

Study	Date	Area of interest	Study design/methods	Human or animal	Number studied	Mode of sepsis/entry criteria
Biomarkers						
Teng et al⁹	2012	MMP9 as a biomarker for MODS severity. Relationship between serum and tissue MMP9	ELISA Immunohistochemistry	Rat	36	Left eyeball removal followed by LPS
Li et al¹⁰	2015	Prognostic value of natriuretic peptides in with MODS	BNP and ANP assays	Human	26	Polytrauma (ISS>16)
Sugita et al¹¹	2017	Correlation of HMGB1, NSE and IL-6 with SOFA score to determine their prognostic value	Prospective observational study	Human	128	Post-cardiac arrest
Cellular Biology						
Gu et al¹³	2018	Differential expression of genes between tissues in MODS and healthy controls	Microarray analysis	Murine	27	MV and <i>S.aureus</i> pneumonia
Oive et al¹⁴	2010	Monocyte signalling profiles in acute pancreatitis and organ failure	Flow cytometry	Human	13	Acute pancreatitis complicated by organ dysfunction
Uhlig et al¹⁶	2002	Ventilation induced changes in MAPK phosphorylation	Western blot analysis	Rat and mouse		High pressure ventilation in isolated lung
Di Paola et al¹⁷	2009	Effect of PD98059 (MAPK inhibitor) on non-septic shock. Cell surface changes, iNOS, Bcl2 among others assessed.	Assessment of acute inflammation in the abdomen. Various laboratory	Mouse	120	Zymosan
Altemeier et al¹⁸	2005	Gene expression in ALI and the influence mechanical ventilation has on this.	Microarray analysis	Mouse	24	Aspirated LPS
Jabandziev et al¹⁹	2014	SNPs of five genes.	PCR and restriction analysis.	Human (children)	1127	Variable
Gharib et al²⁰	2016	Identification of differentially expressed genes in organs in SIRS	Microarray qPCR	Mouse		<i>S.aureus</i> inoculation and MV (VAP)
Madach et al²¹	2010	Polymorphisms of PAI-1 gene	Prospective data collection. PCR analysis.	Human	208	Due to pneumonia
Protti et al²⁶	2007	Mitochondrial dysfunction and MODS. Complex I dysfunction and the use of succinate	Measurement of mitochondrial complex activity and oxygen consumption.	Rat		Fecal peritonitis
Fredrikss	2006	Mitochondrial dysfunction in muscle	Muscle biopsies with spectrophotometric	Human	10	Sepsis induced multiple organ failure

on et al²⁸		of critically ill patients	and microscopic analysis			
Carre et al²⁹	2010	Interaction of mitochondrial biogenesis and critical illness.	Muscle biopsies from patients in ICU.	Human	16	Critical illness and multiple organ failure.
Malaisse et al³⁰	1997	The potential therapeutic utility of succinic acid in endotoxemia		Rat		LPS injections
Miyaji et al³¹	2003	Ethyl pyruvate and sepsis induced organ dysfunction	Histology Reverse transcription PCR Western blot	Mouse		LPS and CLP
Lowes et al³²	2008	Mitochondria specific antioxidants and organ damage secondary to sepsis		Rat		LPS
Piel et al³³	2007	Cytochrome oxidase inhibition and reduced substrate availability and the relationship to myocardial dysfunction.		Mouse	75	CLP
Fauvel et al³⁴	2002	Protective effects of cyclosporin	Spectrophotometer Western blot ELISA	Rats		Endotoxin
Vinokurov et al³⁶	2011	The role of HSP70 and protection against inflammatory changes	Assays for ROS, TNF- α and CD11 expression	Rat		LTA injections
Wang et al³⁷	2016	Effect of 17-DMAG on MODS through HSP90 inhibition	ELISA Western blot	Rat		
Zeng et al³⁸	2015	Rs1800625 association with sepsis mortality and MODS development.	Genotyped using pyrosequencing	Human	837	Major trauma
Gunst⁴¹	2013	The role of hyperglycemia and autophagy, mitochondrial dysfunction and repair In critical illness.	Prospective randomised study.	Rabbits	3	
Chung et al⁴²	2017	Effect of oestrogen on autophagy in ovariectomised rats	Various laboratory techniques	Rat	90	LPS infusion
Nakahira et al⁴³	2011	Autophagic proteins and their role in regulation of caspase 1 mediated innate immune responses.	Flow cytometry ELISA Immunoblot Transmission electron microscopy qPCR and more	Rat Human		LPS infusion CLP

Cui et al⁴⁵	2017	Determination of the role that necroptosis has in MODS Measurement of lung, liver and kidney damage	Western blotting ELISA Staining and immunohistochemistry Immunofluorescence	Rats		Fracture trauma and haemorrhage
Inflammation and immune response						
Cabrera et al⁴⁸	2017	Comparison of the transcriptome among patients with trauma and healthy volunteers	Whole blood transcriptome and flow cytometry	Human	70	Critically injured patients (ISS>25)
Jun et al⁴⁹	2011	NFkB activity and cytokine levels	Flow cytometry ELISA	Human	71	Multiple injuries (ISS>16)
Uchida et al⁵⁰	2018	Ulnistatin and 28-day all cause mortality in multiple organ failure (MOF).	Retrospective observational study Multivariable regression analysis	Human	212	Diagnosis of MOF within 24hrs of ICU admission
Bakopoulos et al⁵²	2017	Expression of TLRs in lung during sepsis	Immunofluorescence and PCR of lung tissue.	Mouse	72	CLP
Lv et al⁵³	2014	Splenic dendritic cell model	Immunohistochemistry and flow cytometry	Mouse	165	Intraperitoneal zymosan
Andruszkow et al⁵⁴	2014	Correlation of IL-6 and MODS development in children	Immunoassay	Human	59	Trauma patients (ISS>9).
Manson et al⁵⁶	2016	Populations of different lymphocytes and cytokines in trauma	Observational cohort Flow cytometry ELISA	Human	38	Blunt trauma (ISS>25)
Kirchhoff et al⁵⁷	2009	Cytokine synthesis	Flow cytometry	Human	13	LPS
Sapan et al⁵⁸	2017	Plasma levels of IL-6 and IL-10 . mRNA expression.	Prospective multicentre trial.	Human	54	Polytrauma patients (ISS>16).
Luan et al⁵⁹	2015	Tregs and effect on apoptosis. CTLA-4, Foxp3 and TGF	Flow cytometry	Mouse	180	CLP
Hazeldine et al⁶⁰	2017	Ultra-early changes in composition and function of immune cells and cytokines	Various	Human	89	Trauma patients (mean ISS 24)
Hall et al⁶¹	2010		Multicentre cohort trial	Human		
Kim et al⁶²	2014	Mesenchymal stromal cells and cytokine production		Mouse		Staphylococcal enterotoxin B
Jia et al⁶³	2013	Number of Tregs Cytokines	Western blot ELISA	Mouse	80	Zymosan

			PCR			
Gao et al⁶⁴	2017	Vitamin C and immunosuppression in sepsis induced MODS	Flow cytometry RT-PCR	Mouse		CLP
Guo et al⁶⁵	2017	Th17/Treg imbalance in sepsis. Effects of high-volume hemofiltration	Flow cytometry ELISA	Human	48	Admission with sepsis
Namas et al⁶⁷	2016	Multiple inflammatory mediators to derive “inflammatory barcodes”.	Principle component analysis/hierarchical clustering	Human	472	Blunt trauma
Endothelial dysfunction						
Bomsztyk et al⁶⁸	2015	Epigenetic modifications of angiogenic genes in endothelial dysfunction in sepsis.	Western blot RNA extraction and cDNA synthesis Chromatin preparation and ChIP assay	Mouse		<i>S.aureus</i> pneumonia
Wada et al⁶⁹	2012	Angiogenic factors and their use to predict organ dysfunction	Assays for VEGF, VEGF receptor, Ang1, Ang2, Tie2 receptor	Human	52	Post cardiac arrest
Lin et al⁷⁰	2015	Determine relationship between levels of Ang-1/2, Tie2 and VEGF in MODS	Prospective ELISA	Human	96	Diagnosis of sepsis
Call et al⁷¹	2017	Extracellular superoxide dismutase and it's protective role in endothelial activation in MODS	Variable	Mouse		LPS injection
Coletta et al⁷²	2014	Effect of aging on endothelial dysfunction and MODS development. Indices of organ dysfunction also measured.	CVD panel Aortic ring assay Various other biochemical assays	Mouse		CLP
Peng et al⁷³	2013	The effect of serum from patients with SIRS and MODS on endothelial progenitor cells.	PCR Angiogenesis assay Migration assay	Humans	20	Patients with either SIRS or MODS from various causes
Gut and MODS						
Loui et al⁷⁶	2013	Bacterial translocation and MODS	Variable	Mouse	139	LPS infusion followed by zymozan.
Moore et al⁷⁷	1991	The association between injury and gut translocation into the portal venous system.	Portal venous blood sampling		20	Injured patients requiring emergency laparotomy.
Senthil et al⁷⁸	2007	The gut derived lymphatic fluid, and its ability to induce lung injury.	Lung permeability and lung histology	Rat		Trauma/haemorrhagic shock

Badami et al⁷⁹	2008	The contribution in terms of lethality of mesenteric lymph factors		Rat		Splanchnic artery occlusion shock model
Yoseph et al⁸¹	2016	Time course and mechanisms of intestinal barrier dysfunction through tight junction protein changes	Western blot PCR Immunohistochemistry	Mouse		CLP
Cheng et al⁸²	2013	Intra-abdominal hypertension and intestinal mucosal injury	Doppler measurement of microcirculatory blood flow Intestinal injury assay	Rabbit	96	Pneumoperitoneum
Osuka et al⁸³	2017	Intestinal damage following burn. Use of I-FABP as a biomarker of intestinal damage.	Prospective cohort study. I-FABP assay. Other biomarkers recorded.	Human	32	TBSA>20%
Management						
Nguyen et al⁸⁶	2008	The role of plasma exchange in children with thrombocytopenic - associated multi organ failure.	Observational Randomised control trial	Human	37	>2 organ dysfunction
Kawai et al⁸⁷	2015	The effect of plasma exchange on haemodynamic and organ failure	Retrospective analysis	Human	14	MODS
Rajasekar an et al⁸⁸	2014	Description of experience with anakinra, a recombinant interleukin-1 receptor antagonist.	Retrospective case series	Human	8	Children with secondary hemophagocytic lymphohistiocytosis
Chang et al⁸⁹	2014	Anti-programmed cell death ligand 1 (PD-1) in patients with sepsis.	Flow cytometry	Human	58	Sepsis as per a consensus panel definition.
Brahmam dam et al⁹⁰	2010	Anti-PD-1 and survival in sepsis.	Flow cytometry	Mice	8	CLP
Inoue et al⁹¹	2012	Anti CTLA-4 therapy and survival in sepsis.	Flow cytometry	Mice		CLP
Banares et al⁹³	2013	Extracorporeal albumin dialysis in acute on chronic liver failure.	Multicentre RCT	Human	189	Acute on chronic liver failure (AOCLF)
Kribben et al⁹⁴	2012	Fractionated plasma separation and adsorption and its survival impact on patients with acute on chronic liver failure.	RCT	Human	145	AOCLF
Reviews and others (in bold)						
		Main focus of article				
Giannoni	2013	To summarise and compare commonly used organ dysfunction scores.				

et al ¹²		
McGhan et al ¹⁵	2012	The role of TLR4 in the pathogenesis of multi organ failure in haemorrhagic shock and resuscitation
Thiessen et al ²²	2018	The role of mitochondria in critical illness induced multiple organ failure
Fink ²³	2001	The role of altered cellular metabolism in MODS pathogenesis.
Zheng et al ²⁴	2015	The current experimental treatment of mitochondrial dysfunction and sepsis.
Szabo et al ²⁵	2014	The role of peroxynitrate in haemorrhagic and endotoxic shock.
Brownlee et al ²⁷	2005	A unifying mechanism for diabetic complications
Dare et al ³⁵	2009	The range of mitochondrial therapies which could be used in MODS and sepsis.
Yang et al ³⁹	2017	The contribution of HMGB1 and histones towards systemic inflammation and organ injury during acute pancreatitis.
Gunst ⁴⁰	2017	Editorial. The role of autophagy in critical illness. The implication of artificial feeding and autophagy.
Galluzzi et al ⁴⁴	2017	The molecular mechanisms of necroptosis and it's relevance to disease
Robinson et al ⁴⁶	2019	Pyroptosis, necroptosis and programmed cell death in general
Gao et al ⁴⁷	2018	The molecular mechanisms of pyroptosis in sepsis
Zhou et al ⁵¹	2019	Meta-analysis. Resveratrol and its efficacy and safety in sepsis treatment in animal models.
Jaffer et al ⁵⁵	2010	The pro- and anti-inflammatory cytokine profile of sepsis and organ dysfunction
Qiu et al ⁶⁶	2013	Meta-analysis. Anti-TNF therapy in sepsis and effects on survival.
Spapen et al ⁷⁴	2017	Proposed pathways of MODS development
Carrico et al ⁷⁵	1986	
Klingensmith et al ⁸⁰	2016	The cellular and molecular mechanisms by which the gut contributes to MODS development.
Ronco et al ⁸⁴	2003	The role of the peak concentration hypothesis in continuous renal replacement therapy in sepsis.
Rimmer et al ⁸⁵	2014	Meta-analysis. Evaluation of the efficacy and safety of plasma exchange in patients with sepsis.

Lee et al⁹²	2016	Description a range of extracorporeal liver support devices.
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