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# Predictors of Mortality in Acute Mesenteric Ischemia: A Systematic Review and Meta-Analysis

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## Abstract

*Background:* Acute mesenteric ischemia (AMI) is a life-threatening medical and surgical emergency, Despite improvement in diagnosis and a recent multidisciplinary approach, there has not been any considerable improvement in mortality in patients suffering from AMI, and the overall mortality rates are high in comparison to other surgical emergencies.

*Aim of Study:* The aim of this review was to determine the clinical predictors of mortality in patients with acute mesenteric ischemia.

*Patients and Methods:* The review considered case-control studies, case report studies, prospective cohort studies and retrospective case follow-up clinical predictors of mortality in patients with acute mesenteric ischemia since 2010 till 2022 that involve patients with acute mesenteric ischemia. The following electronic databases were searched up to 2022: PubMed, Google Scholar search engine, Cochrane database of systematic reviews, EMBASE and Science Direct, Wiley Online Library, The Journal of Ankle and Foot Surgery and Clinical Key database searching keywords and terms listed below: "Mesenteric ischemia; acute ischemia, acute mesenteric ischemia, mortality of acute mesenteric ischemia, comorbidities with mesenteric ischemia".

*Results:* In our study, the Etiology of AMI was also variable among patients. 915 patients had arterial occlusive mesenteric ischemia (AOMI), 354 patients had mesenteric venous thrombosis and 193 patients had non-occlusive mesenteric ischemia (NOMI) while 7678 patients had either other secondary cause of AMI or the etiology was unspecified. In our study, age and gender were factors related to demographics included in the current review.

Age was reported by 15 studies and was significantly associated with mortality (OR 1.19, 95% CI 1.09 - 1.29; $p$<0.00001; $I^2$=82%). Gender was assessed in 18 studies. It was analyzed as male versus female but it could not achieve statistical significance (OR 0.96, 95% CI 0.85-1.07; $p$=0.46; $I^2$=34%).

*Conclusion:* This comprehensive review investigated clinical predictors of mortality in patients with acute mesenteric ischemia (AMI) from studies conducted between 2010 and 2022.

***Key Words:*** *Mortality – Acute Mesenteric Ischemia.*

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## Introduction

Intestinal ischemia refers to insufficient blood flow within the mesenteric circulation to meet the metabolic demands in the bowel **[1]**. Acute mesenteric ischemia (AMI) is an emergency condition, which is accompanied by fatal complications, and defined as extremely reduced blood flow to the intestine or part of the intestine that may progress to intestinal necrosis, septic shock, and eventually death **[2]**. Patients with AMI normally present in acute settings with abdominal pain out of proportion to clinical findings. Diagnosis of AMI has always been a challenge as no single biomarker can completely diagnose AMI with both high sensitivity and specificity **[3]**.

The mortality rate in AMI remains high due to challenges in early diagnosis, the lack of specific markers, and irreversible intestinal ischemia secondary to delay in diagnosis. Although significant advances in its diagnosis and treatment have been made over the last decade, mortality rates are still reported to be around 40-70% for acute mesenteric ischemia mainly due to a low index of suspicion **[4]**. The etiologic cause in 70-80% of cases with AMI is intestinal ischemia that occurs as a result of occlusion of the mesenteric artery due to an embolus or thrombus. Embolic occlusion results in earlier ischemia and trans mural necrosis as compared with other causes, due to the absence of a well-developed collateral circulation **[5]**. Strangulated hernia, ve-

nous thrombosis and non-occlusive causes are rare reasons of AMI **[6].**

CT angiography remains the diagnostic method of choice since it is a rapid, noninvasive and easily available radiological modality with a sensitivity of 93% and specificity of 100% **[7]**, with a confirmed diagnosis, the patient is managed with an infusion of intravenous fluids, anticoagulants, and antibiotics, **[8].** Both Endovascular and open treatment methods are employed based on specific patient settings and etiology, **[9]**. In the case of Non-occlusive mesenteric ischemia (NOMI), treatment with vasodilators is useful in combating vasospasm and laparotomy is only used when there is suspected intestinal necrosis.

Therefore, to sort out increasing discrepancies among existing literature and figure out a prognostic model, we aim to conduct a systematic review that will pool data from all the original articles to identify predictors of mortality in AMI.

*Aim of the work:*

The aim of this review is to determine the clinical predictors of mortality in patients with acute mesenteric ischemia.

## Patients and Methods

The review will consider case-control studies, case report studies, prospective cohort studies and retrospective case follow-up clinical predictors of mortality in patients with acute mesenteric ischemia. This review will consider all studies since 2010 till 2022 that involve patients with acute mesenteric ischemia.

The following electronic databases were searched up to 2022: PubMed, Google Scholar search engine, Cochrane database of systematic reviews, EMBASE and Science Direct, Wiley Online Library, The Journal of Ankle and Foot Surgery and Clinical Key database searching keywords and terms listed below: “mesenteric ischemia; acute ischemia, acute mesenteric ischemia, mortality of acute mesenteric ischemia, comorbidities with mesenteric ischemia”. Also full copies of articles of available medical journals and other published studies identified by the search, discussion with several investigators expert in the field and published case reports, considered to meet the inclusion criteria, based on their title, abstract and subject descriptors, will be obtained for data synthesis. Our review will be restricted to studies conducted in English language.

Methods of the review:

*Data extraction:*

Studies that fit the inclusion criteria will be manually reviewed and data will be analysed. All the primary research studies that come out from the search will be screened regarding the title to remove any duplicate. Included studies will be categorized according to level of evidence and evaluated for quality.

*Statistical analysis:*

Review Manager (Version 5.3; The Cochrane Collaboration; London, United Kingdom) was used to perform statistical analysis. OR/HR and 95% confidence interval (CI) were extracted from multivariate analysis of original studies if reported. Otherwise, they were extracted from univariate analysis or calculated based on reported numbers, and then they were pooled together in a random-effects model due to expected heterogeneity due to variable setting and etiologies. Forest plots were used for a visual representation of the pooled results. We only pooled those variables that were reported by two studies or more. To summarize the analysis, we grouped these predictors into seven groups, namely demographics, comorbidities and past illness, cardiovascular diseases, disease presentation, radiological findings, biochemical parameters, and management (medical and surgical). Age was analyzed as a categorical variable with a cut-off equal to or more than 60 years, and delay to surgery had a cutoff of a minimum of 6h. Heterogeneity was assessed using the $I^2$ statistic, and a value of $I^2$ greater than 75% was considered significant heterogeneity. Publication bias was assessed by the Egger test and funnel plot.

## Results

*Literature search:*

The initial search yielded 1524 articles. After de-duplication and title/abstract screening, 100 articles were left that underwent full-text review. At last, 36 potential articles were selected. The detailed literature search is represented in the PRISMA flow chart (Fig. 1).

*Study characteristics:*

In 36 studies 9164 patients suffering AMI were included. 35 studies reported on the number of people who died. Out of the included patients, there were 3067 cases died. 34 studies were retrospective cohort and two was prospective cohort. Expression of mortality was variable among different studies. In-hospital mortality was reported by 11 studies, while 30-day mortality was reported by 14 studies. Three studies reported perioperative or postoperative mortality. Expression of mortality was variable in one study while five studies did not report any expression of mortality. The Etiology of AMI was also variable among patients. 915 patients had arterial occlusive mesenteric ischemia (AOMI), 354 patients had mesenteric venous thrombosis and 193 patients had non-occlusive mesenteric ischemia (NOMI) while 7678 patients had either other secondary cause of AMI or the etiology was unspecified. Detailed study characteristics are presented in Tables (1,2).

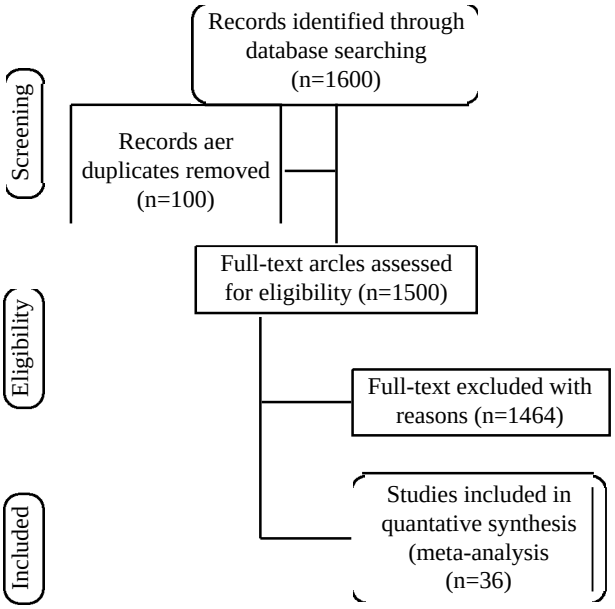


Fig. (1): Flow diagram of the literature search and study selection processes.

*Risk of bias and publication bias:*

Study quality was assessed by NOS score. All studies have a low risk of bias with a median score of 7 (Table 3).

Meta-analysis:

*Predictors of mortality:*

Overall, we identified 33 predictors of mortality that underwent statistical analysis. Predictors were further divided into the following categories.

*Demographic:*

Age and gender were factors related to demographics included in the current review. Age was reported by 15 studies and was significantly associated with mortality (OR 1.19, 95% CI 1.09-1.29; $p<0.00001$; $I^2=82\%$). Gender was assessed in 18 studies. It was analyzed as male versus female but it could not achieve statistical significance (OR 0.96, 95% CI 0.85-1.07; $p=0.46$; $I^2=34\%$) (Fig. 2).

There was no significant publication bias since there was no asymmetry seen on the funnel plot, and the Egger test was non-significant ($p>0.05$).

*Comorbidities and past illnesses:*

Comorbidities and past illnesses included were cancer, chronic renal disease, diabetes mellitus, hypertension, patient dependency, peripheral vascular disease, previous surgery, and cerebrovascular disease. Among these factors, chronic renal disease was not significantly related to mortality, while patient dependency was among the factors that were significantly related to mortality. Chronic renal disease was reported by five studies (OR 2.25, 95% CI 0.97-5.21; $p=0.06$; $I^2=64\%$). Patient dependency was reported by five studies (OR 2.84, 95% CI 1.99-4.07; $p<0.00001$; $I^2=24\%$). Diabetes was reported by 10 studies (OR 1.54, 95% CI 1.00-2.39; $p=0.05$; $I^2=69\%$). Additionally, comorbidities and past illnesses that were significantly related to mortality included cancer that was reported by two studies (OR 2.01, 95% CI 1.05-3.85; $p=0.04$; $I^2=0\%$). Hypertension didn't significantly related to mortality and reported by 10 studies (OR 1.60, 95% CI 0.82-3.15; $p=0.17$; $I^2=87\%$). Peripheral vascular disease (PVD) was not significantly related to mortality and mentioned by six studies (OR 0.74, 95% CI 0.52-1.04; $p=0.08$; $I^2=54\%$). Previous surgery was not significantly related to mortality and was reported by five studies (OR 1.11, 95% CI 0.56-2.17; $p=0.77$; $I^2=74\%$) and cerebrovascular disease that was reported by two studies (OR 0.77, 95% CI 0.27-2.24; $p=0.64$; $I^2=4\%$). There was no significant publication bias since there was no asymmetry seen on the funnel plot, and the Egger test was nonsignificant ($p>0.05$).

*Cardiovascular diseases:*

Within cardiovascular diseases, the following diseases were included; arrhythmia, atrial fibrillation, cardiac failure and coronary artery disease. Out of these arrhythmias and cardiac failure attained a statistically significant relationship with mortality. Arrhythmia was reported by three studies (OR 2.33, 95% CI 1.16-4.70; $p=0.02$; $I^2=60\%$), coronary artery disease that was reported by three studies (OR 1.68, 95% CI 1.35-2.10; $p<0.00001$; $I^2=0\%$), and cardiac failure was mentioned in five studies (OR 2.01, 95% CI 1.36-2.98; $p=0.0005$; $I^2=77\%$) while those factors that failed to establish a statistically significant relation with mortality include atrial fibrillation that was reported by four studies (OR 1.00, 95% CI 0.77-1.31; $p=0.98$; $I^2=33\%$). There was no significant publication bias since there was no asymmetry seen on the funnel plot, and the Egger test was non significant ($p>0.05$).

*Disease presentation:*

Abdominal pain, hypotension, small bowel involvement, small & large bowel involvement, and large bowel involvement were included as part of the disease presentation. Abdominal pain and large bowel involvement were significantly associated with mortality. Small and large bowel involvement was reported in three studies (OR 2.25 95% CI 0.96-5.27; $p=0.06$, $I^2=63\%$) large bowel involvement was reported by seven studies (OR 2.74, 95% CI 1.14-6.59; $p=0.02$; $I^2=79\%$) while abdominal pain was reported by five studies and had a significant association with mortality (OR 0.31, 95% CI 0.14-0.72; $p=0.006$; $I^2=0\%$). Small bowel involvement was reported in three studies showed no significant relation with mortality (OR 1.15, 95% CI 0.40-3.27; $p=0.8$, $I^2=78\%$). There was no significant publication bias since there was no asymmetry seen on the funnel plot, and the Egger test was non-significant ($p>0.05$).

Table (1): Basic Characteristics of the selected studies.

| Study | Country | Study design | Sample size (n) | Mortality (n) | Female (%) | Mean age (n) | Expression of mortality | NOS score |
|---|---|---|---|---|---|---|---|---|
| (Arnalich et al., 2010) | Spain | Prospective | 99 | 46 | 33.07 | N/A** | 30-day mortalty | 9 |
| (Gupta et al., 2011) | USA | Retrospective | 861 | 240 | 53.66 | N/A** | 30-day mortality | 7 |
| (Newton et al., 2011) | | Retrospective | 142 | 43 | 45.77 | 66 | Postoperative | 7 |
| (Park et al., 2012) | Korea | Retrospective | 40 | 13 | 40 | 64.05 | Perioperative | 7 |
| (Aliosmanoglu et al., 2013) | Turkey | Retrospective | 95 | 40 | 41.05 | 68.4 | N/A** | 6 |
| (Paladino et al., 2014) | Italy | Retrospective | 149 | 57 | N/A** | 76.4 | N/A** | 7 |
| (Yun et al., 2013) | Korea | Retrospective | 30 | 8 | 50 | N/A** | In hospital mortality | 6 |
| (Dinc et al., 2015) | Turkey | Retrospective | 73 | 40 | 42.46 | 69.3 | 30-day mortality | 7 |
| (Adaba et al., 2016) | UK | Retrospective | 113 | N/A** | 53.98 | N/A** | 30-day mortality | 7 |
| (Akyıldız et al., 2015) | Turkey | Retrospective | 104 | 69 | 44.23 | 66 | 30-day mortality | 8 |
| (Bilgiç et al., 2015) | Turkey | Retrospective | 61 | 35 | 40.98 | 69.7 | N/A** | 7 |
| (Eslami et al., 2016) | USA | Retrospective | 1563 | 277 | 65 | 68.7 | N/A** | 7 |
| (Leone et al., 2015) | France | Retrospective | 780 | 454 | 42 | 69 | N/A** | 6 |
| (Nagaraja et al., 2015) | India | Retrospective | 117 | 46 | 27.35 | N/A** | In hospital mortality | 6 |
| (Studer et al., 2015) | Germany | Retrospective | 91 | 39 | 53.84 | 66.7 | In hospital mortality | 6 |
| (Crawford et al., 2016) | USA | Retrospective | 2255 | 551 | N/A** | 67 | In hospital mortality | 7 |
| (Yıldırım et al., 2017) | Turkey | Retrospective | 46 | 27 | 52.17 | 67.5 | In hospital mortality | 8 |
| (Yılmaz & Cartı, 2017 | Turkey | Retrospective | 34 | 19 | 44.11 | N/A** | In hospital mortality | 7 |
| (Salim et al., 2018) | Sweden | Retrospective | 120 | 13 | 57.5 | N/A** | 30-day mortality | 7 |
| (Caluwarts et al., 2019) | Belgium | Retrospective | 214 | 145 | 49.06 | 72 | 30-day mortality | 7 |
| (Grotelüschen et al., 2019) | Germany | Retrospective | 302 | 204 | 63.9 | 70.9 | Postoperative | 7 |
| (Lemma et al., 2019) | Finland | Retrospective | 81 | 50 | 48.15 | N/A** | In hospital mortality | 7 |
| (Miyazawa & Kamo, 2020) | Japan | Retrospective | 21 | 11 | N/A** | N/A** | In hospital mortality | 6 |
| (Nakamura et al., 2019) | Japan | Retrospective | 30 | 9 | 43.33 | N/A** | In hospital mortality | 6 |
| (Vural & Vefik Ozozan, 2019) | Turkey | Retrospective | 37 | 9 | 48.64 | 67.8 | 30-day mortality | 6 |
| (Yang et al., 2019) | China | Retrospective | 199 | 35 | 48.24 | 48.1 | 30-day mortality | 6 |
| (Jagielski et al., 2020) | Poland | Retrospective | 41 | 26 | 65.85 | 65.4 | In hospital mortality | 6 |
| (Miao et al., 2020) | China | Retrospective | 88 | 10 | 14.77 | 58.8 | 30-day mortality | 8 |
| (Sindall et al., 2020) | Czech republic | Retrospective | 221 | 55 | N/A** | 61.9 | Variable | 6 |
| (Wu et al., 2020) | Western China | Retrospective | 77 | 23 | 44.44 | N/A** | 30-day mortality | 8 |
| (Ozturk et al., 2021) | Turkey | Retrospective | 140 | 74 | 45 | 66.6 | In hospital mortality | 8 |
| (Ksouri et al., 2022) | France | Prospective | 114 | 15 | 39 | 58 | 12-month mortality | 9 |
| (Wu & Zhou, 2021) | China | Retrospective | 338 | 117 | 52.1 | 67.9 | Hospital mortality | 8 |
| (Pedersoli et al., 2021) | Germay | Retrospective | 40 | 25 | 55 | 74 | 30-day mortality | 7 |
| (Tolonen et al., 2021) | Finland | Retrospective | 145 | 57 | 65 | 75 | 30-day mortality | 8 |
| (Chou et al., 2021) | United States | Retrospective | 303 | 185 | 55 | 72 | 30-day mortality | 7 |

SD* = Standard deviation. N/A** = Not applicable.

Table (2): Etiology of AMI.

| Study | Total population (n) | AOMI (n) | MVT (n) | NOMI (n) | Other/Not specified (n) |
|---|---|---|---|---|---|
| (Arnalich et al., 2010) | 99 | 63 | 15 | 21 | – |
| (Gupta et al., 2011) | 861 | – | – | – | 861 |
| (Newton et al., 2011) | 142 | 142 | – | – | – |
| (Park et al., 2012) | 40 | 24 | 2 | 14 | – |
| (Aliosmanoglu et al., 2013) | 95 | – | – | – | 95 |
| (Paladino et al., 2014) | 149 | – | – | – | 149 |
| (Yun et al., 2013) | 30 | – | – | – | 30 |
| (Dinc et al., 2015) | 73 | 73 | – | – | – |
| (Adaba et al., 2016) | 113 | 74 | 25 | – | 14 |
| (Akyıldız et al., 2015) | 104 | 74 | 15 | 12 | 3 |
| (Bilgiç et al., 2015) | 61 | – | – | – | 61 |
| (Eslami et al., 2016) | 1563 | – | – | – | 1563 |
| (Leone et al., 2015) | 780 | – | – | – | 780 |
| (Nagaraja et al., 2015) | 117 | 61 | 56 | – | – |
| (Studer et al., 2015) | 91 | – | – | – | 91 |
| (Crawford et al., 2016) | 2255 | 37 | – | – | 2218 |
| (Yıldırım et al., 2017) | 46 | 34 | 8 | 4 | – |
| (Yılmaz & Cartı, 2017 | 34 | – | – | – | 34 |
| (Salim et al., 2018) | 120 | – | 120 | – | – |
| (Caluwarts et al., 2019) | 214 | – | – | – | 214 |
| (Grotelüschen et al., 2019) | 302 | – | – | – | 302 |
| (Lemma et al., 2019) | 81 | – | – | – | 81 |
| (Miyazawa & Kamo, 2020) | 21 | – | – | 21 | – |
| (Nakamura et al., 2019) | 30 | – | – | 30 | – |
| (Vural & Vefik Ozozan, 2019) | 37 | – | – | – | 37 |
| (Yang et al., 2019) | 199 | 149 | 13 | 6 | 31 |
| (Jagielski et al., 2020) | 41 | 14 | 2 | – | 25 |
| (Miao et al., 2020) | 88 | 14 | 10 | – | 37 |
| (Sindall et al., 2020) | 221 | – | – | – | 221 |
| (Wu et al., 2020) | 77 | 45 | 32 | – | – |
| (Ozturk et al., 2021) | 140 | – | 11 | 17 | 112 |
| (Ksouri et al., 2022) | 114 | 71 | 45 | 1 | – |
| (Wu & Zhou, 2021) | 338 | – | – | – | 338 |
| (Pedersoli et al., 2021) | 40 | 40 | – | – | – |
| (Tolonen et al., 2021) | 145 | – | – | – | 145 |
| (Chou et al., 2021) | 303 | – | – | 67 | 236 |

SD* = Standard deviation. N/A** = Not applicable.

*Radiological findings:*

Radiological findings selected were bowel wall thickening, mesenteric or portal venous gas, and pneumatosis intestinalis. Bowel wall thickening was reported by three studies and was not associated with a significant decrease in mortality (OR 0.62, 95% CI 0.35-1.07; $p$=0.08; $I^2$=0%), furthermore, mesenteric or portal venous gas and pneumatosis intestinalis could not establish relation with mortality. Mesenteric or portal venous gas was reported by three studies (OR 1.35, 95% CI 0.68-2.70; $p$=0.39; $I^2$=0%) and pneumatosis intestinalis was reported by three studies (OR 0.58, 95% CI 0.09-3.83; $p$=0.58; $I^2$=76%). There was no significant publication bias since there was no asymmetry seen on the funnel plot, and the Egger test was nonsignificant ($p$>0.05).

*Biochemical parameters:*

Creatinine and lactate are two biochemical parameters that were included and were significantly associated with increased mortality. Creatinine was reported in five studies (OR 1.59, 95% CI 1.18-2.14; $p$=0.0002; $I^2$=69%) and lactate was reported as a risk factor in four studies (OR 1.40, 95% CI 1.23-1.60; $p$<0.00001; $I^2$=0%). There was no significant publication bias since there was no asymme-

try seen on the funnel plot, and the Egger test was nonsignificant ($p$>0.05).

*Management (medical and surgical):*

Factors related to medical and surgical management related to mortality included in this review were Anticoagulation, antiplatelet, bowel resection, inotropes, revascularization, second-look surgery, primary anastomosis, and delay to surgery. Treatment with anticoagulation was associated with decreased mortality. It was reported in five studies (OR 0.30, 95% CI 0.10-0.88; $p$=0.03; $I^2$=82%). Revascularization was not significantly related to decreased mortality and was reported in two studies (OR 0.55, 95% CI 0.09-3.35; $p$=0.52; $I^2$=2%). On the other hand, management with inotropes was reported by two studies and was related with significantly increased mortality (OR 10.29, 95% CI 3.24-32.67; $P$<0.0001; $I^2$=31%). Delay to surgery that was reported by four studies and also established a significant association to mortality (OR 6.35, 95% CI 1.32-30.60 $p$=0.02; $I^2$=94%). Antiplatelet was reported by two studies and was significantly related to mortality (OR 1.21, 95% CI 0.70-2.09; $p$=0.049; $I^2$=35%). Bowel resection was reported by 11 studies and could not establish a statistically significant association with mortality (OR 0.93, 95% CI 0.45-1.93; $p$=0.84; $I^2$=94%). Primary anastomosis was reported by two studies and was not a significant predictor of mortality (OR 1.13, 95% CI 0.49-2.63; $p$=0.78; $I^2$=60%). Second look surgery was reported by four studies and was not a significant predictor of mortality (OR 1.20, 95% CI 0.73-1.98; $p$=0.46; $I^2$=0%). There was no significant publication bias since there was no asymmetry seen on the funnel plot, and the Egger test was non-significant ($p$>0.05).

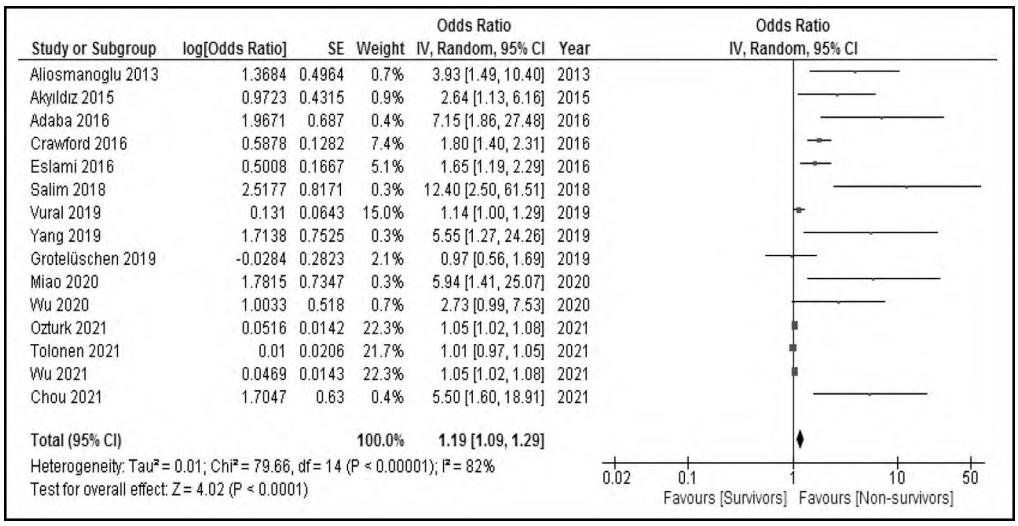


Fig. (2): Forest plot for age.

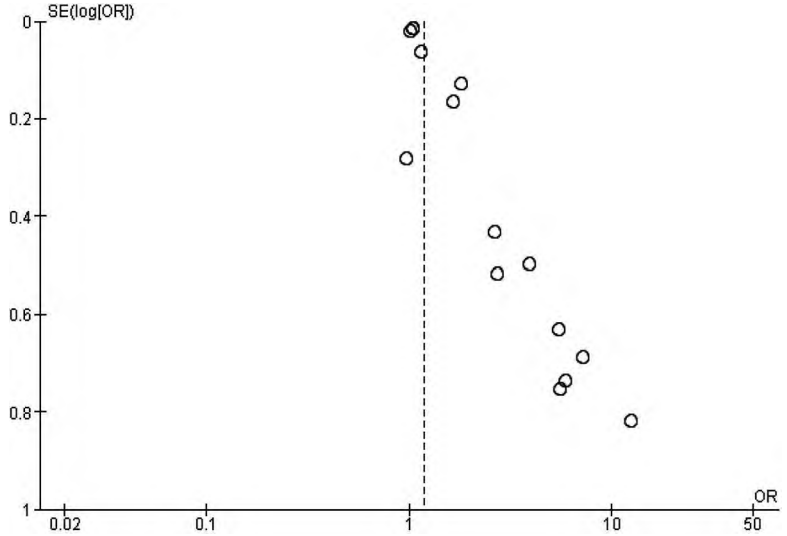


Fig. (3): Funnel plot of age.

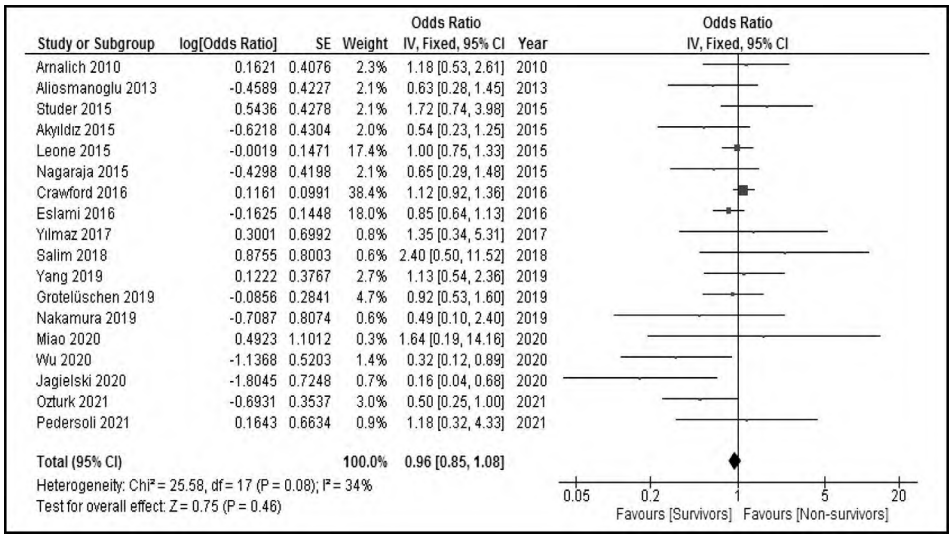


Fig. (4): Forest plot for gender Male vs Female.

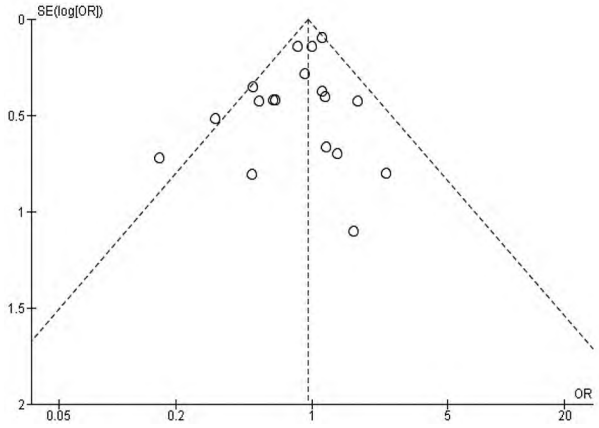


Fig. (5): Funnel plot for gender.

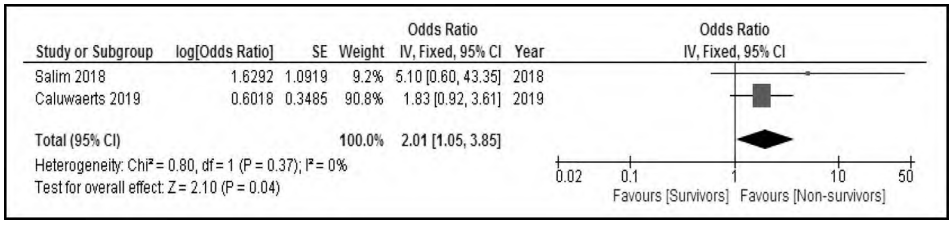


Fig. (6): Forest plot for cancer.

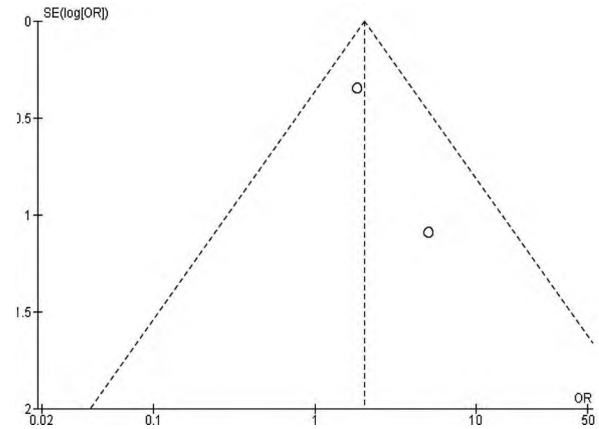


Fig. (7): Funnel plot for cancer.

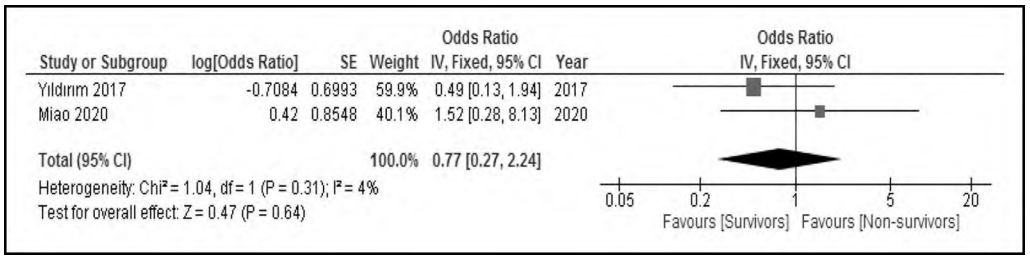


Fig. (8): Forest plot for cerebrovascular disease.

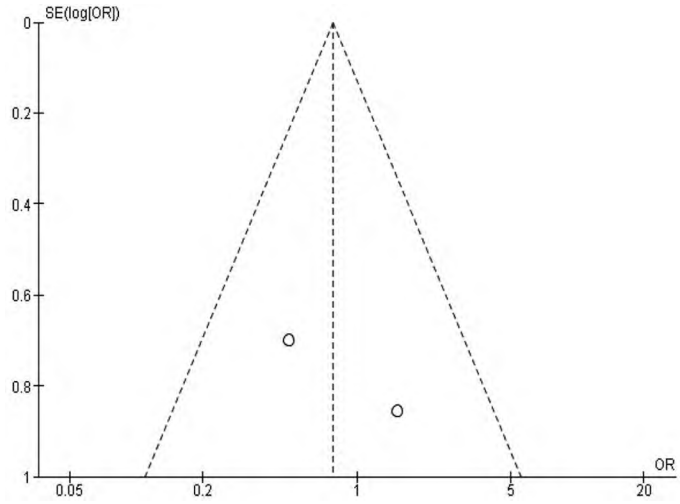


Fig. (9): Forest plot for cerebrovascular disease.

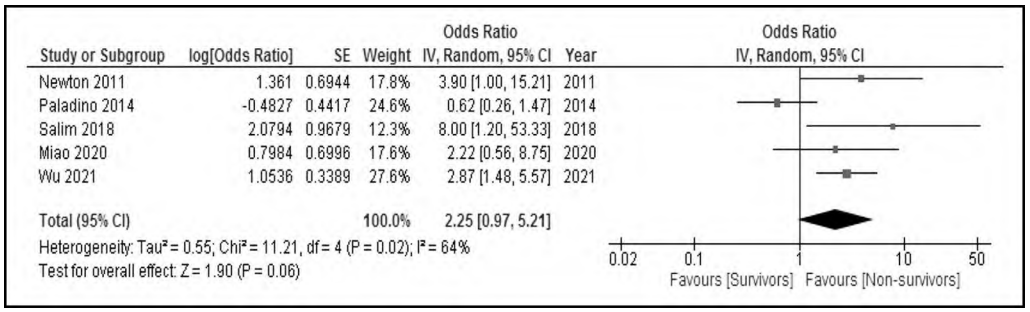


Fig. (10): Forest plot for chronic renal disease.

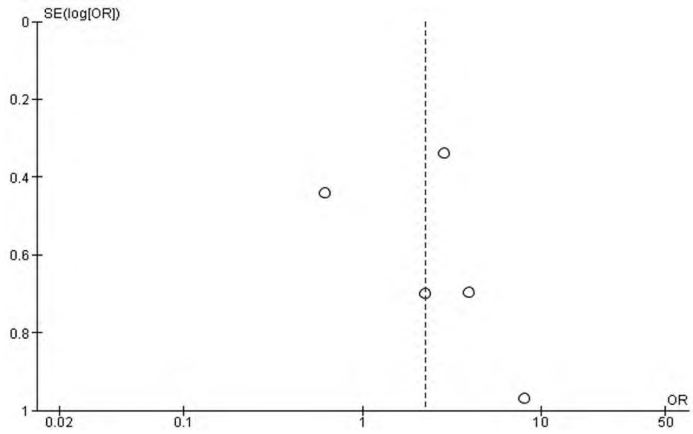


Fig. (11): Funnel plot for chronic renal disease.

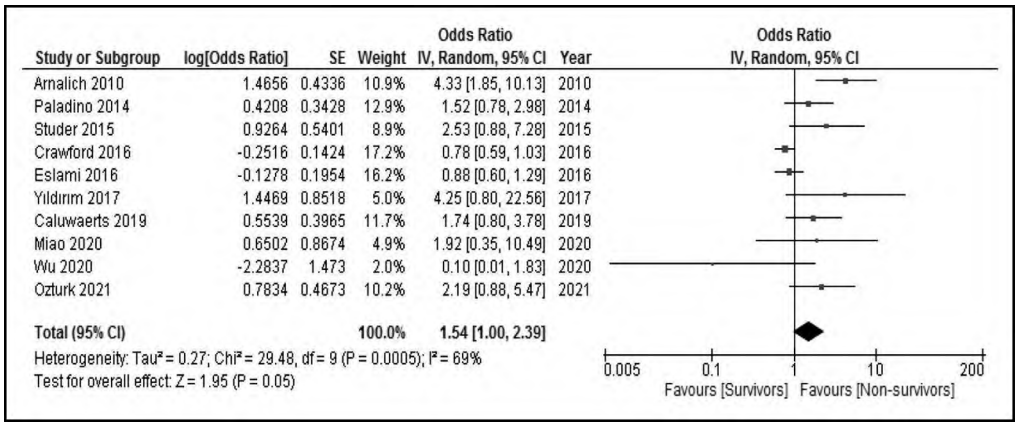


Fig. (12): Forest plot for diabetes.

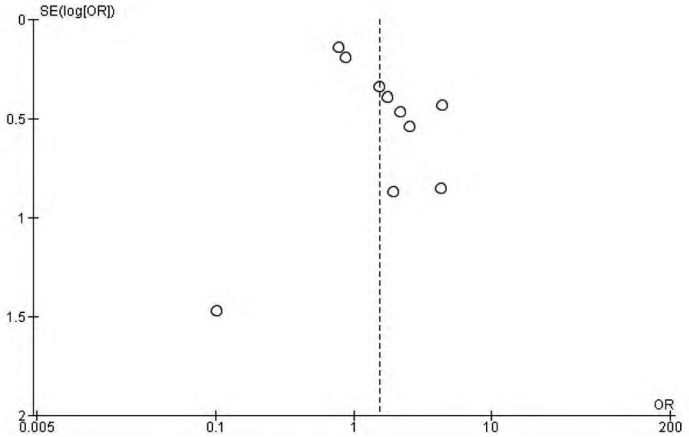


Fig. (13): Funnel plot for diabetes.

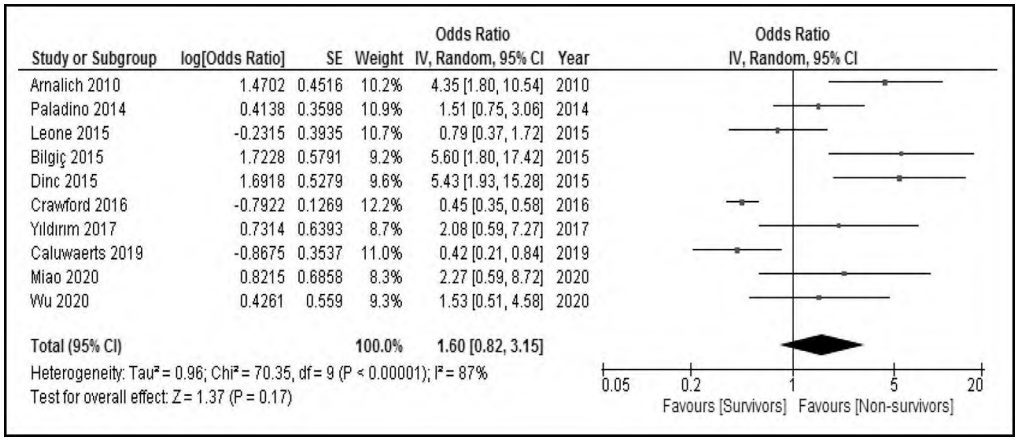


Fig. (14): Forest plot for hypertension.

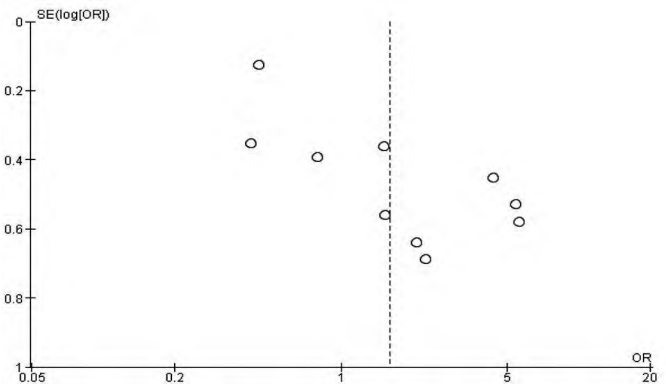


Fig. (15): Funnel plot for hypertension.

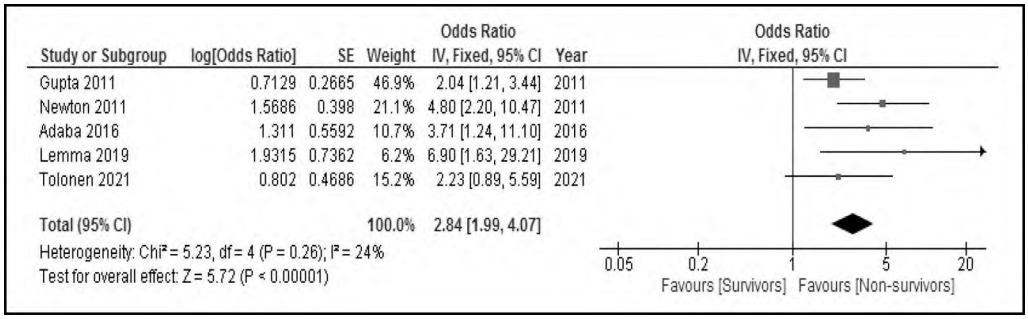


Fig. (16): Forest plot for patient dependency.

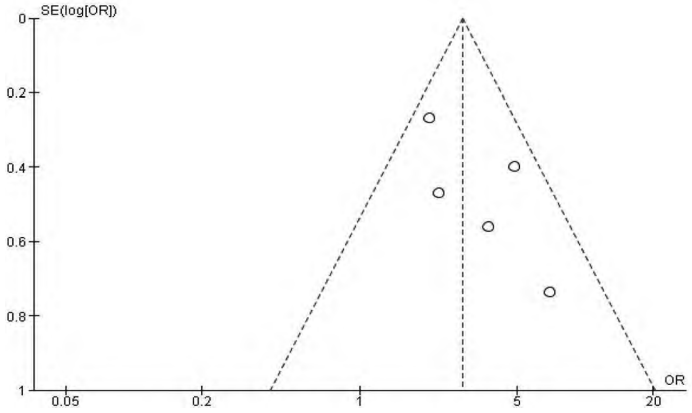


Fig. (17): Funnel plot for patient dependency.

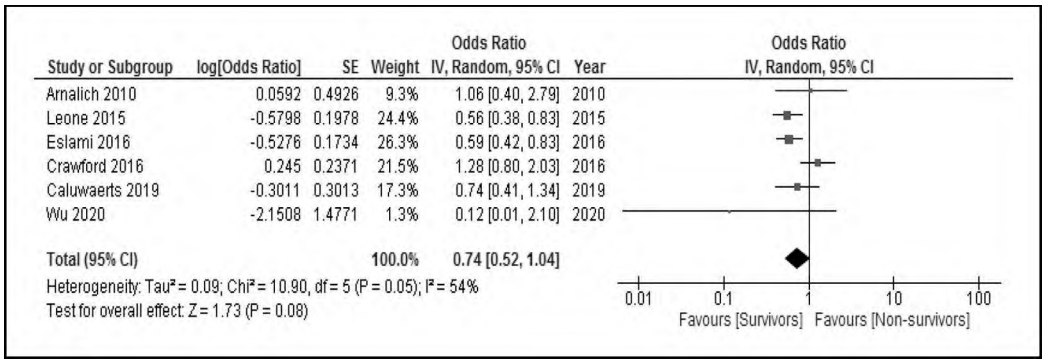


Fig. (18): Forest plot for peripheral vascular disease.

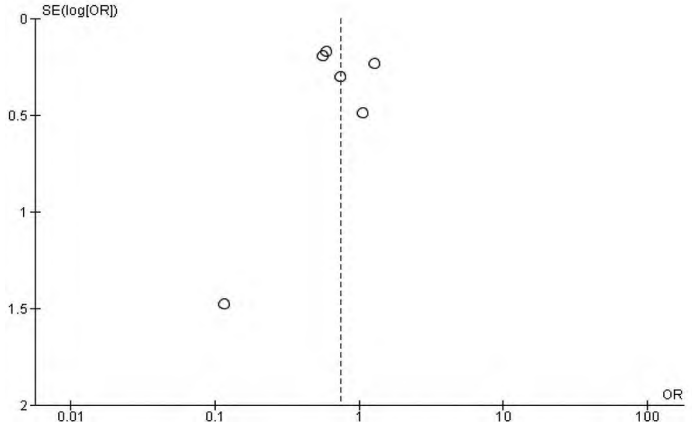


Fig. (19): Funnel plot for peripheral vascular disease.

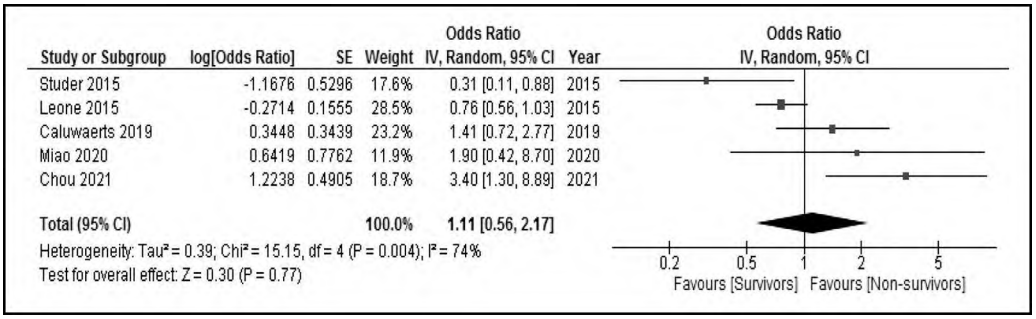


Fig. (20): 20: Forest plot for previous surgery.

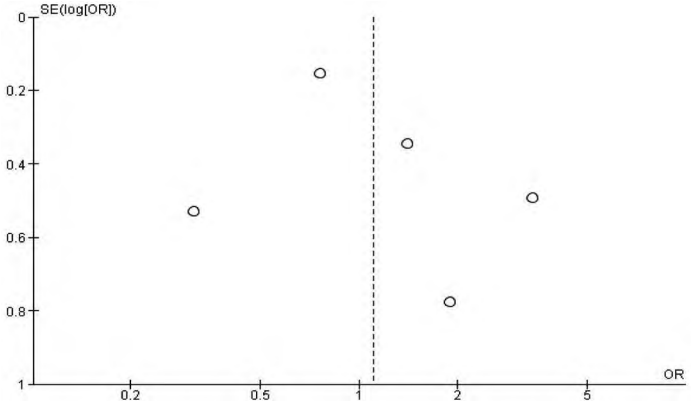


Fig. (21): Funnel plot for previous surgery.

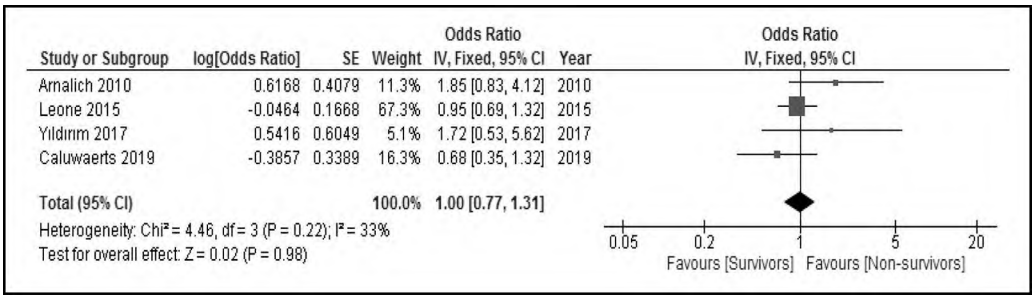


Fig. (22): Forest plot for Atrial fibrillation.

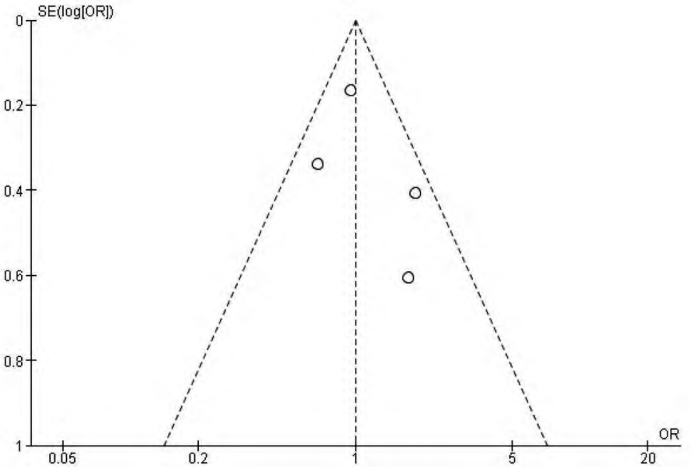


Fig. (23): Funnel plot for Atrial fibrillation.

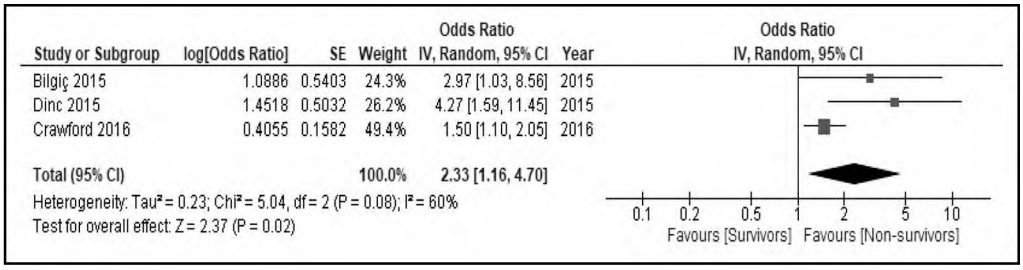


Fig. (24): Forest plot for Arrhythmias.

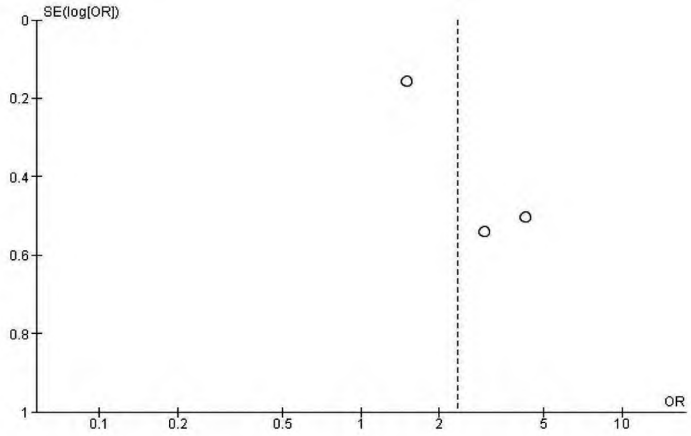


Fig. (25): Funnel plot for Arrhythmias.

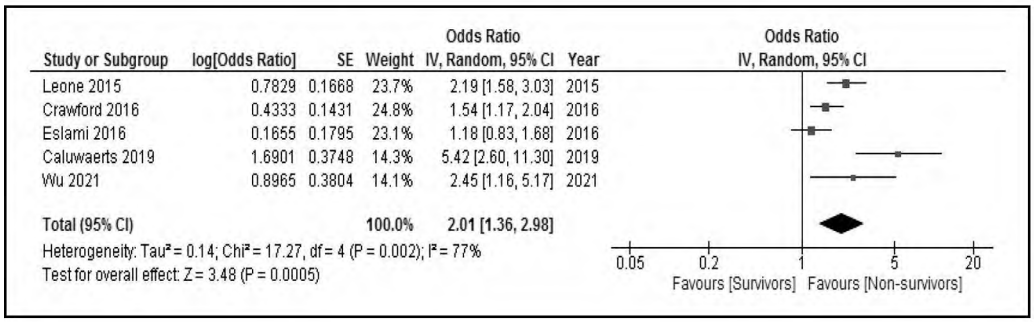


Fig. (26): Forest plot for cardiac failure.

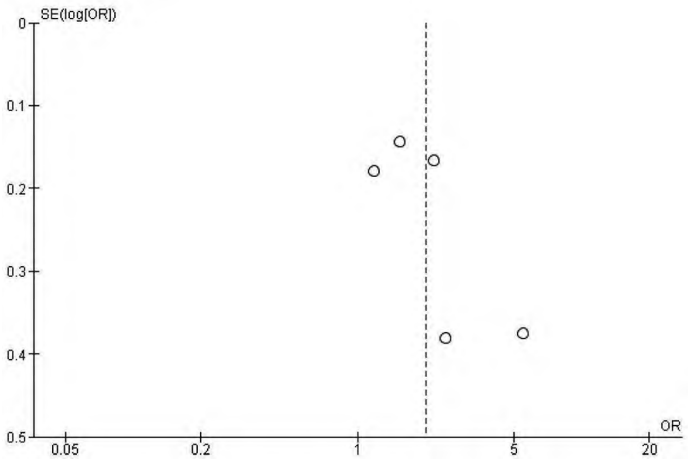


Fig. (27): Funnel plot for cardiac failure.

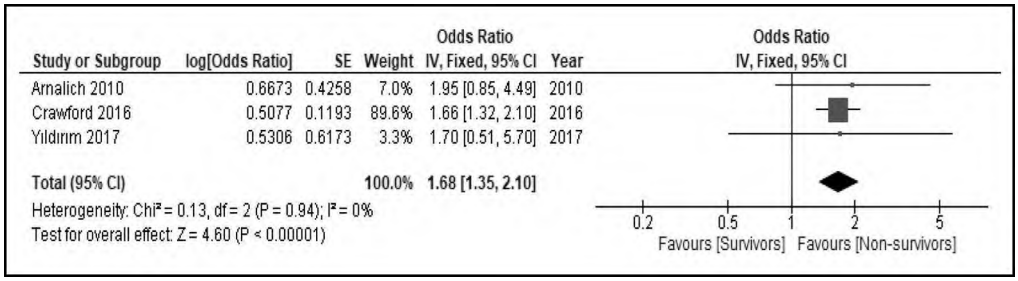


Fig. (28): Forest plot for coronary artery disease.

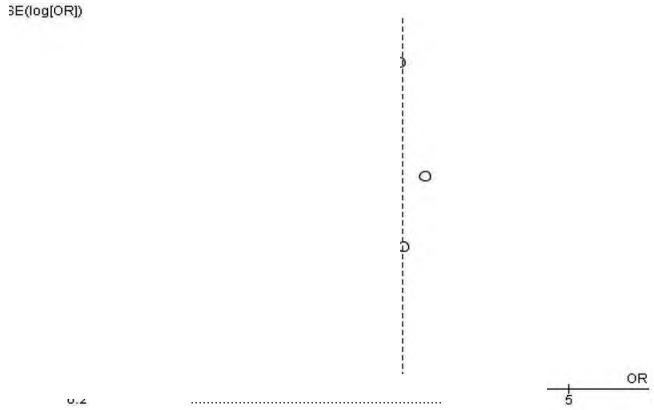


Fig. (29): Funnel plot for coronary artery disease.

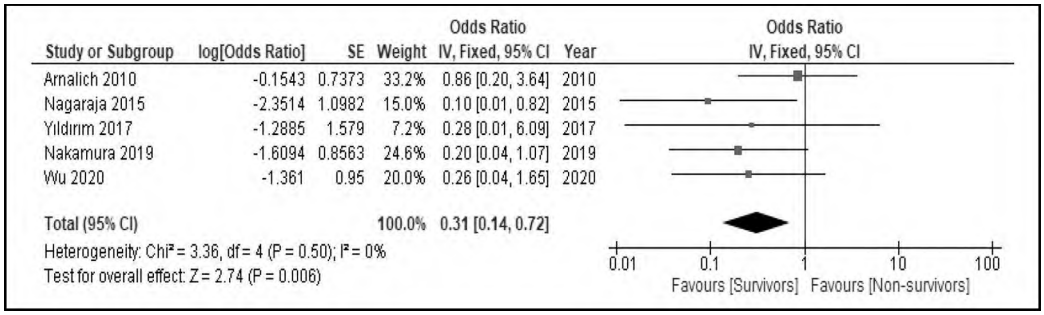


Fig. (30): Forest plot for Abdominal pain.

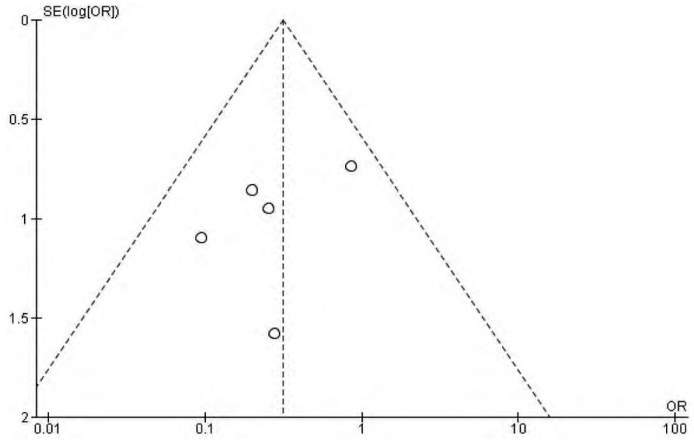


Fig. (31): Funnel plot for Abdominal pain.

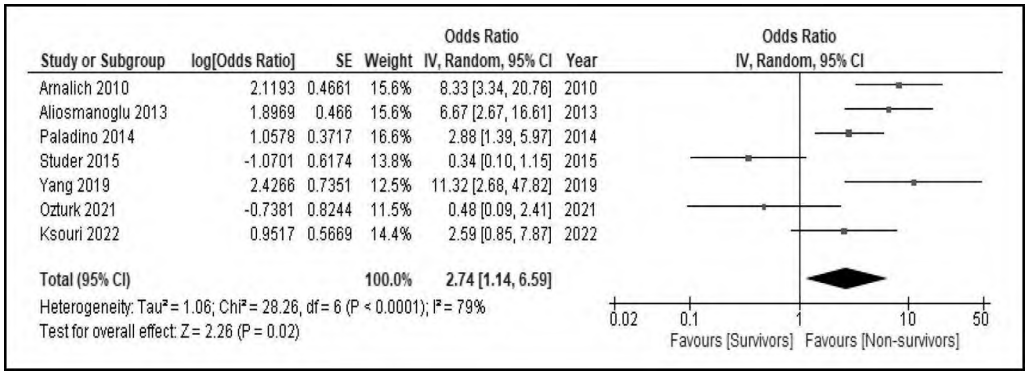


Fig. (32): Forest plot for large bowel involvement.

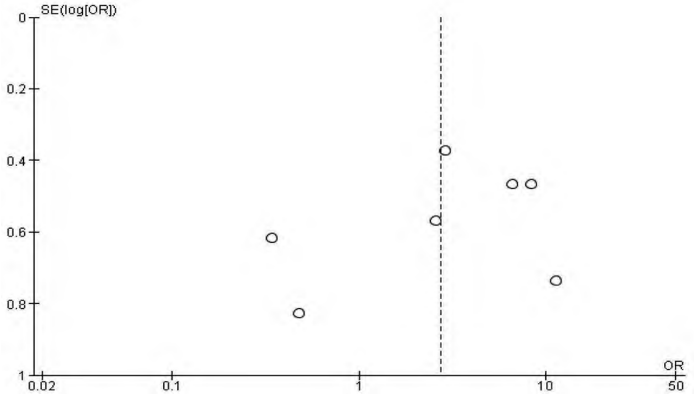


Fig. (33): Funnel plot for large bowel involvement.

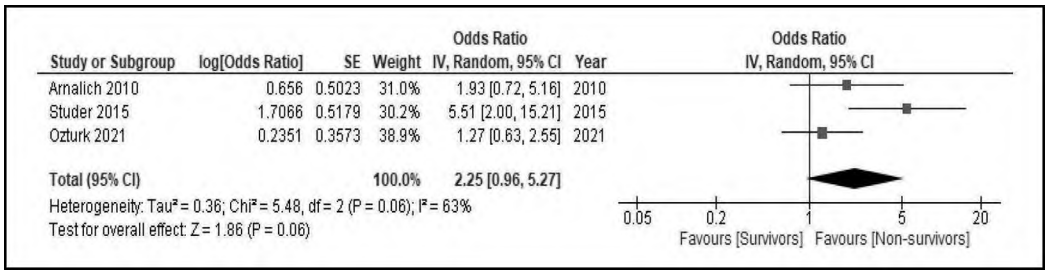


Fig. (34): Forest plot for small and large bowel involvement.

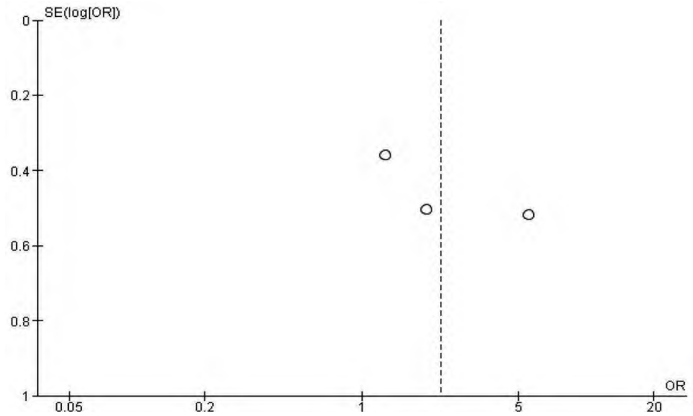


Fig. (35): Funnel plot for small and large bowel involvement.

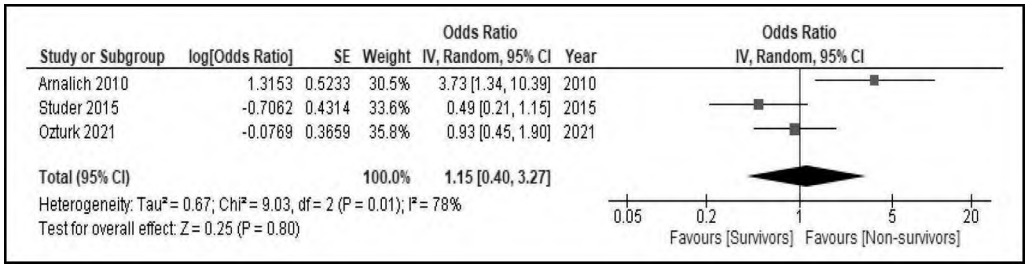


Fig. (36): Forest plot for small bowel involvement.

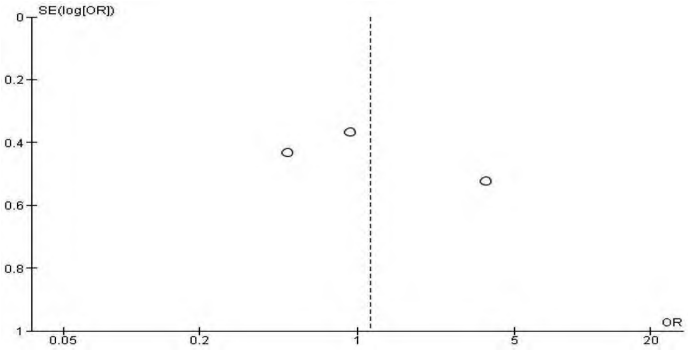


Fig. (37): Funnel plot for small bowel involvement.

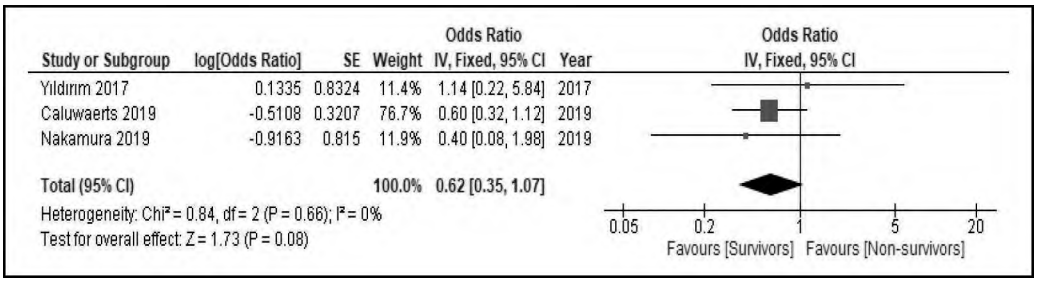


Fig. (38): Forest plot for Bowel wall thickening.

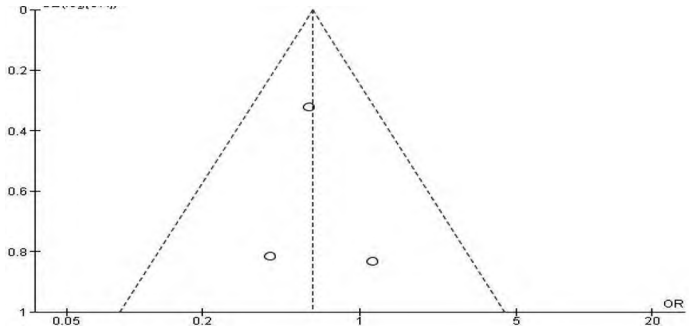


Fig. (39): Funnel plot for Bowel wall thickening.

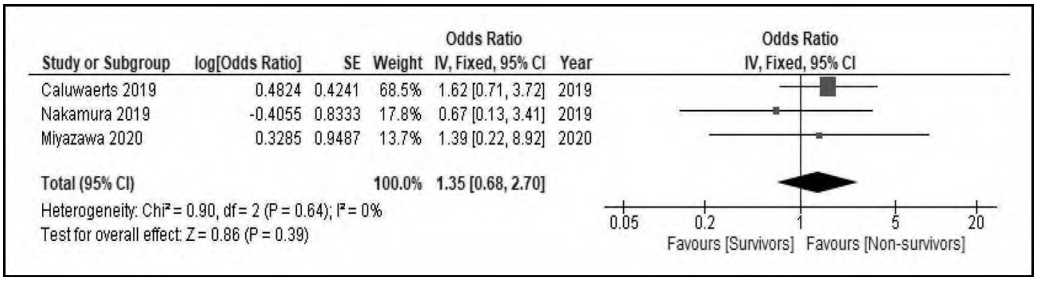


Fig. (40): Forest plot for Mesenteric or portal venous gas.

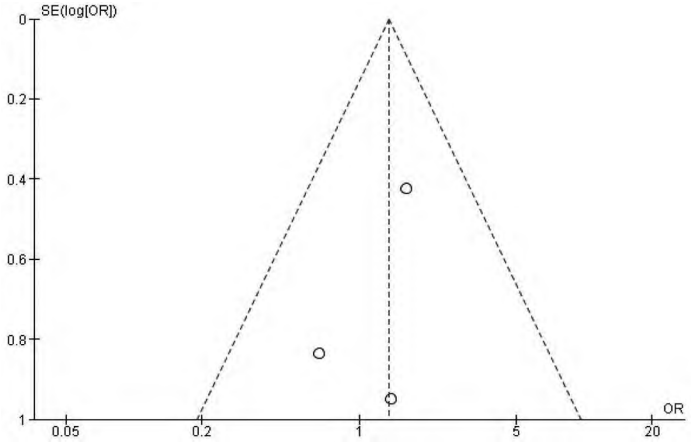


Fig. (41): Funnel plot for Mesenteric or portal venous gas.

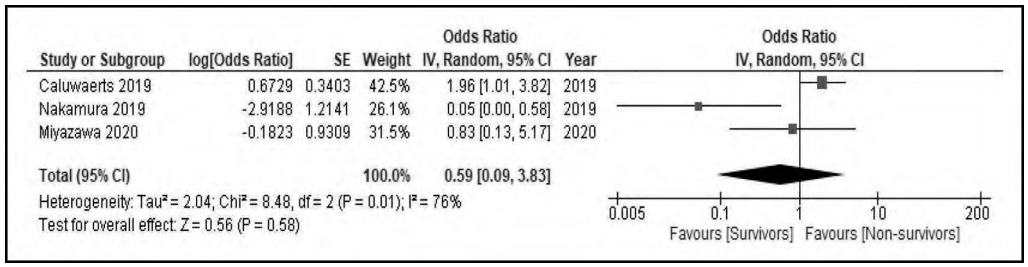


Fig. (42): Forest plot for Pneumatosis intestinalis.

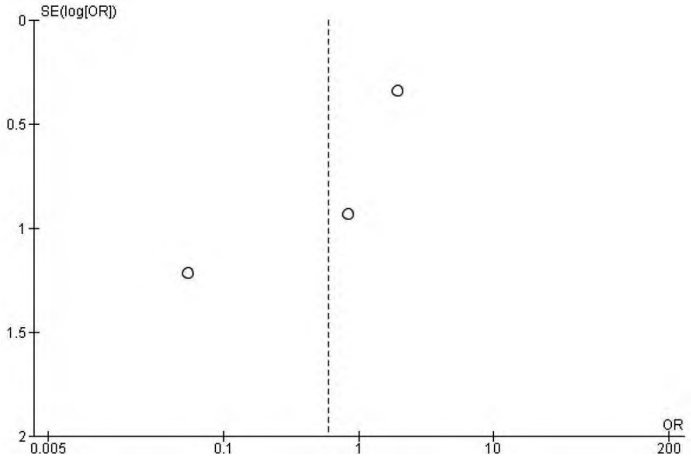


Fig. (43): Funnel plot for Pneumatosis intestinalis.

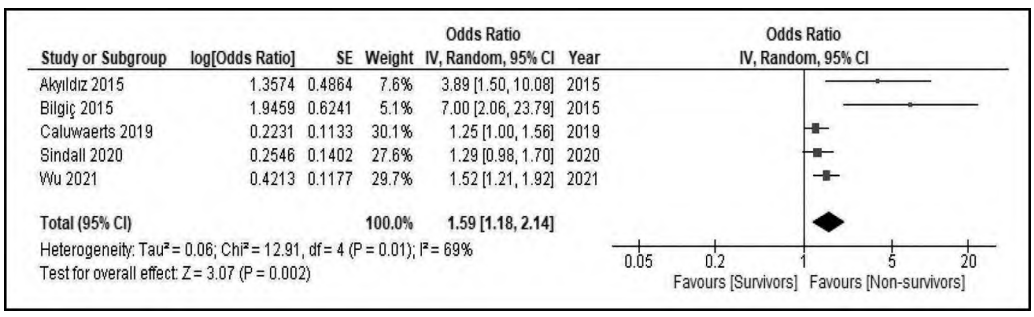


Fig. (44): Forest plot for Creatinine.

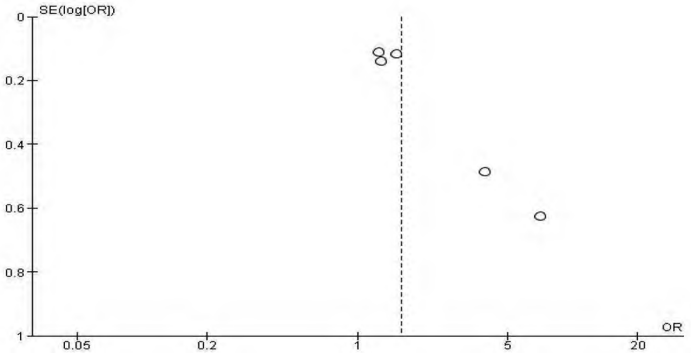


Fig. (45): Funnel plot for Creatinine.

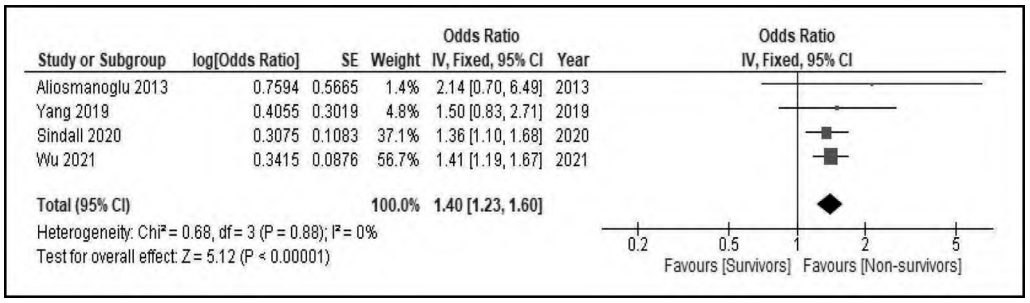


Fig. (46): Forest plot for Lactate.

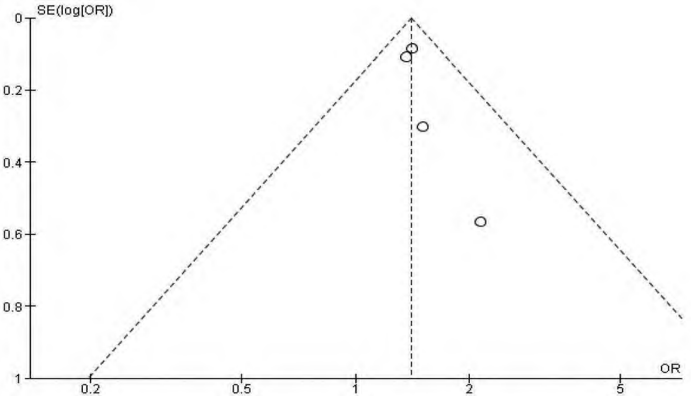


Fig. (47): Funnel plot for Lactate.

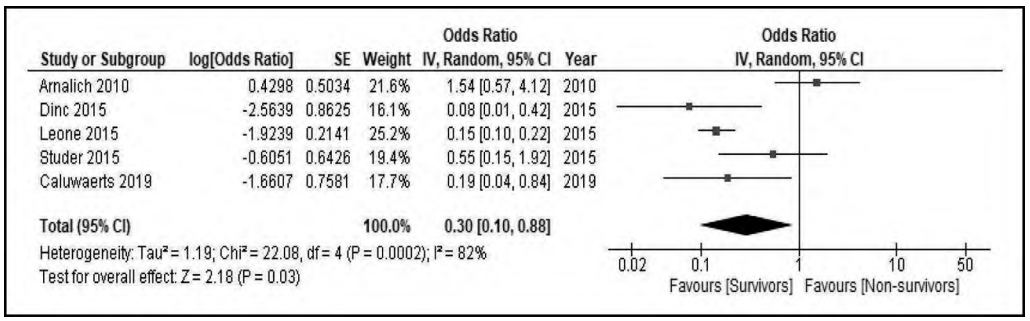


Fig. (48): Forest plot for Anti-coagulant.

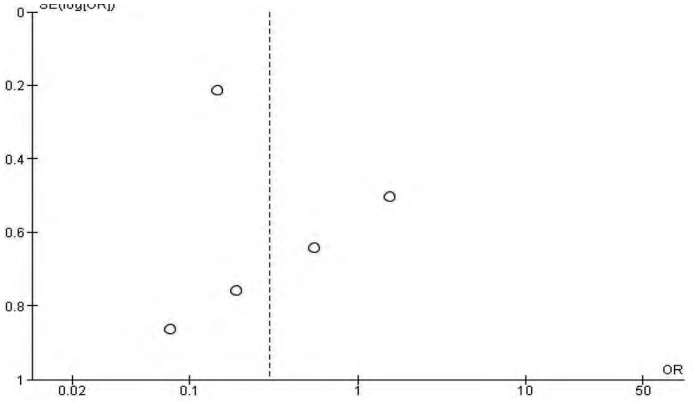


Fig. (49): Funnel plot for Anti–coagulant.

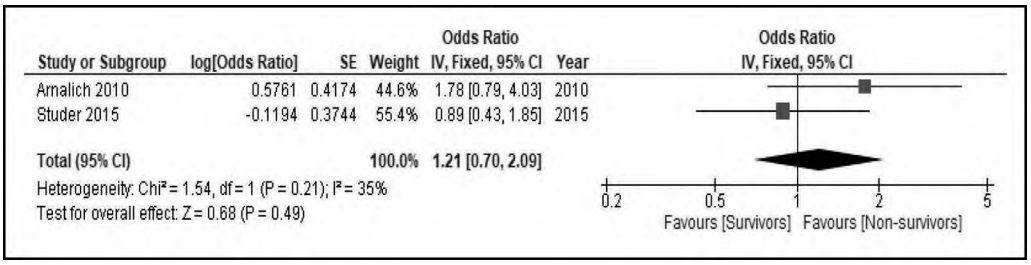


Fig. (50): Forest plot for Anti platelet.

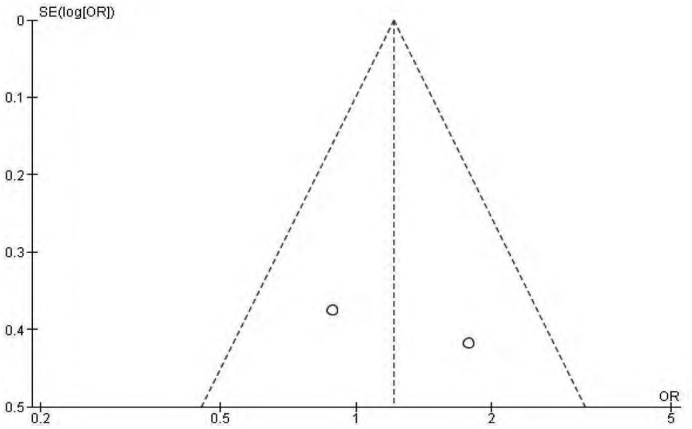


Fig. (51): Funnel plot for Anti platelet.

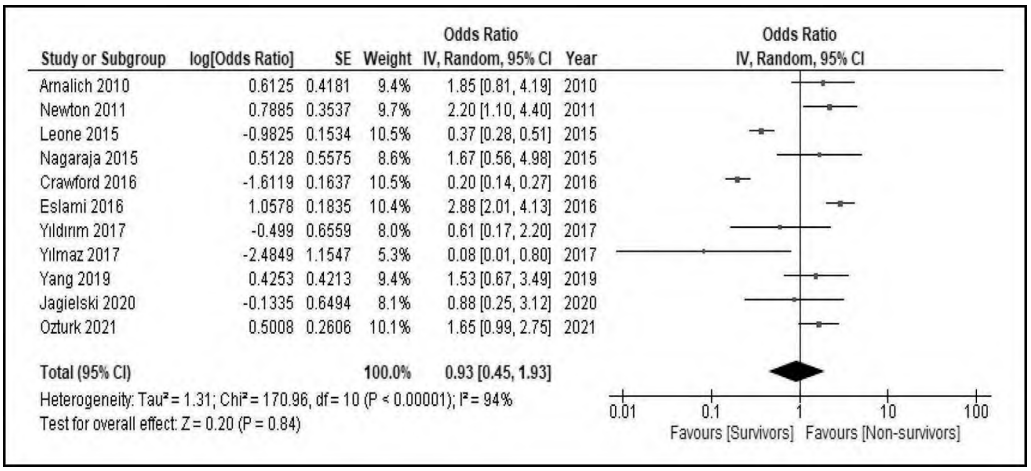


Fig. (52): Forest plot for Bowel resection.

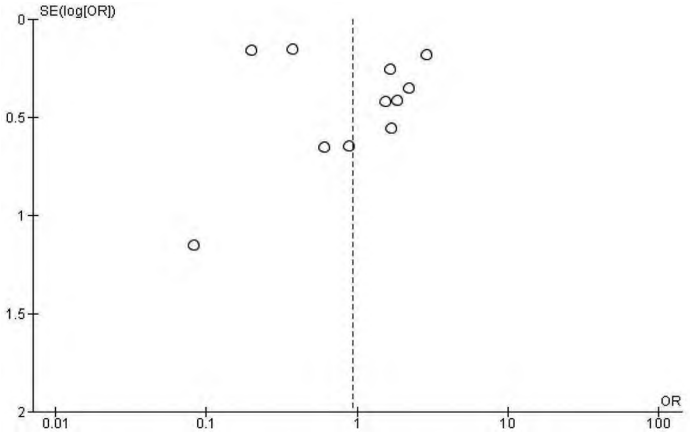


Fig. (53): Funnel plot for Bowel resection.

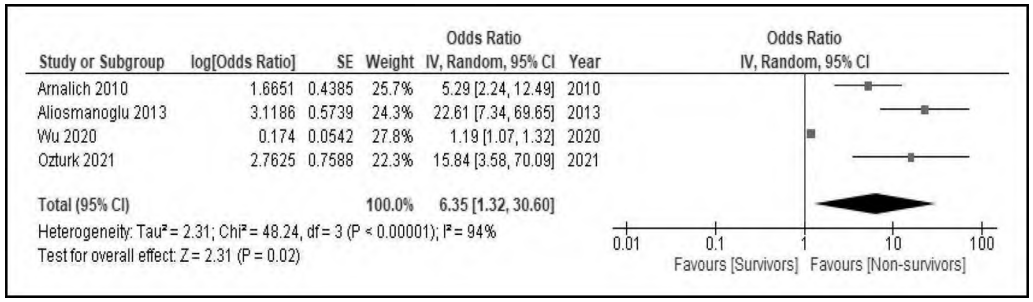


Fig. (54): Forest plot for Delay to surgery.

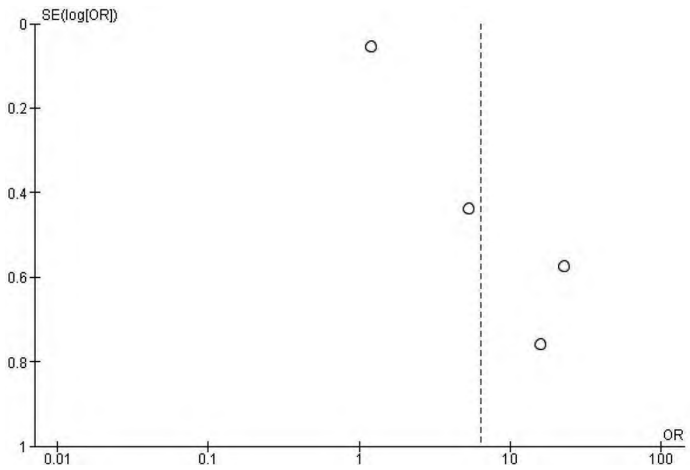


Fig. (55): Funnel plot for Delay to surgery.

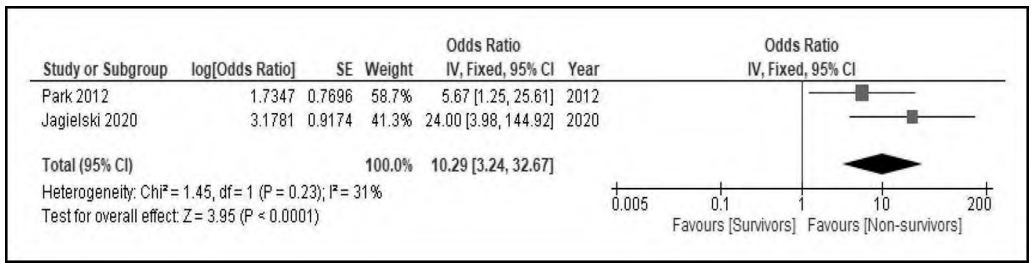


Fig. (56): Forest plot for Inotropes.

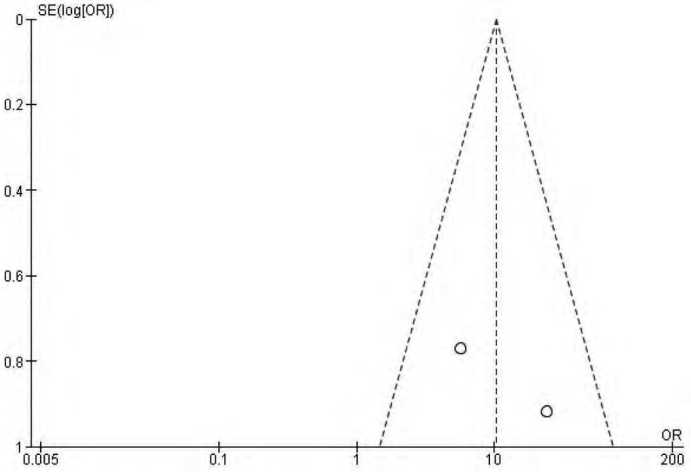


Fig. (57): Funnel plot for Inotropes.

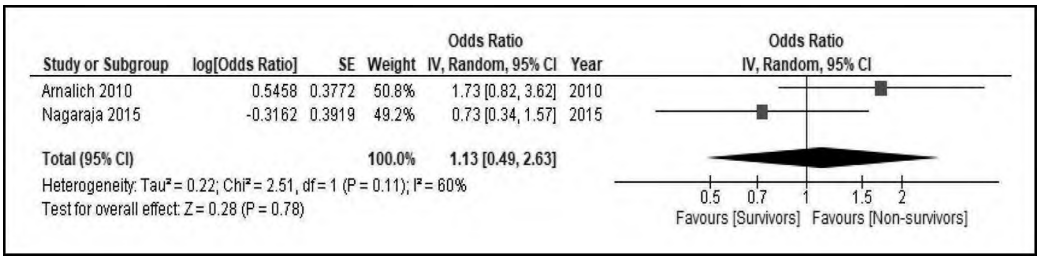


Fig. (58): Forest plot for Primary anastomosis.

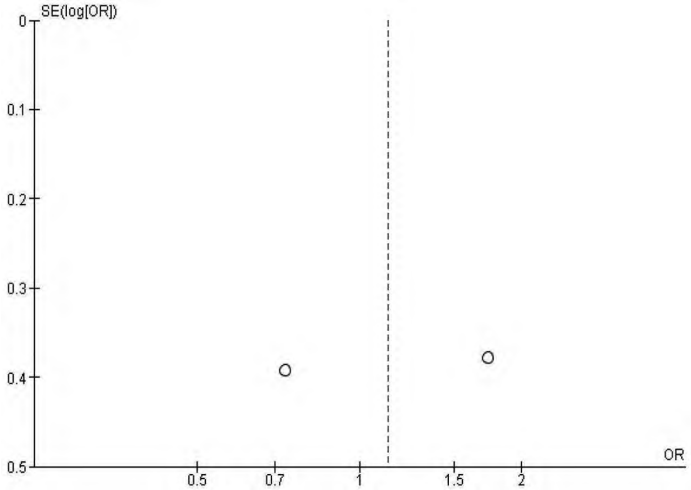


Fig. (59): Funnel plot for Primary anastomosis.

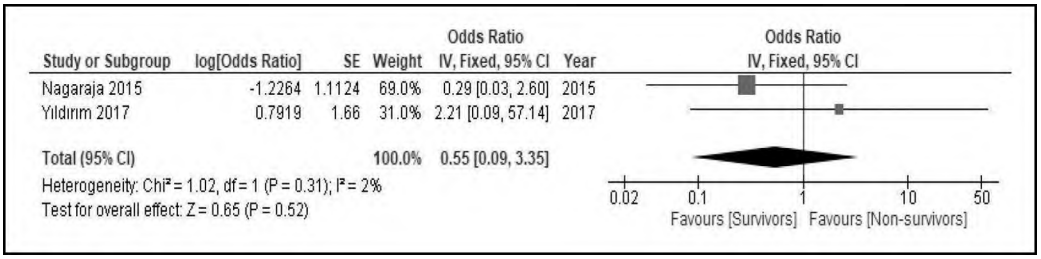


Fig. (60): Forest plot for Revascularization.

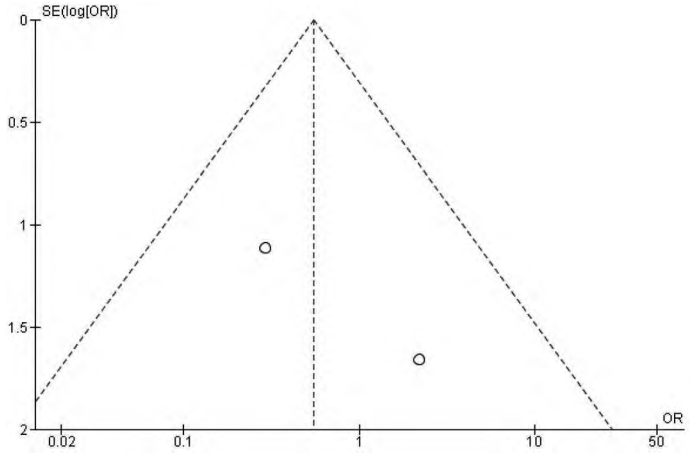


Fig. (61): Funnel plot for Revascularization.

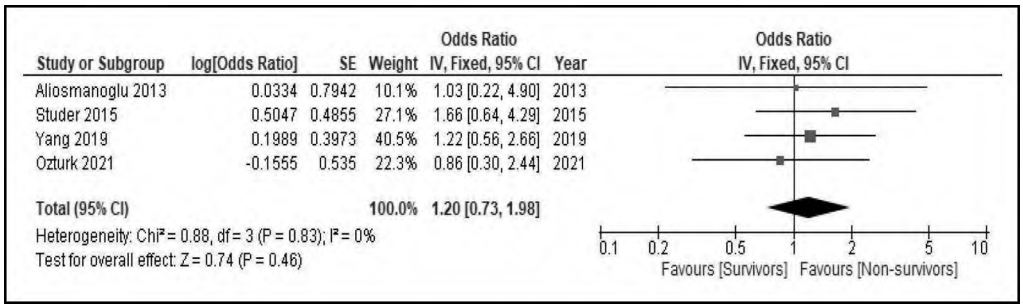


Fig. (62): Forest plot for Second look surgery.

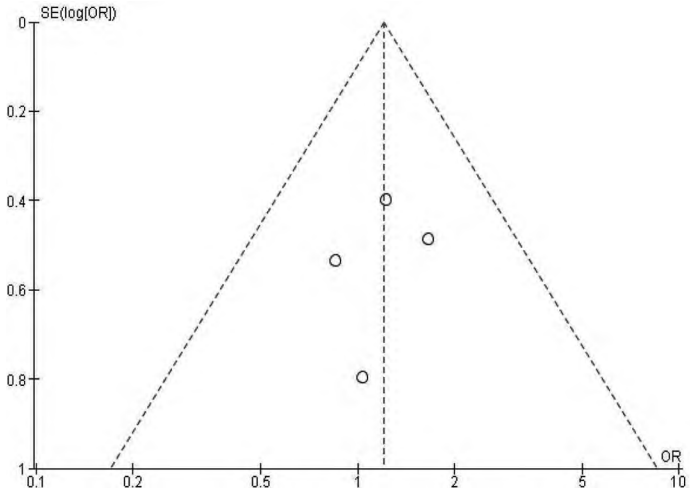


Fig. (63): Funnel plot for Second look surgery.

## *Discussion*

Acute mesenteric ischemia (AMI) is a condition where blood supply to the intestines is suddenly disrupted, resulting in tissue damage and potentially life-threatening complications *[10]*. Predicting mortality in AMI patients is important for guiding treatment decisions. Several predictors have been identified, including advanced age, delayed presentation or diagnosis, hemodynamic instability, abnormal laboratory markers (e.g., elevated lactate levels, metabolic acidosis), the presence of comorbidities (e.g., cardiovascular disease, diabetes), and radiological findings indicating extensive bowel necrosis or absence of arterial flow *[11]*. These predictors help assess the risk of mortality and guide clinicians in providing timely intervention and close monitoring to improve outcomes for individuals with AMI *[12]*.

The aim of this review was to determine the clinical predictors of mortality in patients with acute mesenteric ischemia.

The review considered case-control studies, case report studies, prospective cohort studies and retrospective case follow-up clinical predictors of mortality in patients with acute mesenteric ischemia since 2010 till 2022 that involve patients with acute mesenteric ischemia. The following electronic databases were searched up to 2022: PubMed, Google Scholar search engine, Cochrane database of systematic reviews, EMBASE and Science Direct, Wiley Online Library, The Journal of Ankle and Foot Surgery and Clinical Key database searching keywords and terms listed below: "mesenteric ischemia; acute ischemia, acute mesenteric ischemia, mortality of acute mesenteric ischemia, comorbidities with mesenteric ischemia".

A retrospective study by Adaba et al. *[13]* of 113 patients (61 women, median age 54 years) treated for mesenteric infarction from 2000-2010 aimed to determine a etiological factors and the effects of restoring bowel continuity on long-term parenteral nutrition (PN) requirements. 74 (65%) patients had superior mesenteric artery thromboembolism, 25 (22%) had superior mesenteric vein thrombosis, and 4 (3%) had superior mesenteric artery stricture/spasm. Patients under 60 years commonly had a clotting abnormality (50%) while older patients commonly had a cardio logical risk factor (65%). All patients with a jejunostomy required long-term PN. Of 57 (49%) patients who had restoration of bowel continuity, PN was stopped within 1 year in 35%, within 2 years in 50%, and within 5 years in 77% ($p$=0.001), showing that restoring continuity significantly reduced long-term PN requirements.

Akyıldız et al. *[14]* aimed to identify factors associated with adverse outcomes in 104 patients (46 females, 58 males; mean age 66±13.4 years) with acute mesenteric ischemia (AMI) over a 4-year period. The cause was arterial pathology in 71% of patients, venous thrombosis in 14%, and non-occlusive ischemia in 12%. Abdominal pain occurred in 97%. The 30-day mortality rate was 66%. Univariate analysis showed mortality was associated with renal insufficiency ($p$=0.004), age over 70 years ($p$=0.02), comorbidities ($p$=0.001), leukocyte count over 18,000/mL ($p$=0.04), and small bowel necrosis over 100 cm ($p$<0.0001). Logistic regression analysis revealed independent predictors of mortality were small bowel necrosis over 100cm ($p$=0.002) and serum creatinine over 2 mg/dL ($p$=0.04).

Aliosmanoglu et al. *[15]* aimed to discuss the effective factors on morbidity and mortality in patients who were operated on for acute mesenteric ischemia. Between 2006 and 2011, 95 patients, who underwent emergent surgery for acute mesenteric ischemia, were analyzed retrospectively. The study group consisted of 56 men (58.9%) and 39 women (41.1%), with an average age of 68.4±14.4 years. Elapsed time between the onset of the symptoms and the surgical operation was less than 24 hours in 47 (49.5%) cases, and more than 24 hours in 48 cases (50.5%) ($p$<0.001). Although all of the patients had intestinal necroses, colon involvement was seen in 38 patients, and mortality was higher in this group of patients ($p$<0.001). Mortality rate was 42.1%. This was higher in older patients, those with increased leukocyte levels, increased elapsed time to laparotomy, and when the colon was involved.

Arnalich et al. *[16]* assessed the usefulness of plasma DNA for predicting outcomes in 130 patients undergoing laparotomy, 99 with confirmed acute mesenteric ischemia (AMI) and 31 non-AMI. The 30-day mortality rate was higher in AMI patients than non-AMI patients (46.6% vs 19.4%, $p$<0.05). Median plasma DNA levels were also higher in AMI patients (7340 vs 2735 GE/ml, $p$<0.01) and AMI non-survivors (8830 vs 4970 GE/ml, $p$<0.05). The area under the ROC curve for plasma DNA predicting AMI was 0.708 (95% CI 0.701-0.890) and for 30-day mortality was 0.815 (95% CI 0.735 -0.894). Multiple logistic regression analysis revealed a 1.52-fold increased risk of hospital mortality for every 1000 GE/ml increase in plasma DNA.

Bilgiç et al. *[17]* who aimed to investigate whether MPV was associated with outcome of acute mesenteric ischemia (AMI). Sixty-one patients who were operated for AMI were retrospectively evaluated. Patients were divided into two groups: survivors and non-survivors, according to the outcome, and the two groups were compared in terms of MPV levels and other prognostic factors. Urea, creatinine, alkaline phosphatase, amylase, gamma-glutamyl transferase and MPV levels were significantly higher in nonsurvivors, when compared to that of survivors. In addition, hypertension, atherosclerotic heart diseases and rhythm disorders were statistically significant risk factors for mortality. AMI is an uncommon but highly lethal surgical emergency. Our results indicate that an elevated MPV is associated with a worse outcome in patients with AMI.

A retrospective study by Caluwaerts et al. *[18]* of 214 ICU patients investigated prognostic factors for arterial acute mesenteric ischemia (AMI), which had a high 30-day mortality rate (71%). Non-occlusive AMI was particularly prevalent, with AMI as a secondary diagnosis in 58% and half being surgical patients requiring urgent procedures. Mortality was not different for those with aortic surgery. Three factors were associated with higher or lower mortality: maximal vasopressor (VP) dose (OR 1.20 per unit increase), arterial lactate change in first 24h (OR 1.24 per unit increase), and anticoagulation (OR 0.19).

Table (2): Etiology of AMI.

| Study | Year | Sample size | Outcome |
|---|---|---|---|
| Adaba et al. | 2016 | 113 patients | Restoring bowel continuity after mesenteric infarction significantly reduced long-term PN requirements. 74% had arterial thromboembolism. |
| Akyıldız et al. | 2015 | 104 patients | 30-day mortality was 66%. Mortality associated with renal insufficiency, age >70 years, comorbidities, high leukocyte count, and bowel necrosis >100 cm. |
| Aliosmanoglu et al. | 2013 | 95 patients | 42.1% mortality rate. Higher in older patients, increased leukocytes, delayed laparotomy, and colon involvement. |
| Arnalich et al. | 2010 | 130 patients | Plasma DNA levels predicted mortality in AMI patients. |
| Bilgiç et al. | 2015 | 61 patients | Elevated MPV associated with worse outcomes in AMI. |
| Caluwaerts et al. | 2019 | 214 ICU patients | 71% 30-day mortality. Mortality associated with max vasopressor dose, lactate change, lack of anticoagulation. |
| Chou et al. | 2021 | 303 patients | 61% 30-day mortality unchanged over 23 years. Elevated WBC and lactate predicted mortality. |
| Crawford et al. | 2016 | 2,255 patients | 24% inpatient mortality. Mortality risk factors included age, illness severity, comorbidities. |
| Dinc et al. | 2015 | 73 patients | Mortality associated with gamma glutamyl transferase, RDW, anticoagulant use. |
| Eslami et al. | 2016 | National inpatient sample | Endovascular surgery increased 1.45-fold. Lower mortality than open surgery but overall mortality unchanged. |
| Grotelüschen et al. | 2019 | 302 surgical AMI patients | 68% postoperative mortality. Preoperative lactate, CRP, ICU stay predicted mortality. |
| Gupta et al. | 2011 | 861 bowel resection patients | Variables predicted postoperative mortality (C-statistic 0.84) and morbidity (C-statistic 0.79). |
| Jagielski et al. | 2020 | 41 surgical AMI patients | 63.4% mortality, 100% if operated >24 hours after symptoms. |
| Ksouri et al. | 2022 | 114 AMI patients | Colonic involvement associated with worse long-term outcomes. Inferior mesenteric artery occlusion predicted colonic involvement. |
| Lemma et al. | 2019 | 81 intervention patients | Presenting to non-surgical services associated with delays and higher mortality. |
| Leone et al. | 2015 | 780 ICU AMI patients | 58% mortality. Age, SOFA score, lactate predicted mortality. |
| Miao et al. | 2019 | 88 surgery patients | Low psoas muscle density predicted complications and 30-day mortality. |
| Miyazawa & Kamo | 2020 | 21 NOMI patients | Earlier vasodilator treatment after CT associated with better 1-month survival. |
| Nagaraja et al. | 2015 | 117 MI patients | Venous etiology nearly as common as arterial in this population and had lower mortality. Mortality predicted by etiology, residuals, etc. |
| Nakamura et al. | 2019 | 30 NOMI laparotomy patients | Intestinal pneumatosis on CT and high DIC score predicted poorer outcomes. Open abdomen strategy improved outcomes. |
| Newton et al. | 2011 | 142 AAMI revascularization patients | 69% morbidity, 30% mortality. Embolic etiology had higher morbidity and mortality than thrombotic. Several variables predicted outcomes. |
| Ozturk et al. | 2021 | 140 AMI patients | Shock, exploration, hospital stay predicted morbidity. Several factors including age, time delay predicted mortality. |
| Paladino et al. | 2014 | 149 AMI surgery patients | Older age, LDH, WBC, greater necrosis extent associated with higher mortality. Colon infarction and perforation also increased mortality risk. |
| Park et al. | 2012 | 40 AMI surgery patients | 32.5% in-hospital mortality. Hyperglycemia and high ASA grade were independent mortality predictors. |
| Pedersoli et al. | 2021 | 40 endovascular AMI patients | 62.5% 30-day mortality. No assessed variable significantly predicted mortality. |
| Salim et al. | 2018 | 120 MVT patients | 85% success with anticoagulation monotherapy. Mortality decreased from 19% to 3.2% over time. Age, timing, renal insufficiency predicted mortality. |
| Sindall et al. | 2020 | AMI patients 2008-2015 | AAST grading scale had weak correlation with complications and mortality. Custom model better predicted mortality. |
| Studer et al. | 2015 | 91 AMI patients | Mean lactate higher and pH lower within 6 hours pre-surgery. Lactate level and necrosis extent predicted mortality. |
| Tolonen et al. | 2021 | AMI patients pre- and post-pathway | Pathway implementation improved processes and reduced 30-day mortality from 51% to 25%. |
| Vural & Ozozan | 2021 | 37 All | Independent Predictors (multivariate): Age Postoperative Mortality. |
| Wu et al. | 2020 | 108 obstructive AMI | Independent Predictors (multivariate): Time to surgery, Platelet count, AOMI diagnosis 30-day Postoperative Mortality. |
| Wu & Zhou | 2021 | 338 AMI | Independent Predictors (multivariate): Diastolic BP, Blood lactate, Blood creatinine, Age, Blood pH, RDW Hospital Death. |
| Yang et al. | 2019 | AMI (with/without colon involvement) | Independent Predictors (mortality/recurrence): Colon ischemia, Serum procalcitonin level 30-day Mortality, Short Bowel Syndrome (SBS). |
| Yıldırım et al. | 2017 | AMI | Independent Predictors (mortality/recurrence): Mannheim Peritonitis Index (MPI) score Mortality. |
| Yılmaz & Cartı | 2017 | AMI | Independent Predictors (mortality/recurrence): MPI score, Platelet-to-lymphocyte (P/L) ratio Mortality. |
| Yun et al. | 2013 | SMA embolic AMI | Independent Predictors (mortality/recurrence): Not applicable In-hospital mortality (surgical intervention). |

A single center study by Chou et al. [19] evaluated presentation, management and outcomes of 303 acute mesenteric ischemia (AMI) patients over 23 years, excluding venous etiologies. Etiologies were 49% embolic, 29% thrombotic, 22% non-occlusive (NOMI). 55% were women, 50% had atrial fibrillation, 23% were anticoagulated. Mean age was 72± 13 years. 321 open and 24 endovascular procedures were performed in 242 patients; 85 (45%) embolic/thrombotic patients had revascularization while 39 (21%) had non-survivable bowel necrosis (NSBN). 30-day mortality remained unchanged at 61% ($p$=0.91) but was worse for thrombotic etiology ($p$=0.04). Since 2000, embolic events decreased ($p$=0.04) while more patients were made comfort measures only (CMO) preoperatively (50% to 70%, $p$=0.02); 55% were ultimately CMO. Elevated white blood cell count and lactate predicted 30-day mortality (OR 3.0 and 2.8) and NSBN (OR 3.4 and 3.6).

A population-based retrospective analysis by Crawford et al. [20] aimed to determine the contemporary incidence and outcomes of acute mesenteric ischemia (AMI) in Maryland during 2009-2013. Of 3,157,499 adult hospital admissions, 2,255 (0.07%) had AMI, an annual rate of 10 per 100,000. Increasing age, hypercoagulability, dysrhythmia, renal insufficiency, illness severity, and tertiary hospital admission were AMI risk factors. Inpatient mortality was high (24%). Multivariate analysis found independent death risk factors were age over 65, critical illness, mechanical ventilation, tertiary hospital admission, hypercoagulability, renal insufficiency, and dysrhythmia.

A retrospective cohort study by Dinc et al. [21] of 73 patients aimed to evaluate factors affecting mortality in acute arterial mesenteric ischemia admitted to a single center between 2008-2013. The mean age was 69.3±12.6 years, 42.46% were female and 57.53% were male. Patients were divided into those who died (Group 1, n=40) and those discharged alive (Group 2, n=33). Multivariate analysis showed that high gamma glutamyl transpeptidase and red cell distribution width levels and presence of anticoagulant use were statistically significant variables ($p$<0.05) associated with mortality.

Eslami et al. [22] utilized the National Inpatient Sample (2003-2011) to evaluate whether increased use of endovascular surgery has affected in-hospital mortality rates for acute mesenteric ischemia patients. Of patients treated with either open vascular surgery or endovascular therapies, there was a 1.45-fold increase in endovascular utilization over the study period. Despite higher comorbidities (Elixhauser index 3±0.1 vs 2.7± 0.1, $p$=0.003), the endovascular group had significantly lower mortality, charges, and length of stay compared to open surgery. However, over the study period, there was no significant change in overall mortality, even with higher endovascular utilization. Factors associated with increased mortality were age, open surgery (OR 1.45, 95% CI 1.10-1.91, $p$=0.016) and bowel resection (OR 2.88, 95% CI 2.01-4.12).

Grotelüschen et al. [23] analyzed data from 302 surgical acute mesenteric ischemia (AMI) patients (2003-2014) to evaluate if AMI markers can predict mortality and guide early treatment initiation. 115 (38%) were in the ICU at AMI diagnosis. 203 (67%) underwent abdominal CT scans, of which 68% showed specific AMI signs. 63 (21%) had embolectomies. The postoperative mortality rate was 68% (204 patients). Among survivors, 87% developed short bowel syndrome. Multivariate analysis revealed preoperative lactate >3mmol/L, C-reactive protein >100mg/L and ICU stay at diagnosis were associated with higher mortality.

Gupta et al. [24] analyzed data on 861 patients who underwent bowel resection for acute mesenteric ischemia (AMI) from the ACS-NSQIP database (2007-2008) to determine if certain variables can predict postoperative death and complications, in order to aid surgical decision-making. The patients had a median age of 69 years, with 30-day morbidity and mortality of 56.6% and 27.9% respectively. Variables significantly associated with mortality (C-statistic 0.84) included preoperative DNR status, open wound, low albumin, dirty case, and poor functional status. Variables significantly associated with morbidity (C-statistic 0.79) included admission from chronic facility, recent MI, COPD, ventilator support, renal failure, prior cardiac surgery, and prolonged operative time. A risk calculator was developed to predict outcomes using these variables.

Jagielski et al. [25] examined outcomes of 41 patients (27 women, 14 men; mean age 65.4 years) undergoing surgery for acute mesenteric ischemia over an unspecified time period. All patients had laparotomy performed; surgery within 24 hours of symptom onset occurred in 31.7%. Procedures included embolectomy in 17.1%, bowel resection for necrosis in 51.2%, and exploratory laparotomy only in 31.7%. In-hospital mortality was 63.4% overall; all patients with surgery >24 hours from symptom onset died. Mortality was significantly lower if operated within 24 hours ($p$=0.001). Female gender, age >65 years, obesity, diabetes, chronic kidney disease, and smoking were identified as factors associated with higher mortality.

Ksouri et al. [10] investigated the prevalence, risk factors, and outcomes associated with colonic involvement among 114 patients with acute mesenteric ischemia (AMI) treated at an intestinal stroke center from 2009-2018. Colonic involvement on CT scan was identified in 28% of patients, with right colon being most commonly involved (91%) and wall thickening the most common finding (84%). Occlusion of the inferior mesenteric artery was the only statistically significant risk factor for colonic involvement (35% vs 15%, $p$=0.02). Compared to

patients without colonic involvement, those with colonic involvement had increased rates of trans mural colonic necrosis (13% vs 0%, p=0.006), short bowel syndrome (16% vs 4%, p=0.04), need for long-term parenteral nutrition (19% vs 5%, p=0.03), and death during follow-up (22% vs 10%, p=0.03).

A single center retrospective study by Lemma et al. *[26]* aimed to evaluate factors affecting treatment delays in 81 patients undergoing intervention for acute superior mesenteric artery thrombosis or embolism during 2006-2015. Overall 30- and 90-day mortality were 62% and 65% respectively. Patients were divided into two groups based on first evaluating physician specialty-surgical (SER) versus non-surgical (non-SER). Presenting first to non-SER was independently associated with door-to-operation time over 12 hours (OR 3.7, p=0.025) compared to SER (median times 15.2 vs 10.1 hours). Length of stay was shorter (median 6.5 vs 10.8 days, p=0.045) and 90-day mortality was lower (50% vs 74.5%, p=0.025) for the SER group.

A multicenter retrospective study by Leone et al. *[27]* aimed to determine risk factors for death among 780 ICU patients with acute mesenteric ischemia (AMI) from 2008-2013. The mortality rate was 58%. Older age, higher SOFA score and lactate >2.7mmol/L at diagnosis were independent risk factors for death. Prior peripheral vascular disease history and initial surgical treatment were protective against mortality. A survival score model was created using age and SOFA cutoffs from recursive partitioning analysis. Patients with a score of 0-2 had significantly higher probability of survival versus a score of 3-4 (p<0.001).

A retrospective study by Miao et al. *[28]* of 88 patients undergoing surgery for acute mesenteric ischemia (AMI) between 2006-2019 investigated if low psoas muscle density (PMD), indicating sarcopenia, is associated with worse short-term postoperative outcomes. PMD was measured on preoperative CT scans and sex-specific cutoffs were used to define low PMD (lowest quartile). Thirty-nine percent of patients developed complications within 30 days and 11.3% died. Patients with low PMD had significantly higher risks of complications and 30-day mortality compared to patients with normal PMD in univariate analysis. In multivariate analysis, low PMD and low psoas muscle area independently predicted complications, while only low PMD was an independent predictor of 30-day mortality.

A single-institution retrospective study by Miyazawa and Kamo, *[29]* of 21 patients diagnosed with non-occlusive mesenteric ischemia (NOMI) on angiography aimed to investigate prognostic factors based on clinical data and CT findings. Patients were divided into “survivor” (n=8) and “non-survivor” (n=11) groups based on 1-month survival. CT findings, including bowel wall abnormalities and vessel diameters, did not significantly differ between groups. The only significant difference was time from CT to vasodilator treatment, which was shorter in survivors (median 187.5 vs 310 min, p=0.048). None of the other clinical information differed significantly between groups.

A retrospective study by Nagaraja et al. *[30]* of 117 patients with acute mesenteric ischemia at an Indian tertiary care center from 1997-2012 examined demographic, clinical, and outcome differences between arterial (52%) and venous (48%) etiology. Unlike Western countries where arterial occlusion predominates in older patients, venous thrombosis was nearly as common here, occurring in younger patients (median age 53 years) with longer symptom duration who were less often hypotensive and had higher platelets, shorter bowel resections, fewer colonic resections, and lower mortality (27%) than arterial occlusion patients (51% mortality). Additional mortality predictors were longer symptom duration, lower albumin, higher creatinine, shorter residual bowel length, and arterial etiology.

A retrospective study by Nakamura et al. *[31]* of 30 patients undergoing emergency laparotomy for non-occlusive mesenteric ischemia (NOMI) from 2013-2017 aimed to determine prognostic factors and examine if an open abdomen second look surgery strategy (OSS) improves outcomes. Multivariate analysis revealed presence of intestinal pneumatosis on CT (odds ratio 0.054, p=0.018) and higher DIC score (odds ratio 1.892, p=0.027) were independently associated with poorer discharge outcome. After instituting an OSS protocol, operation time and bleeding amount were significantly reduced compared to prior standard single laparotomy.

A report by Newton et al. *[32]* investigates outcomes following revascularization for acute arterial mesenteric ischemia (AAMI) utilizing data from the American College of Surgeons National Surgical Quality Improvement Program database. They identified 142 cases of AAMI, with 71 classified as thrombotic and 71 as embolic based on revascularization codes. The mean age of patients was 66 years, with 84% being white and 54% female. Unadjusted major morbidity and mortality rates were 69% and 30%, respectively. Thrombotic AAMI cases were associated with lower body mass index, significant weight loss, and a history of smoking, while embolic cases were more likely to present emergently with sepsis. Morbidity and mortality rates were higher for embolic (78% and 38%) compared to thrombotic AAMI (61% and 23%). Multivariable predictors of morbidity included bowel resection, transfer admission, and involvement of a surgical resident, while predictors of mortality included impaired functional status, increased age, and postoperative sepsis. The cause of AAMI itself did not significantly predict morbidity or mortality.

A retrospective study by Ozturk et al. [11], conducted at Ege University Faculty of Medicine, reviewed the records of 140 patients hospitalized with acute mesenteric ischemia (AMI) between May 1997 and August 2013. Multiple Logistic Regression analysis, employing the Enter method and adjusting for confounding factors, was used to assess demographic and clinical features as predictors of morbidity and mortality. The results revealed that shock, exploration, and length of hospital stay were statistically significant factors affecting morbidity, while age, cardiac comorbidities, ASA scores, time delay to surgery, presence of acidosis and shock, organs involved, type of surgery, medical treatment, and small bowel length under 100 cm were significant predictors of mortality. The study highlights the critical importance of early diagnosis, emphasizing parameters such as age and time delay in predicting mortality, particularly for patients presenting with shock and acidosis.

A retrospective study by Paladino et al. [33], spanning from September 2003 to August 2011, aimed to assess the impact of various risk factors on mortality in 149 patients who underwent surgery for Acute Mesenteric Ischemia (AMI). Among the findings, a significantly higher mortality rate was associated with older age (mean 79.9 years), elevated LDH serum levels (695 UI/L), increased white blood cell count (25.1 X $10^3$/$mm^3$), and a greater extent of necrosis. Comorbidities did not show a significant correlation with mortality. Multivariate analysis highlighted a substantially higher risk of death in patients with right colon and massive small bowel infarction (adjOR=3.58; 95% CI=1.36-9.42) and intestinal perforation (adjOR=31.1; 95% CI= 2.45-395.7).

A study by Park et al. [34], conducted between January 2001 and June 2009, aimed to identify prognostic factors and risk scores influencing in-hospital mortality in acute mesenteric ischemia (AMI) patients. Forty consecutive patients who underwent AMI-related surgery were retrospectively analyzed. The overall in-hospital mortality rate was 32.5%. Univariate analysis revealed several significant predictors of mortality, including decreased mental status, shock at admission, symptom duration, various laboratory parameters, pH, coagulation factors, length of remnant bowel, postoperative inotropics, Acute Physiology and Chronic Health Evaluation II (APACHE II), and American Society of Anesthesiologists (ASA) grading. In the multivariate analysis, hyperglycemia and higher ASA grades (>II) emerged as independent prognostic factors for in-hospital mortality.

In a retrospective analysis by Pedersoli et al. [12] spanning from January 2011 to December 2019, the study aimed to determine 30-day mortality rates and identify predictors for survival in patients undergoing endovascular revascularization for acute mesenteric ischemia (AMI) resulting from thrombotic occlusion of the celiac or superior mesenteric artery due to atherosclerosis at the vessel origin. The analysis included 40 patients, revealing a 30-day mortality rate of 62.5%. However, none of the assessed factors, including sex, age, smoking history, abdominal angina history, pre-interventional CT findings of bowel necrosis, vessel disease, patency of the inferior mesenteric artery, outpatient or inpatient occurrence of ischemia, onset during ITU stay, elevated pre-interventional serum lactate levels, total leukocyte count, platelet/lymphocyte ratio, and neutrophil/lymphocyte ratio, were found to be statistically significantly associated with 30-day mortality.

A retrospective study by Salim et al. [35], conducted between 2000 and 2015, aimed to evaluate the outcomes, prognostic factors, and failure rates of anticoagulation monotherapy in patients with mesenteric venous thrombosis (MVT), identifying instances requiring bowel resection. Among 120 patients diagnosed with MVT, seven died due to autopsy-verified MVT without bowel resection, while 15 underwent immediate bowel resection without anticoagulation therapy. Of the remaining 98 patients treated with anticoagulation monotherapy, 85% were successfully managed, but 15 patients failed, leading to seven bowel resections and eight endovascular therapies. The 30-day mortality rate significantly decreased from 19.0% in the earlier (2000-2007) to 3.2% in the later (2008-2015) part of the study period. Independent predictors of increased mortality included age ≥75 years, management during the earlier time period, and renal insufficiency at admission.

A single-center retrospective chart review by Sindall et al. [36] to assess the correlation between the AAST grading scale for acute mesenteric ischemia (AMI) and the severity of complications. In the study encompassing inpatients aged over 17 from 2008 to 2015, AAST grades (1-5) were assigned based on a comprehensive review of clinical, imaging, operative, and pathology findings. Two independent raters applied the scales, achieving poor interrater agreement. The overall AAST grade demonstrated a weak correlation with both Clavien-Dindo complication severity (rho=0.27) and mortality (rho=0.21). Notably, computed tomography, pathology, and clinical grades did not exhibit significant correlations with mortality or complication severity. However, a mortality prediction model incorporating operative grade, vasopressor use, preoperative serum creatinine, and lactate levels demonstrated excellent discrimination (c-index= 0.93).

A retrospective study by Studer et al. [37], conducted between January 2006 and December 2012, aimed to assess the correlation between repeated preoperative serum lactate levels and bowel necrosis while identifying risk factors for a lethal out-

come in patients with acute mesenteric ischemia (AMI). Among 91 patients with confirmed AMI, the in-hospital mortality rate was 42.9%. Analysis of 209 preoperative lactate measurements revealed that, within six hours before surgery, the mean serum lactate level was significantly higher, and the mean pH lower compared to measurements taken over six hours prior. In a subgroup of 34 patients with at least two lactate measurements within 24 hours before surgery, logistic regression analysis identified the length of necrotic bowel and the highest lactate value 24 hours before surgery as independent risk factors for mortality.

A retrospective comparative study by Tolonen et al. *[38]* aimed to analyze the impact of implementing a pathway on patient management and outcomes in occlusive arterial acute mesenteric ischemia (AMI) cases. Conducted between 2014 and April 2020, the study compared patients treated before pathway implementation (pregroup, 2014-2017) with those treated post-implementation (post group, May 2018 to April 2020) in a secondary and tertiary referral center. The post group, comprising 67 patients, demonstrated improved diagnostic methods with increased use of contrast-enhanced computed tomography. Additionally, the post group experienced a shorter mean in-hospital delay to the operating room, more frequent revascularization, particularly through endovascular treatment, and significantly lower 30-day mortality compared to the pregroup (25% vs. 51%). Multivariate analysis confirmed that being managed in the post group was a protective factor for 30-day mortality.

In a retrospective study by Vural and Vefik Ozozan *[39]*, the clinical utility of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in predicting postoperative mortality among patients undergoing surgery for acute intestinal ischemia (AII) was investigated. The study included 37 consecutive patients operated for AII between January 2014 and September 2019. Prognostic factors such as age, sex, preoperative white blood cell count (WBC), C-reactive protein (CRP), neutrophil, lymphocyte, and platelet counts were examined. Univariate analysis identified age, WBC, and neutrophil count as predictors of postoperative mortality. However, in multivariate analysis, only age (OR =1.14; 95% CI, 1.005-1.303; $p$=0.02) emerged as an independent variable predicting postoperative mortality.

Wu et al. *[40]* aimed to investigate the clinical manifestations and identify risk factors for postoperative mortality in patients diagnosed with obstructive acute mesenteric ischemia (AMI). The study included 108 cases, with an average age of 57.1 years, consisting of 58 arterial occlusive mesenteric ischemia (AOMI) and 50 mesenteric venous thrombosis (MVT) cases. AOMI patients were older and had a higher frequency of comorbidities like heart disease, hypertension, and diabetes, while MVT had more male patients and a higher frequency of liver disease. Of the 77 patients undergoing laparotomy, the 30-day postoperative mortality rate was 29.9%. Multivariate logistic regression analysis revealed that the time interval from admission to surgery, platelet count, and AOMI were independent predictors of 30-day mortality after exploratory laparotomy for obstructive AMI. Further analysis within the AOMI subgroup identified platelet count as independent risk factors for 30-day postoperative mortality.

Wu and Zhou *[41]* utilized both traditional statistics and machine learning approaches to develop and validate prediction models for hospital death in patients with acute mesenteric ischemia (AMI), utilizing data from the Medical Information Mart for Intensive Care (MIMIC III) electronic clinical database. Among 338 eligible AMI patients, the cohort was divided into a training group (n=238) and a validation group (n=100). Independent risk factors for hospital death, including diastolic blood pressure, blood lactate, blood creatinine, age, blood pH, and red blood cell distribution width, were identified through univariate and multivariate logistic regression analyses. The traditional statistics nomogram and the optimal machine learning model both demonstrated good discrimination (AUC=77.0% and 82.9%, respectively) and calibration in the validation cohort. Decision curve analysis indicated that the machine learning model provided a greater net benefit than the nomogram.

In a retrospective cohort study by Yang et al. *[42]* to compare outcomes between patients with isolated acute mesenteric ischemia (AMI) and those with AMI and colon involvement (CI), while identifying predictors of worse outcomes. Among 199 AMI patients, 39 were diagnosed with AMI with CI, and 160 had AMI without CI. Patients with CI exhibited higher 30-day mortality (49% vs. 10%) and short bowel syndrome (SBS) incidence (49% vs. 19%) compared to those without CI. AMI patients with CI had a higher rate of bowel resection and second-look laparotomy. For those with CI, emergent laparotomy was associated with a shorter hospital stay and lower SBS incidence than initial endovascular therapy. Patients with ostomy had lower rates of repeated bowel resection and SBS than those with primary bowel anastomosis. Serum procalcitonin level and colon ischemia were identified as risk factors for 30-day mortality and SBS in AMI patients.

A retrospective study by Yıldırım et al. *[43]* aimed to investigate factors influencing mortality in patients diagnosed with acute mesenteric ischemia (AMI) and treated at the General Surgery Clinic between January 2008 and December 2014. The study included 46 patients, with 27 experiencing mortality (58.7%) and 19 surviving (41.3%). Factors such as

age, gender, accompanying disorders, clinical, laboratory, and radiologic findings, duration until laparotomy, postoperative complications based on the Mannheim Peritonitis Index (MPI), surgical treatment, type of ischemia, and surgical outcomes were evaluated. The mean MPI score was significantly higher in the deceased group (25.0±6) compared to the survivors (16.8±4.7), with a notable correlation between increased MPI score and mortality ($p$<0.001). Specifically, patients with an MPI score of 26 or higher had a higher mortality rate (51.9%), while those with a score of 25 or lower had a higher survival rate (89.5%).

A retrospective study Yılmaz and Cartı [44]aimed to evaluate the predictive value of the Mannheim Peritonitis Index (MPI) and platelet-to-lymphocyte (P/L) ratio in the prognosis of acute mesenteric ischemia (AMI). The study included 34 patients diagnosed with AMI between September 2014 and April 2016, categorized into survival and non-survival groups. Among the patients, 55.9% were male, and 44.1% were female. Of the total, 55.9% were discharged with complete recovery, while 44.1% succumbed to the condition. The mean MPI value was significantly higher in those who died (21.13±7.55) compared to survivors (16.00±5.24, $p$=0.026). Similarly, the P/L ratio was higher in non-survivors (288.48±233.01) compared to survivors (373.82± 389.62, $p$=0.045).

This retrospective study by Yun et al. [45] aimed to investigate the treatment outcomes and identify post-treatment prognostic factors in acute mesenteric ischemia caused by superior mesenteric artery (SMA) embolism. Clinical data from 32 episodes in 30 patients, including 2 recurrent cases were reviewed. The median patient age was 74 years, with 50% being male. Conservative treatment was pursued in 5 patients without clinical evidence of bowel gangrene, resulting in no deaths. Surgical interventions, including 25 embolectomies and 2 bowel resections alone, were performed in 27 patients, with 30% in-hospital mortality. Most bowel resections were limited, and the overall 1-, 3-, and 5-year survival rates after successful treatment were 96%, 73%, and 44%, respectively, regardless of treatment type. Notably, no variables, including age, gender, presence of bowel gangrene, and symptom duration, were associated with mortality after surgical intervention.

In our study, the Etiology of AMI was also variable among patients. 915 patients had arterial occlusive mesenteric ischemia (AOMI), 354 patients had mesenteric venous thrombosis and 193 patients had non-occlusive mesenteric ischemia (NOMI) while 7678 patients had either other secondary cause of AMI or the etiology was unspecified.

In our study, age and gender were factors related to demographics included in the current review. Age was reported by 15 studies and was significantly associated with mortality (OR 1.19, 95% CI 1.09 -1.29; $p$<0.00001; $I^2$=82%). Gender was assessed in 18 studies. It was analyzed as male versus female but it could not achieve statistical significance (OR 0.96, 95% CI 0.85-1.07; $p$=0.46; $I^2$=34%).

In our study, comorbidities and past illnesses included were cancer, chronic renal disease, diabetes mellitus, hypertension, patient dependency, peripheral vascular disease, previous surgery, and cerebrovascular disease. Among these factors, chronic renal disease was not significantly related to mortality, while patient dependency was among the factors that were significantly related to mortality. Chronic renal disease was reported by five studies (OR 2.25, 95% CI 0.97-5.21; $p$=0.06; $I^2$=64%). Patient dependency was reported by five studies (OR 2.84, 95% CI 1.99-4.07; $p$<0.00001; $I^2$=24%). Diabetes was reported by 10 studies (OR 1.54, 95% CI 1.00-2.39; $p$=0.05; $I^2$=69%). Additionally, comorbidities and past illnesses that were significantly related to mortality included cancer that was reported by two studies (OR 2.01, 95% CI 1.05-3.85; $p$=0.04; $I^2$=0%). Hypertension didn't significantly related to mortality and reported by 10 studies (OR 1.60, 95% CI 0.82-3.15; $p$=0.17; $I^2$=87%). Peripheral vascular disease (PVD) was not significantly related to mortality and mentioned by six studies (OR 0.74, 95% CI 0.52-1.04; $p$=0.08; $I^2$=54%). Previous surgery was not significantly related to mortality and was reported by five studies (OR 1.11, 95% CI 0.56-2.17; $p$=0.77; $I^2$=74%) and cerebrovascular disease that was reported by two studies (OR 0.77, 95% CI 0.27-2.24; $p$=0.64; $I^2$=4%).

In our study, within cardiovascular diseases, the following diseases were included; arrhythmia, atrial fibrillation, cardiac failure and coronary artery disease. Out of these arrhythmias and cardiac failure attained a statistically significant relationship with mortality. Arrhythmia was reported by three studies (OR 2.33, 95% CI 1.16-4.70; $p$=0.02; $I^2$=60%), coronary artery disease that was reported by three studies (OR 1.68, 95% CI 1.35-2.10; $p$<0.00001; $I^2$=0%), and cardiac failure was mentioned in five studies (OR 2.01, 95% CI 1.36-2.98; $p$=0.0005; $I^2$=77%) while those factors that failed to establish a statistically significant relation with mortality include atrial fibrillation that was reported by four studies (OR 1.00, 95% CI 0.77-1.31; $p$=0.98; $I^2$=33%).

In our study, abdominal pain, hypotension, small bowel involvement, small & large bowel involvement, and large bowel involvement were included as part of the disease presentation. Abdominal pain and large bowel involvement were significantly associated with mortality. Small and large bowel involvement was reported in three studies (OR 2.25, 95% CI 0.96-5.27; $p$=0.06, $I^2$=63%) large bowel involvement was reported by seven studies (OR

2.74, 95% CI 1.14-6.59; p=0.02; $I^2$=79%) while abdominal pain was reported by five studies and had a significant association with mortality (OR 0.31, 95% CI 0.14-0.72; p=0.006; $I^2$=0%). Small bowel involvement was reported in three studies showed no significant relation with mortality (OR 1.15, 95% CI 0.40-3.27; p=0.8, $I^2$=78%).

In our study, radiological findings selected were bowel wall thickening, mesenteric or portal venous gas, and pneumatosis intestinalis. Bowel wall thickening was reported by three studies and was not associated with a significant decrease in mortality (OR 0.62, 95% CI 0.35-1.07; p=0.08; $I^2$=0%), furthermore, mesenteric or portal venous gas and pneumatosis intestinalis could not establish relation with mortality. Mesenteric or portal venous gas was reported by three studies (OR 1.35, 95% CI 0.68-2.70; p=0.39; $I^2$=0%) and pneumatosis intestinalis was reported by three studies (OR 0.58, 95% CI 0.09-3.83; p=0.58; $I^2$=76%).

In our study, creatinine and lactate are two biochemical parameters that were included and were significantly associated with increased mortality. Creatinine was reported in five studies (OR 1.59, 95% CI 1.18-2.14; p=0.0002; $I^2$=69%) and lactate was reported as a risk factor in four studies (OR 1.40, 95% CI 1.23-1.60; p<0.00001; $I^2$=0%).

In our study, factors related to medical and surgical management related to mortality included in this review were Anticoagulation, antiplatelet, bowel resection, inotropes, revascularization, second-look surgery, primary anastomosis, and delay to surgery. Treatment with anticoagulation was associated with decreased mortality. It was reported in five studies (OR 0.30, 95% CI 0.10-0.88; p=0.03; $I^2$=82%). Revascularization was not significantly related to decreased mortality and was reported in two studies (OR 0.55, 95% CI 0.09-3.35; p=0.52; $I^2$=2%). On the other hand, management with inotropes was reported by two studies and was related with significantly increased mortality (OR 10.29, 95% CI 3.24-32.67; p<0.0001; $I^2$=31%). Delay to surgery that was reported by four studies and also established a significant association to mortality (OR 6.35, 95% CI 1.32-30.60 p=0.02; $I^2$=94%). Antiplatelet was reported by two studies and was significantly related to mortality (OR 1.21, 95% CI 0.70-2.09; p=0.049; $I^2$=35%). Bowel resection was reported by 11 studies and could not establish a statistically significant association with mortality (OR 0.93, 95% CI 0.45-1.93; p=0.84; $I^2$=94%). Primary anastomosis was reported by two studies and was not a significant predictor of mortality (OR 1.13, 95% CI 0.49-2.63; p=0.78; $I^2$=60%). Second look surgery was reported by four studies and was not a significant predictor of mortality (OR 1.20, 95% CI 0.73-1.98; p=0.46; $I^2$=0%).

Conclusion:

In conclusion, this comprehensive review investigated clinical predictors of mortality in patients with acute mesenteric ischemia (AMI) from studies conducted between 2010 and 2022. The review encompassed a diverse range of factors, including demographics, comorbidities, cardiovascular diseases, disease presentation, radiological findings, biochemical parameters, and medical and surgical management.

Noteworthy findings included the significant association of age, patient dependency, diabetes, cancer, arrhythmia, cardiac failure, abdominal pain, large bowel involvement, elevated creatinine, and lactate levels with increased mortality. Conversely, anticoagulation treatment demonstrated a significant decrease in mortality, while inotropic support and delayed surgery were associated with elevated mortality. The study underscores the multifactorial nature of AMI prognosis, emphasizing the importance of a holistic approach considering various clinical elements for risk assessment and management decisions.

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# التنبئ بالوفيات فى نقص تروية المساريق الحاد : دراسة منهجية و تحليل تجميعى

نقص التروية المساريقى الحاد (AMI) هو حالة طبية وجراحية طارئة تهدد الحياة، على الرغم من التحسن فى التشخيص والنهج من التخصصات الحديث، لم يكن هناك أى تحسن كبير فى معدل الوفيات بين المرضى الذين يعانون من AMI، ومعدلات الوفيات الإجمالية مرتفعة فى مقارنة بحالات الطوارئ الجراحية الأخرى.

كان الهدف من هذه المراجعة هو تحديد المنبئات السريرية للوفيات لدى المرضى الذين يعانون من نقص تروية المساريقى الحاد.

تناولت المراجعة دراسات الحالات والشواهد، ودراسات تقرير الحالة، ودراسات الأتراب المرتقبة، ومتابعة الحالة بأثر رجعى، والمنبئات السريرية للوفيات لدى المرضى الذين يعانون من نقص تروية المساريقى الحاد منذ عام ٢٠١٠ حتى ٢٠٢٢ والتى تشمل المرضى الذين يعانون Google، ومحرك بحث PubMed من نقص تروية المساريقى الحاد. تم البحث فى قواعد البيانات الإلكترونية التالية حتى عام ٢٠٢٢، ومجلة جراحة Wiley Online، ومكتبة Science Direct و EMBASE للمراجعات المنهجية، وCochrane، وقاعدة بيانات Scholar. الكاحل والقدم، وقاعدة بيانات المفاتيح السريرية للبحث عن الكلمات الرئيسية والمصطلحات المدرجة أدناه: نقص تروية المساريقى. نقص تروية المساريقى الحاد، نقص تروية المساريقى الحاد، الوفيات الناجمة عن نقص تروية المساريقى الحاد، الأمراض المصاحبة لنقص تروية المساريقى.

ويمكن تلخيص نتائج دراستنا الحالية على النحو التالى:

- فى دراستنا، كانت مسببات AMI متغيرة أيضًا بين المرضى. كان ٩١٥ مريضًا يعانون من نقص تروية المساريقى الانسدادى (AOMI)، وكان ٣٥٤ مريضًا يعانون من تجلط الدم الوريدى المساريقى، وكان ١٩٣ مريضًا يعانون من نقص تروية المساريقى غير الانسدادى (NOMI) بينما كان لدى ٧٦٧٨ مريضًا إما سبب ثانوى آخر لـ AMI أو كانت المسببات غير محددة.
- فى دراستنا، كان العمر والجنس من العوامل المتعلقة بالتركيبة السكانية المدرجة فى المراجعة الحالية. تم الإبلاغ عن العمر فى ١٥ دراسة وارتبط بشكل كبير بالوفيات ($I^2$=82%, $p$<0.0001, 95% CI 1.09-1.29, OR 1.19). تم تقييم الجنس فى ١٨ دراسة. تم تحليله على أنه ذكر مقابل أنثى ولكنه لم يتمكن من تحقيق دلالة إحصائية ($I^2$=34%, $p$=0.46, 95% CI 0.85-1.07, OR 0.96).