificial [MeSH Terms] OR bioartificial liver	exp Bioartificial liver/	Artificial Liver [MeSH Terms] OR Bioartificial Liver OR Bioartificial Livers OR Liver, Bioartificial OR Livers, Bioartificial OR Artificial Liver