

Supplementary Online Content

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

Supplementary Table 1. Search strategy details

Supplementary Table 2. Main characteristics of the studies included in the review

Supplementary Table 3. Newcastle-Ottawa Scale scoring of studies included in the review

Supplementary Figure 1. Funnel plot for meta-analysis for overall mortality in patients with or without lymphopenia

Supplementary Figure 2. Funnel plots for meta-analysis for mortality based on two different definitions of lymphopenia: A. Lymphocyte count $< 1.0 \times 10^9/L$ B. Lymphocyte count $< 1.5 \times 10^9/L$

Supplementary Figure 3. Funnel plot for meta-analysis for mortality based on lymphocyte count

Supplementary Figure 4 Funnel plots for meta-analysis for lymphopenia and different post-operative complications

This supplementary material has been provided by the authors to give readers additional information about their work.

31 **Supplementary Table 1.** Search strategy details

32

Strategy	Cohort studies
Outcome	Lymphopenia OR lymphocytopenia OR lymphocyte count OR leukocyte count
Search filter	None
Databases searched	MEDLINE, EMBASE, WEB OF SCIENCE, GOOGLE SCHOLAR, and COCHRANE. Search terms were applied as MeSH and free text. To validate the search strategy a sampled cross-search strategy with the search terms “mortality” OR “death” AND “surgery” OR “preoperative” OR “perioperative” OR “postoperative” was applied.

33

34 Abbreviations: MeSH, medical subject headings

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50 **Supplementary Table 2. Main characteristics of the studies included in the review**

51

First author	Year	Surgery type	Sample size	Age*	Gender	Study type	Comorbidities reported	Outcome(s) reported	Follow-up period	Definition of lymphopenia	Timing of lymphopenia	Mortality	Q.A.
Ackland ²¹	2019	Non-cardiac	1654	66 (±9)	841 (M) 813 (F)	Prospective	NR	Mortality, post-operative complications, wound morbidity, infection morbidity, lymphocyte levels, Length of hospital stay	30 days	< 1.00 x10 ⁹ /L	Pre-operative: Day of surgery	39/1654	2/5
Pierre-Louis ²²	2019	Vascular	410	64 (±12)	327 (M) 83 (F)	Retrospective	Coronary artery disease 200, Stroke 68, Diabetes mellitus 243, Congestive heart failure 90, Hyperlipidemia 209, Chronic obstructive pulmonary disease 72, Chronic renal disease 122, Hypertension 361	Mortality, Revision rate	30 days	N/A	Pre-operative: < 7 days	19/410	3/5
Edwards ¹⁰	2015	Orthopaedic	745	70 (±11)*	265 (M) 480 (F)	Prospective	NR	Mortality, post-operative complications, wound morbidity, infection morbidity, lymphocyte levels, Length of hospital stay	30 days	<1.3x10 ⁹ /L or <20% of the total leucocyte count	Pre-operative: Day of surgery	1/745	2/5
Lomivorotov ²³	2011	Cardiac	1368	56 (±10)	870 (M) 498 (F)	Retrospective	Diabetes mellitus 4/40 lymphopenic group – 167/1328 non-lymphopenic group Chronic renal disease 3/40 lymphopenic group – 93/1328 non-lymphopenic group	Mortality, morbidity, infectious complications, Inotropic support, Dialysis dependent ARF, Cardiac arrhythmia, Ventilation, Bleeding	In-hospital admission period	< 1.00 x10 ⁹ /L	Pre-operative: < 72 hours	51/1368	3/5

First author	Year	Surgery type	Sample size	Age*	Gender	Study type	Comorbidities reported	Outcome(s) reported	Follow-up period	Definition of lymphopenia	Timing of lymphopenia	Mortality	Q.A.
O'Daly ²⁴	2010	Orthopaedic	200	81 (±10)*	83 (M) 294 (F)	Retrospective	NR	Mortality	In-hospital admission period, 3 months, 12 months	< 1.5 x10 ⁹ /L	Pre-operative: < 48 hours	In-hospital 14/200 3 months 30/200 12 months 59/200	3/5
Masuo ²⁶	1998	Abdominal	45	83 (±4)	NR	Retrospective	NR	Mortality	In-hospital admission period	N/A	Pre-operative: Admission	6/45	3/5
Conlan ²⁰	1989	Orthopaedic	126	79 (NR)	26(M) 100(F)	Retrospective	NR	Mortality	In-hospital admission period	N/A	Pre-operative: Admission	62/126	3/5
Seltzer ²⁵	1979	Cardiac and Non-cardiac	263	NR	NR	Retrospective	NR	Mortality, complications	In-hospital admission period	< 1.5 x10 ⁹ /L	Pre-operative: Admission	2/263	3/5

52
53

*Age reported as mean (standard deviation), asterisk denotes estimation from median and interquartile range.⁴³

54
55

Abbreviations: F, Female; M, Male; N/A, Not applicable; NOS, Newcastle-Ottawa Scale; NR, Not reported; Q.A. Quality appraisal of the methodology of the included studies

56

57

58

59

60

61

62 **Supplementary Table 3.** Newcastle-Ottawa Scale scoring of studies included in the review

63

Source	Study type	Selection	Comparability	Outcome or Exposure	Total Score
Ackland et al. 2019 ²¹	Prospective cohort study	***	**	***	8
Pierre-Louis et al. 2019 ²²	Retrospective cohort study	***	**	***	8
Edwards et al. 2015 ¹⁰	Prospective cohort study	***	*	***	7
Aghdaii et al. 2014*	Prospective cohort study	***	*	*	5
Lomivorotov et al. 2011 ²³	Retrospective cohort study	****	*	***	8
O'Daly et al. 2010 ²⁴	Retrospective cohort study	****	**	***	9
Masuo et al. 1998 ²⁶	Retrospective cohort study	****	*	***	8
Conlan 1989 ²⁰	Retrospective cohort study	***	**	**	7
Seltzer et al. 1979 ²⁵	Retrospective cohort study	****	*	**	7

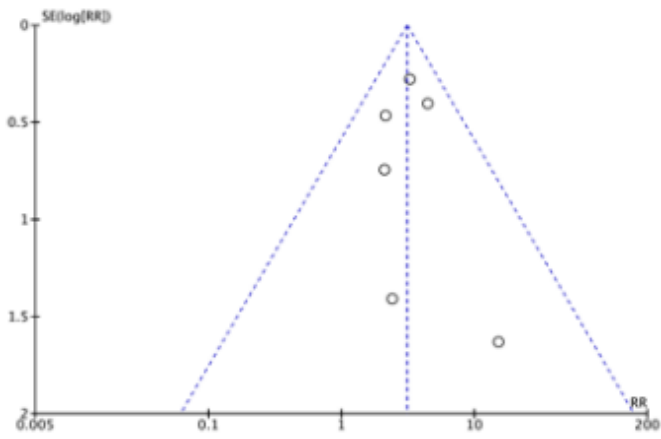
64
65 For Selection, possible scores are 0 to 4 asterisks, 0 to 2 asterisks for Comparability, and 0 to 3 * for Outcome or Exposure.

66 *The study by Aghdaii et al. was excluded from our meta-analysis due to NOS < 7.

67

68 **Supplementary Figure 1.** Funnel plot for meta-analysis for overall mortality in patients with
69 or without lymphopenia

70



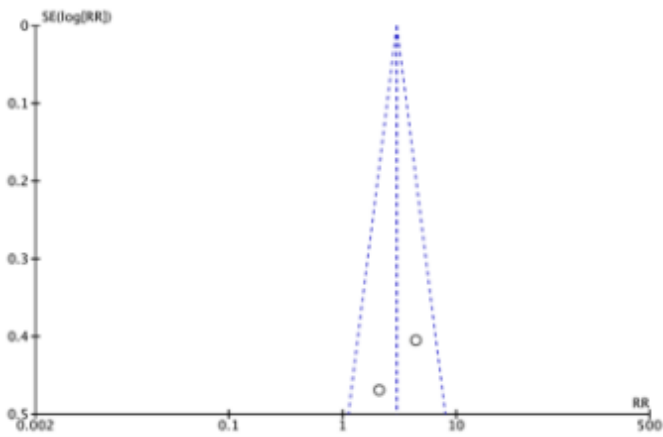
71

72 *Funnel plot analysis showed symmetrical shape.

73 **Supplementary Figure 2.** Funnel plots for meta-analysis for mortality based on two different
74 definitions of lymphopenia:

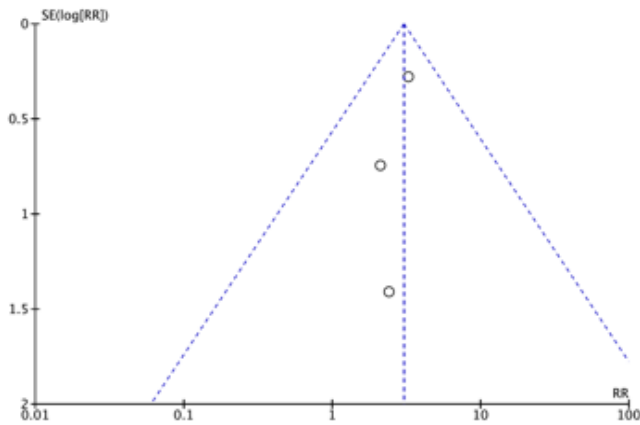
75

76 **A. Lymphocyte count < 1.0 x10⁹/L**
77



78

79 **B. Lymphocyte count < 1.5 x10⁹/L**
80



81

82

83 *Funnel plots analysis showed symmetrical shape for both groups.

84

85

86

87

88

89

90

91

92

93

94

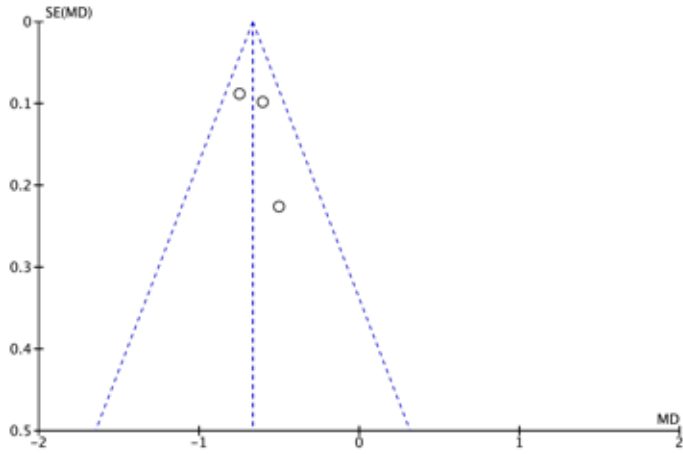
95

96

97 **Supplementary Figure 3.** Funnel plot for meta-analysis for mortality based on lymphocyte

98 count

99



100

101 *Funnel plot analysis showed symmetrical shape.

102

103

104

105

106

107

108

109

110

111

112

113

114

115

116

117

118

119

120

121

122

123

124

125

126

127

128

129

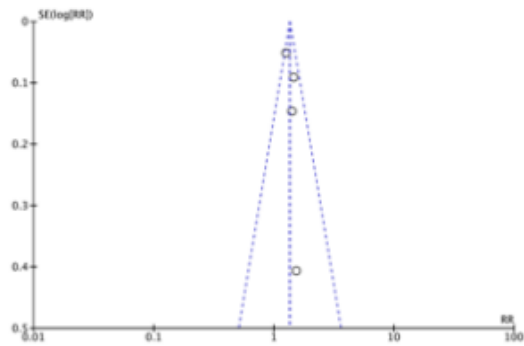
130

131

132 **Supplementary Figure 4.** Funnel plots for meta-analysis for lymphopenia and different post-
133 operative complications

134 **All complications**

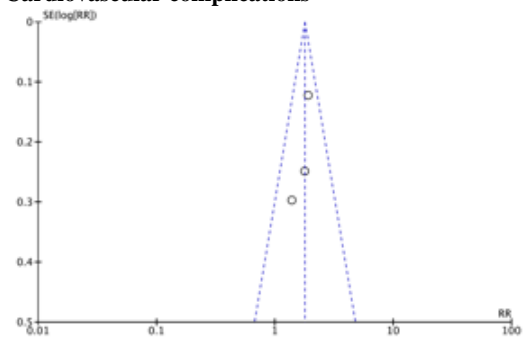
135



136

137

138 **Cardiovascular complications**

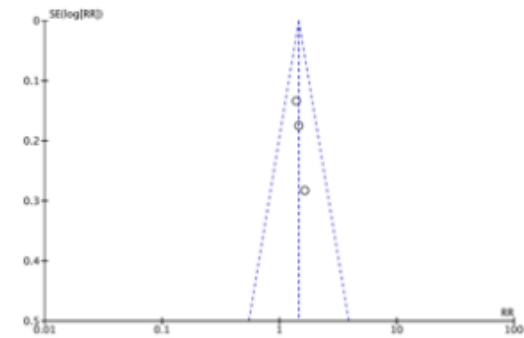


139

140

141 **Infectious complications**

142

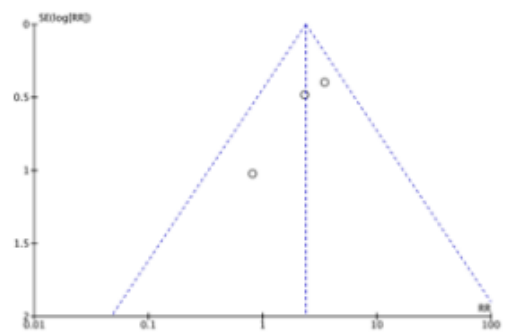


143

144

145 **Acute renal failure**

146



147

148 * Funnel plots analysis showed symmetrical shape for all groups.