



Systematic Surgical Exploration or Observation and Selective Exploration of Suspected Traumatic Mesenteric and Bowel Injuries: A Meta-analysis

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Abstract

Context: Mesenteric and bowel injuries (MBI) are rare and dangerous presentations of blunt abdominal trauma and often cause clinical uncertainty since their diagnosis is difficult and operative treatments are often delayed. No clear guidelines exist regarding this topic, and due to the rarity of the injury, few and highly low-quality data are available. This study aimed to compare early surgical exploration, delayed surgical exploration, and non-operative management in patients with proven and suspected blunt MBI.

Evidence Acquisition: Detailed research was performed on Medline, Embase, PubMed, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews databases until 29th November 2019. The studies that were considered eligible to be included in this systematic review and consequent meta-analysis were those focusing on patients with proven MBI or computed tomography (CT) signs suspected for them and comparing early surgical exploration (EOR) with delayed one (DOR) or with selective surgical exploration (SOR) after clinical observation. The eligible studies were sub-grouped into those using a delay cut-off (to distinguish "early" and "deferred" surgical intervention) higher than 12 h and those using a cut-off lower than 12 h, as well as those focusing on patients with high-risk CT signs (pneumoperitoneum and active mesenteric bleeding) and those focusing on patients with low-risk ones.

Results: Finally, 16 studies fulfilled the inclusion criteria and were included in the meta-analysis with a total of 2,702 patients. All studies, although not randomized, were considered to be at the acceptable risk of bias in the important domains. It was found that in patients with proven MBI, in the subgroup of studies with a delay cut-off for surgical intervention lower than 12 h, the complication rate was significantly lower in EOR, compared to DOR (risk ratio [RR]=0.47, 95% CI=0.29-0.79, P=0.004). In patients with suspected MBI with low-risk CT signs, the complication rate was significantly lower in SOR, compared to EOR (RR=1.79, 95% CI=1.27-2.53, P=0.001). It was also revealed that in patients with high-risk CT signs, the complication rate and the length of stay (LOS) were significantly lower in EOR, compared to DOR (complication: RR=0.38, 95% CI=0.17-0.84, P=0.02; LOS: mean difference=-12.00, 95% CI=-21.44-2.56, P=0.01).

Conclusion: The present meta-analysis confirmed that in patients with proven blunt MBI a delay of surgical intervention higher than 12 h would lead to a higher complication rate and a longer LOS. Based on the results, in blunt trauma patients with pneumoperitoneum or active mesenteric bleeding at the admission CT scan, complications and LOS could be reduced by performing an early surgical exploration. On the other hand, in blunt trauma patients with low-risk CT signs of suspected MBI, a clinical observation with selective surgical exploration in case of clinical or radiological worsening could reduce the complication rate without increasing mortality and LOS.

Keywords: Abdominal trauma index, Bowel

1. Context

The management of traumatic solid organ injury, with the majority of patients being managed non-operatively, has been regulated by shared international guidelines (1-4), and indication for conservative or operative management in this group of patients is well understood. On the contrary, mesenteric and bowel injuries (MBI) are rare consequences of blunt abdominal trauma and often cause clinical uncertainty. Although MBIs are rare (5), patients with bowel injuries have a high mortality rate, ranging from 1.3%-19.8% (5, 6). Despite technological innovation, MBI diagnosis remains challenging. Computed tomography (CT) scans fail to detect MBI in a significant number of patients in 4%-25% of cases (5, 7, 8), with reported insufficient sensibility and specificity of CT scans (5, 8). As a result of the difficult diagnosis and sporadic

exposure of surgeons (especially of non-trauma surgeons) to MBIs and the rarity of these injuries, their treatment is often subjected to delay.

There is a considerable debate regarding distinguishing patients with suspected MBI needing urgent surgical exploration from those who can receive clinical observation, to prevent septic complications and, at the same time, minimizing negative exploration rates. Furthermore, no consensus exists among researchers on the real relationship between the delay of operative intervention in MBI and the increase in mortality and complication rate (6, 7, 9-14), as well as on the rate of non-therapeutic surgical intervention (negative surgical exploration or findings which do not require surgical repair) (7, 9-12, 15, 16). Some pieces of evidence are available for penetrating hollow-viscus injuries (17); however, no clear guidelines exist for the diagnosis and treatment of

MBI after blunt trauma. Nevertheless, in trauma and emergency surgery setting, it is very difficult to perform randomized controlled trials and obtain high-quality data. To the best of our knowledge, no meta-analysis has been performed on the mentioned issues yet to collect and analyze them. The present meta-analysis aimed to compare, in blunt trauma patients undergoing surgery with proven MBI or with CT signs of suspected MBI, the outcomes of early surgical intervention (Early Operative Room [EOR]) with outcomes of deferred surgery (Deferred Operative Room [DOR]). Moreover, it was conducted to compare, in blunt trauma patients with CT signs of suspected MBI, the outcomes of EOR with those of clinical observation and selective surgical exploration in patients with clinical or radiological worsening (onset of sepsis or peritonism, worsening of CT-scan signs) (Selective Operative Room [SOR]).

2. Evidence Acquisition

2.1. Literature search strategy

Electronic searches were performed in Medline, Embase, PubMed, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews databases until 29th November 2019. The search process was conducted using the following keywords: "Bowel", "Hollow viscus", "Mesenteric trauma", "Mesenteric injury", "Mesenteric bleeding", "Mesenteric hematoma", "Mesenteric hemorrhage", "Mesenteric embolization", and "Blunt trauma" combined with AND/OR. The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. Review articles were also obtained to determine other possible studies.

2.2. Selection criteria

The studies determined as eligible for this systematic review and consequent meta-analysis were those comparing EOR with DOR or SOR in patients with proven MBI or CT signs suspected for MBI after blunt abdominal trauma. In this study, EOR means immediate surgical exploration (exploratory laparoscopy or laparotomy) for bowel or mesenteric injuries after a patient's arrival in the Emergency Department (ED) and possibly performing a CT scan. With SOR, it means clinical observation of patients with CT signs of suspected MBI (i.e., extraluminal air, bowel wall thickening, arterial vessel extravasation, mesenteric stranding, bowel wall discontinuity, reduced bowel wall enhancement, free fluid without solid organ injuries, and mesenteric hematoma) and selective deferred surgical exploration only in patients with clinical deterioration after repeated CT scan with worsened radiological signs. The term DOR means surgical exploration for MBI after a delay from patient's arrival in the ED, failed non-operative

management, or delayed diagnosis. No language restrictions have been applied, and either prospective or retrospective comparative cohort studies were initially selected to maximize the number of patients. On the other hand, the studies considering only penetrating trauma or only pediatric patients were excluded from the research. The eligibility for study inclusion into the meta-analysis and study quality assessment were performed independently by two authors, namely PF and MT. Study data were extracted into standard forms independently by the mentioned authors. Discrepancies between the two investigators were resolved by discussing and evaluating the question with other investigators. Studies were divided into two groups, including those analyzing patients with proven MBI comparing EOR and DOR (sub-grouped according to the delayed cut-off used to distinguish "early" and "deferred" surgical intervention in each study: <12 h vs \geq 12 h) and those focusing on patients with CT signs of suspected MBI comparing EOR and SOR and comparing EOR and DOR (sub-grouped according to the presence of high risk or low-risk CT signs for suspected MBI (Table 1)).

The primary outcomes for the meta-analysis were mortality, complication rate, length of stay (LOS), the necessity of stoma formation, necessity of bowel resection, failure rate, and non-therapeutic surgical exploration rate (negative surgical exploration or findings which do not require surgical repair). The outcome "failure" means non-therapeutic surgical exploration for EOR and the necessity of surgical exploration during observation for SOR.

2.3. Risk of bias assessment

Data quality of studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS) (18). By considering 12 items (8 for non-comparative and 4 for comparative studies) the total score was calculated by summing the values attributed as follows: 0=not reported, 1=reported but inadequate, 2=reported and adequate. Global ideal scores for non-comparative and comparative studies were obtained at 16 and 24, respectively.

2.4. Statistical analysis

Data from the individual eligible studies were

Table 1. High-risk and low-risk computed tomography signs for suspected mesenteric and bowel injuries (12)

High-risk computed tomography signs	Low-risk computed tomography signs
Pneumoperitoneum	Bowel wall thickening
Active mesenteric bleeding	Mesenteric stranding
	Bowel wall discontinuity
	Reduced bowel wall enhancement
	Free fluid without solid organ injuries
	Mesenteric hematoma

entered into a spreadsheet for further analysis. The Review Manager software (Version 5.3., Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011) was used to perform the statistical analysis. Risk Ratio (RR) was calculated for discrete variables (19) and Mean Difference (MD) was assessed for continuous variables. The random and fixed-effects models were used to calculate the outcomes. Heterogeneity amongst the trials was determined employing the Cochrane Q value and quantified using the I^2 inconsistency test.

3. Results

Finally, 17 studies fulfilled the inclusion criteria

and were included in the meta-analysis, which were all observational studies, including 15 retrospective and 2 prospective studies (publication dates 1998–2019) (Figure 1).

Among these studies, ten studies focused on patients with proven MBI and seven studies on patients with CT signs of suspected MBI. There were a total of 2,702 patients, including 2,119 cases with proven MBI (1,402 in the EOR group and 717 in the DOR group) (Table 2) and 583 subjects with CT signs of suspected MBI (173 in the EOR group and 410 in SOR group) (Table 3). The inclusion and exclusion criteria, considered CT signs, mean scores age and injury severity score, and the cut-off delay of each study are reported in Table 1-2. For studies on patients with proven MBI, the range of delay varied

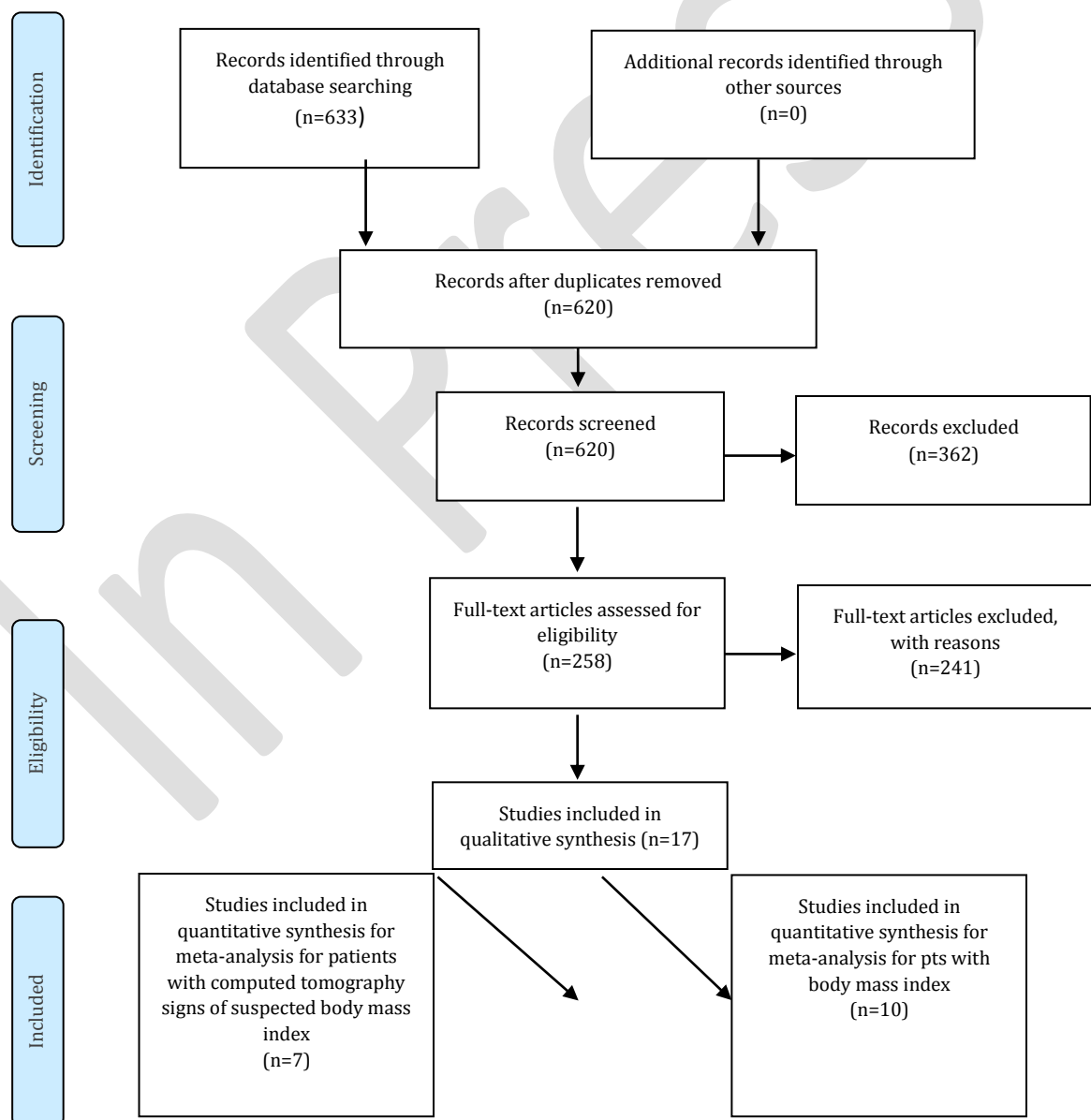


Figure 1. PRISMA flow diagram

Table 2. Comparative table of trauma patients undergone surgery for proven mesenteric and bowel injuries

First author (year)	Study type	Inclusion criteria	Exclusion criteria	Trauma patients undergone surgery for bowel/mesenteric injuries															
				Number of patients		Delay cut-off (hours)	Age, years (mean±SD)	ISS mean±SD (min-max)	Bowel resection		Stoma formation		LOS (days: mean±SD)		Complication rate		Mortality		
				EOR	DOR				EOR	DOR	EOR	DOR	EOR	DOR	EOR	DOR	EOR	DOR	
Liao 2010	Prospective	Blunt operated bowel or mesenteric injuries	Expired in ED, no operation, age<16, absence of CT scan	161	27	24	45.3±18.3	17.2±11.2	42.161	8.27	4.161	2.27	17.1±15.4	18.3±16.6	17.161	7.27	18.161	3.27	
Al-Hassani 2013	Retrospective	Blunt operated bowel or mesenteric injuries	Penetrating trauma, age<16	83	26	8	35±9.5	16±10	39.83	11.26	12.83	0.26	/	/	21.83	10.26	7.74	1.25	
Alsayali 2009	Retrospective	Blunt operated bowel or mesenteric injuries		170	52	8	35 (14-95)	29 (4-75)	/	/	/	/	/	/	13.170	7.52	1.170	4.52	
Xeropotamos 2001	Retrospective	Blunt operated mesenteric injuries		21	10	6	/	/	/	/	/	/	11 (3-24)	23 (10-61)	0.21	7.10	/	/	
Ahmed 2018	Retrospective	Patients with blunt injuries and underwent a small bowel resection within 24 hours of arrival		482	482	4	EOR: 37.2±18.8 DOR: 36.4±21.2	EOR: 17.7±12.0 DOR: 18.2±12.1	/	/	/	/	9 (6-15)	10 (7-19)	29.224*	41.224*	40.482	38.482	
Govender 2010	Prospective	All patients found at laparotomy to have colon and/or rectal injuries after abdominal trauma (Blunt and perforating)		138	39	12	29.8±10.9	12.5±6.3	/	/	/	/	/	/	48.138	12.39	27.138	2.39	
Frick 1999	Retrospective	Small-bowel and mesentery injuries in blunt trauma patients		54	9	12	35±21.4	29±16.7	/	/	/	/	/	/	46.54	3.9	15.54	0.9	
Malinoski 2009	Retrospective	Blunt hollow viscus injuries	Non-perforation injuries, (such as hematomas or serosal tears), patients who died within 24 hours	136	55	8	35±16	17±11	/	/	/	/	/	/	/	/	10.136	7.55	
Allen 1998 Oct	Retrospective	Blunt duodenal injuries		28	7	6	DOR: 16.9±4.5 EOR: 8.8±2.5	DOR: 20±2 EOR: 27±2	/	/	/	/	25.0±5.2	25.1±9.4	3.28	4.7	4.28	0.7	
Allen 1998 Jul	Retrospective	Hollow viscus injuries after blunt trauma		129	10	6	27±1.4	30.1±1.1	/	/	/	/	/	/	7.129	2.10	/	/	

* Complication rates among pairs of patients who both had complication records available by the timing of small bowel resection
LOS: Length of stay; ISS: Injury severity score; EOR: Early surgical exploration; DOR: Delayed surgical exploration; ED: Emergency department; CT: Computed tomography

Table 3. Comparative table of trauma patients with computed tomography signs of suspected mesenteric and bowel injuries

First author (year)	Study type	computed tomography signs	Exclusion criteria	Bowel/ mesentery	Trauma patients with computed tomography signs of suspected mesentery/hollow viscus injuries										LOS (days: mean±SD)			Complication rate			Mortality		
					Number of patients		Age, years (mean±SD)	ISS mean±SD (min-max)	Nontherapeutic EOR/total EOR (EOR failure)	Delayed laparotomy/Observed patients (SOR failure)	Nontherapeutic DOR/total DOR (DOR failure)	Delay (days; mean±SD)	IOR	SOR	DOR	IOR	SOR	DOR	IOR	SOR	DOR		
					EOR	SOR																	
Lannes 2019	Retrospective	Hemoperitoneum, mesenteric pneumoperitoneum, bowel wall thickening, arterial mesenteric vessel extravasation, mesenteric stranding, bowel wall discontinuity, reduced bowel wall enhancement, and anterior abdominal wall injury	Penetrating trauma	B+M	22	62	43(8-84)	27.2 (5.2-18.3)	3.22	18.62	3.18	2.5 days ± 2 (range 0-7)	22	40	53	3.22	8.62	6.18	1.22	7.62	1.18		
Park 2018	Retrospective	Mesenteric hematoma, mesenteric fat infiltration, bowel wall thickening, or free fluid in the peritoneal cavity	Patients who required emergency surgery for large pneumoperitoneum, bowel ischemia, other complicated solid organ injuries, or large extravasation of contrast from bowel or mesenteric injury by CT scan at the admission, hemodynamical instability	B+M	35	42	41±15 (17-78)	13 ± 4	13.35	18.42	3.18	3±2 days (range, 2-9 days)	15±14	18±23	/	14.35	7.42	7.18	/	/	/		
McNutt 2014	Retrospective	Bowel wall discontinuity, abnormal bowel wall enhancement, and extraluminal air, infiltration, haematoma, intravenous contrast extravasation, mesenteric vascular beading appearance, and occlusion of a mesenteric vessel	Lack of abdominal CT scan, abdominal operation before CT scan, off-protocol CT scan, and CT Grade 5 injury (active extravasation or pneumoperitoneum), hemodynamical instability	B+M	43	67	42(23-55)	19(9-34)	4.43	17.67	1.17	18.8 hours (range, 5.2 hours to 8.2 days)	14(8-24)	10 (4-23)	17(9-23)	15.43	13.67	6.17	3.43	1.67	1.17		
Bège 2014	Retrospective	Bowel wall discontinuity, abnormal bowel wall enhancement, and extraluminal air, infiltration, haematoma, intravenous contrast extravasation, mesenteric vascular beading appearance, and occlusion of a mesenteric vessel	Patients who underwent abdominal surgery without an initial CT scan	B+M	11	32	43(15-82)	20(4-50)	1.11	12.32	0.12	3 (1-21)	20(8-26)	21	32 (2-66)	3.11	-/-	9.12	2.11	2.32	2.12		
Marek 2014	Retrospective	Free intraabdominal air		B	38	36	38.9	21.9	10.38	2.36	1.2	/	/	/	/	/	/	/	/	/	/		
Jost 2017	Retrospective	Intraperitoneal free fluid without solid organ injuries	Hemodynamical instability, contiguous solid organ injury, obvious extravasation of oral contrast from a HVI or other obvious hollow viscus injury, observed mesenteric hemorrhage, and intraperitoneal bladder ruptures, pts dead in the first 24 hour	M+B	14	25	34(23-50)	25(18-32)	3.14	7.25	3.7	9(4-14)	17.8 (5.5-43)	35 (14.5-43)	12.14	15.25	7.7	/	/	/	/		
Gonser-Hafertepen 2014	Retrospective	Patients with free fluid and no sign of solid organ injuries or hollow viscus injury (defined as bowel wall thickening, contrast extravasation, or extraluminal air)	Bowel wall thickening, contrast extravasation, or extraluminal air, hemodynamically unstable, peritonitis, traumatic abdominal wall hernia, solid organ injuries	M+B	10	146	35	14	1.10	4.146	0.4	/	/	/	/	/	/	/	/	/	/		

ai exploration; IOR: Immediate surgical exploration; LOS: Length of stay; CT: Computed tomography

Table 4. Adopted criteria for early surgical exploration for each study focused on patients with CT signs of suspected mesenteric and bowel injuries

First author (year)	Criteria for immediate surgical exploration in included patients with CT signs of suspected mesenteric and bowel injuries
Lannes 2019	Surgical indication was collegially determined based on clinical, laboratory, and CT scan findings (unspecified)
Park 2018	Treatment was determined by either surgeon or patient preference after full clinical consideration and discussion
McNutt 2014	Bowel injury on CT scan, hemodynamic instability, seatbelt sign with a tender examination, a free fluid of unclear etiology, and equivocal CT scan with unreliable physical examination
Bège 2014	Hemodynamic instability despite fluid resuscitation, clinical signs of peritoneal irritation, radiological evidence of intestinal perforation
Marek 2014	In addition to having free air on CT, there existed clinical and/or radiologic suspicion of intra-abdominal injury: haemodynamic instability, seatbelt sign, radiologic signs of bowel injury, free fluid, other obvious organ injuries (e.g. bladder or diaphragm), and/or active bleeding
Jost 2017	Not reported
Gonser-Hafertepe 2014	Not reported

from 4-24 h. For studies on patients with CT signs suspected for MBI, the adopted criteria for EOR for each study are reported in Table 4, and for those undergone a DOR, the range of the mean delay varied from 18 h to 3 days (Table 3).

3.1. Quality of trials

There was good agreement between the reviewers (i.e., PF and MT) about the eligibility and quality of the studies. Table 5 demonstrates the quality of the included studies. All studies, although not randomized, were considered to be at acceptable risk of bias in the important domains.

3.2. Meta-analysis of studies focusing on trauma patients undergone surgery for proven MBI comparing EOR and DOR -Mortality

The mortality rate for EOR versus DOR was reported in seven studies (14, 20-26). Overall, 1,243 and 696 patients received EOR and DOR, respectively. There was no statistical heterogeneity between studies (Figure 2A), and in the fixed-effects model, the mortality rate was not significantly different between EOR and DOR (RR=1.12, 95% CI=0.81-1.55, P=0.48).

Table 5. Quality assessment of non-randomized trials

Study (Ref.) Year	Quality evaluation criteria								Additional criteria in comparative studies					Total
	Clear stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to the study aim	Unbiased assessment of study end-point	Appropriate follow-up period	Loss to follow-up less than 5%	Prospective calculation of the study size	Adequate control group	Contemporary groups	Baseline equivalence	Adequate statistical analysis		
1 Lannes 2019 [9]	2	2	0	2	2	2	0	0	2	2	0	2	16	
2 Park 2018 [10]	2	2	0	2	2	2	0	0	2	2	2	2	18	
3 McNutt 2014 [7]	2	2	0	2	2	2	0	0	2	2	1	2	17	
4 Bège 2014 [11]	2	2	0	2	2	2	0	0	2	2	2	2	18	
5 Marek 2014 [15]	2	2	0	2	2	2	0	0	2	2	2	2	18	
6 Jost 2017 [12]	2	2	0	2	2	2	0	0	2	2	1	2	17	
7 Gonser-Hafertepe 2014 [16]	2	2	0	2	2	2	2	0	2	2	2	2	18	
8 Liao 2010 [26]	2	2	2	2	2	2	0	0	2	2	2	2	20	
9 Al-Hassani 2013 [21]	2	2	0	2	2	2	0	0	2	2	2	2	18	
10 Alsayali 2009 [23]	2	2	0	2	2	2	0	0	2	2	0	0	14	
11 Xerepotamos 2001 [28]	2	2	0	2	2	2	0	0	2	2	0	2	16	
12 Ahmed 2018 [20]	2	2	0	2	2	2	0	0	2	2	2	2	18	
13 Govender 2010 [25]	2	2	2	2	2	2	0	0	1	2	0	2	17	
14 Frick 1999 [24]	2	2	0	2	2	2	0	0	2	2	0	2	16	
15 Malinoski 2009 [14]	2	2	0	2	2	2	0	0	0	2	0	2	14	
16 Allen 1998 Oct [22]	2	2	0	2	2	2	0	0	2	2	2	2	18	
17 Allen 1998 Jul [27]	2	2	0	1	2	2	0	0	1	2	0	2	14	

-Complication rate

The complication rate for EOR versus DOR was reported in nine studies (20-28). Overall, 1,008 and 404 patients received EOR and DOR, respectively. Among the studied pieces of research, 6 (20-23, 27, 28) and 3 studies (24-26) used a cut-off (to distinguish “early” and “deferred” surgical intervention) lower and higher than 12 h, respectively. Considering all studies, there was statistical heterogeneity between studies (Figure 2B), and in the random-effects model, the complication rate was significantly lower in EOR (RR=0.61, 95% CI=0.38-0.98, P=0.04). Considering the studies with a delay cut-off higher or equal to 12 h (i.e., 12 h or 24 h), statistical heterogeneity was observed between studies, and in the random-effects model, the complication rate was not significantly different between EOR and DOR (RR=1.03, 95% CI=0.41-2.58, P=0.95). Focusing on studies with a delay cut-off lower than 12 h (i.e., 4 h, 6 h, or 8 h) there was no statistical heterogeneity between studies, and both in the random-effects model and in the fixed-effects model, the complication rate was significantly lower in EOR, compared to DOR (RR=0.47, 95% CI=0.29-0.79, P=0.004)

-Length of stay

Length of stay was reported in 4 studies (20, 22, 26, 28) for EOR versus DOR. Overall, 434 and 268 patients respectively received EOR and DOR. There was no statistical heterogeneity between studies (Figure 2C), and in the fixed-effects model, the LOS was significantly lower in EOR, compared to DOR (MD=-1.04, 95% CI=-1.53--0.54, P<0.0001).

-Necessity of bowel resection

The necessity of bowel resection was reported in 2 studies (21, 26) for EOR versus DOR. Overall, 244 and 53 patients received EOR and DOR, respectively. No statistical heterogeneity was found between studies (Figure 2D), and in the fixed-effects model, the necessity of bowel resection was not significantly different between EOR and DOR (RR=1.01, 95% CI=0.68-1.50, P=0.97).

-Stoma formation

Stoma formation rate was reported in 2 studies (21, 26) for EOR versus DOR. Overall, 244 and 53 patients received EOR and DOR, respectively. There was statistical heterogeneity between studies (Figure 2E), and in the random-effects model, the stoma formation rate was not significantly different between EOR and DOR (RR=1.41, 95% CI=0.04-51.30, P=0.85).

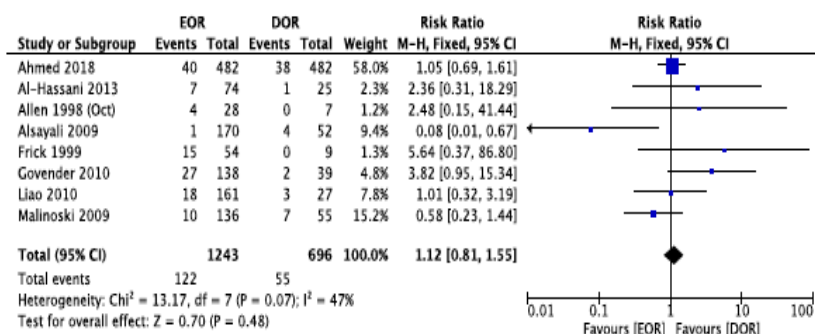
3.3. Meta-analysis of studies focusing on patients with CT-signs of suspected MBI comparing EOR and SOR

- Failure

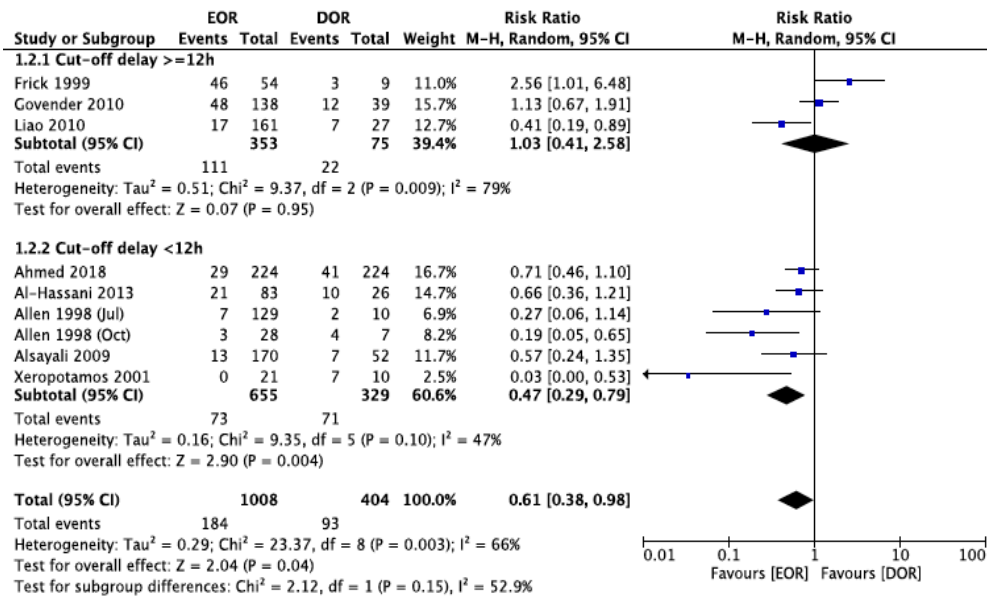
The failure rate was reported in 7 studies (7, 9-12, 15, 16) for EOR versus SOR. Overall, 173 and 410 patients received EOR and SOR, respectively. In 4 studies (7, 10, 12, 16) the focus was on patients with low-risk CT signs of suspected MBI and in 3 studies (9, 11, 15) on patients with high-risk CT signs. Considering all studies, there was statistical heterogeneity between studies (Figure 3A), and in the random-effects model, the failure rate was not significantly different between EOR and SOR (RR=0.82, 95% CI=0.43-1.55, P=0.53). Focusing on studies on patients with low-risk CT-signs, there was no statistical heterogeneity between studies, and in the random-effects model, the failure rate was not significantly different between EOR and SOR (RR=0.76, 95% CI=0.41-1.43, P=0.40). Focusing on studies on patients with high-risk CT-signs, there was statistical heterogeneity between studies, and in the random-effects model, the failure rate was not significantly different between EOR and SOR (RR=0.85, 95% CI=0.15-4.70, P=0.85).

-Mortality

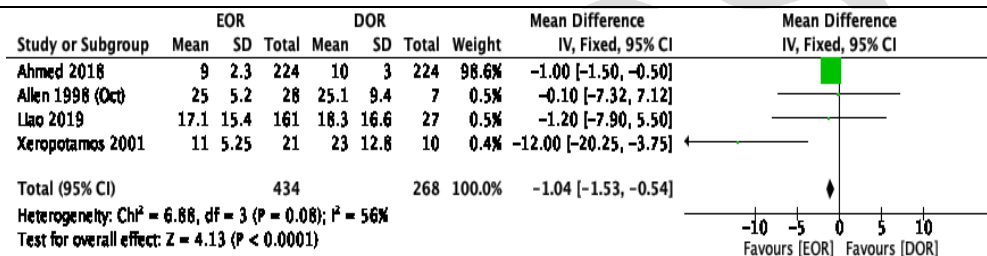
The mortality rate was reported in 3 studies (7, 9, 11) for EOR versus SOR. Overall, 76 and 161 patients received EOR and SOR, respectively. In 1 study (7) the focus was on patients with low-risk CT signs of suspected MBI and in 2 studies (9, 11) on patients with high-risk CT signs. Considering all studies, there was no statistical heterogeneity between studies (Figure 3B), and in the fixed-



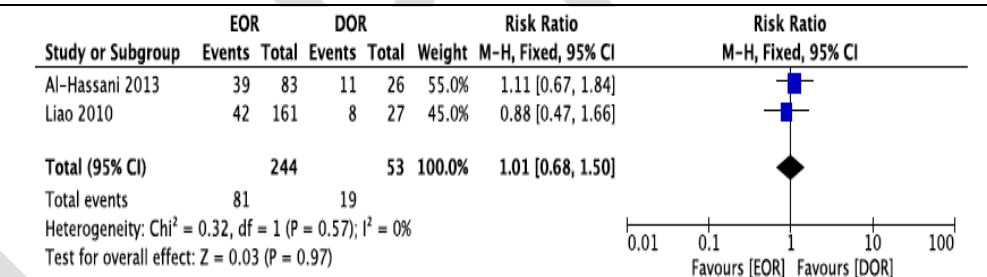
2 A. Mortality



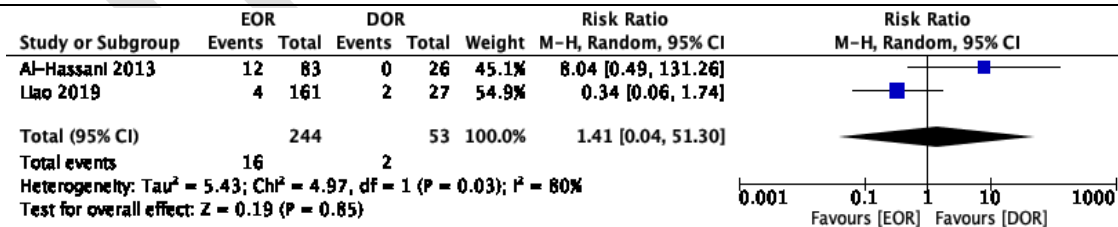
2 B. Complication



2 C. Length of stay



2 D. Necessity of bowel resection

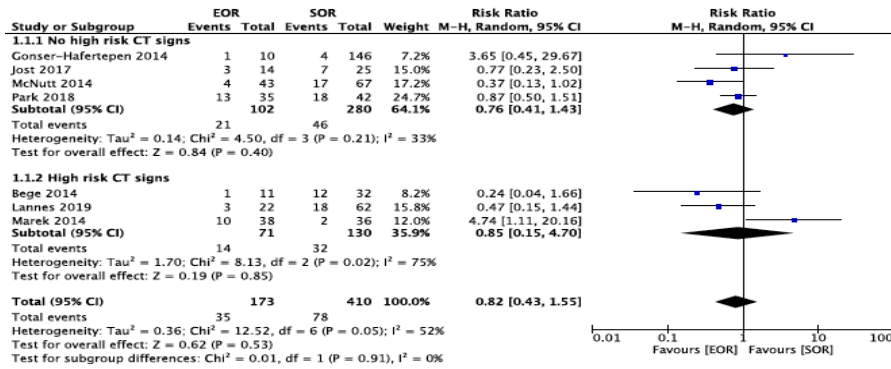


2 E. Stoma formation

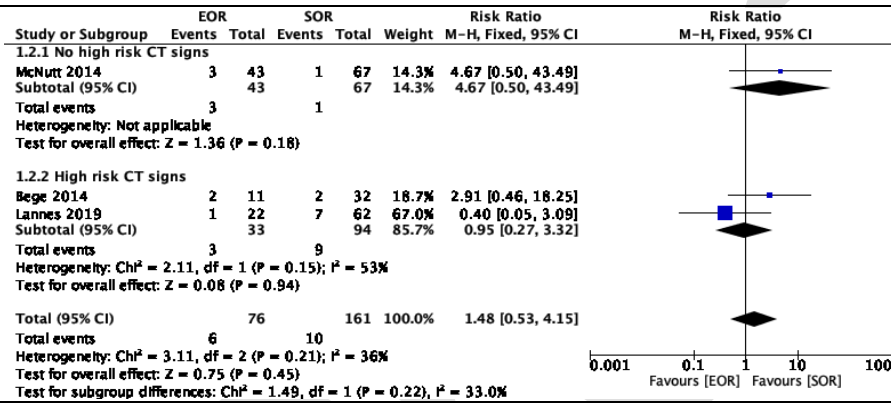
Figure 2. Early Operative Room vs Deferred Operative Room in trauma patients undergone surgery for Bowel/Mesenteric Injuries

effects model, the mortality rate was not significantly different between EOR and SOR (RR=1.48, 95% CI=0.53-4.15, P=0.45). Focusing on the study on patients with low-risk CT signs, the mortality rate was not significantly different between EOR and SOR (RR=4.67, 95% CI=0.50-

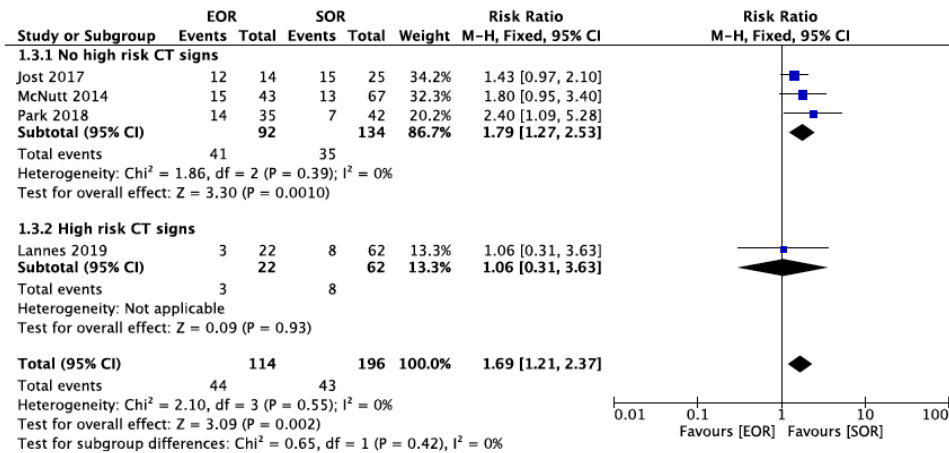
43.49, P=0.18). Considering the studies on patients with high-risk CT-signs, there was no statistical heterogeneity between studies, and in the fixed-effects model, the mortality rate was not significantly different between EOR and SOR (RR=0.95, 95% CI=0.27-3.32, P=0.94).



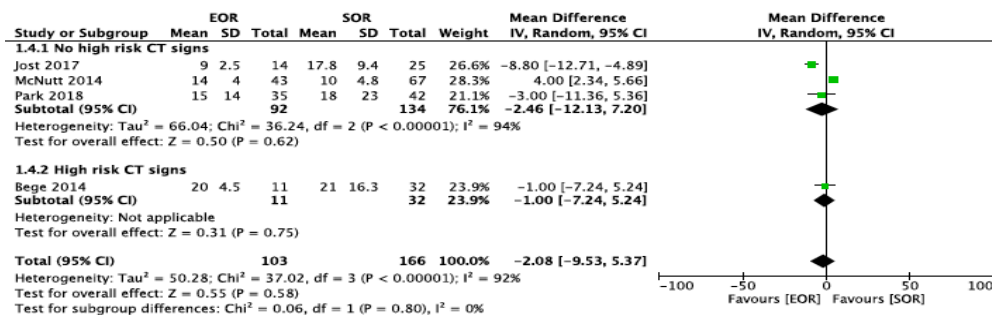
3A. Failure (Early Operative Room failure: non-therapeutic surgical intervention, Selective Operative Room failure: necessity of laparotomy during observation)



3B. Mortality



3C. Complication



3D. Length of stay

Figure 3. Early Operative Room vs Selective Operative Room in trauma patients with computed tomography signs of suspected Bowel/Mesenteric Injuries (High-risk computed tomography signs: pneumoperitoneum and/or arterial mesenteric vessel contrast extravasation)

-Length of stay

The length of stay was reported in 4 studies (7, 10-12) for EOR versus SOR. Overall, 103 and 166 patients received EOR and SOR, respectively. In 3 studies (7, 10,12), the focus was on patients with low-risk CT signs of suspected MBI, and in 1 study (11), on patients with high-risk CT signs. Considering all studies, there was statistical heterogeneity between studies (Figure 3D), and in the random-effects model, LOS was not significantly different between SOR and EOR (MD=-2.08, 95% CI=-9.53-5.37, P=0.58). Focusing on the studies on patients with low-risk CT-signs, there was statistical heterogeneity between studies, and in the random-effects model, LOS was not significantly different between SOR and EOR (MD=-2.46, 95% CI=-12.13-7.20, P=0.62). Considering the study on patients with high-risk CT signs, the complication rate was not significantly different between EOR and SOR (MD=-1.00, 95% CI=-7.24-5.24, P=0.75).

3.4. Meta-analysis of studies focusing on patients undergone surgical exploration for CT-signs of suspected MBI comparing EOR and DOR

-Non-therapeutic surgical exploration

Non-therapeutic surgical exploration rate was reported in 7 studies (7, 9-12, 15, 16) for EOR versus DOR. Overall, 173 and 78 patients received EOR and DOR, respectively. The focus in 4 studies (7, 10, 12, 16) was on patients with low-risk CT signs of suspected MBI and in 3 studies (9, 11, 15), on patients with high-risk CT signs. Considering all studies, there was no statistical heterogeneity between studies (Figure 4A), and in the fixed-effects model, the non-therapeutic surgical exploration rate was not significantly different between EOR and DOR (RR=1.22, 95% CI=0.67-2.23, P=0.51). Focusing on studies on patients with low-risk CT-signs, there was no statistical heterogeneity between studies, and in the fixed-effects model, the non-therapeutic surgical

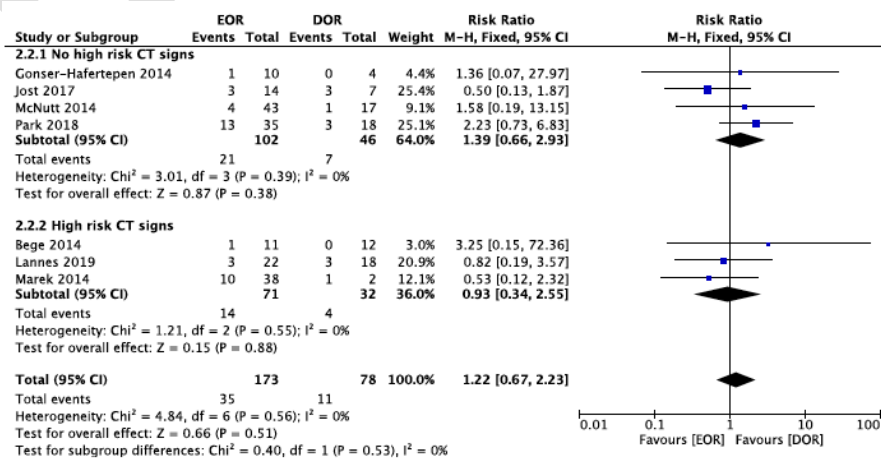
intervention rate was not significantly different between EOR and DOR (RR=1.39, 95% CI=0.66-2.93, P=0.38). Focusing on studies on patients with high-risk CT signs, there was no statistical heterogeneity between studies, and in the fixed-effects model, the non-therapeutic surgical exploration rate was not significantly different between EOR and SOR (RR=0.93, 95% CI=0.34-2.55, P=0.88).

-Mortality

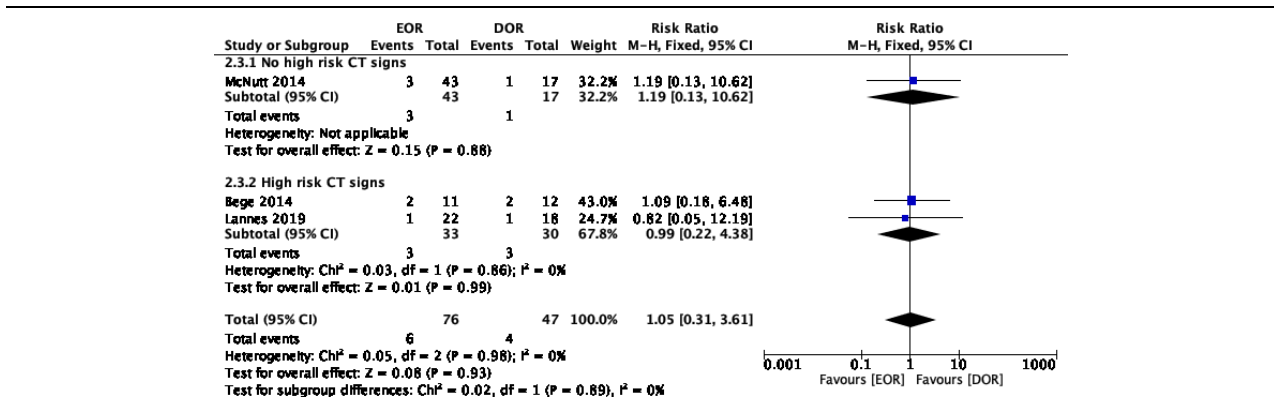
The mortality rate was reported in 3 studies (7, 9, 11) for EOR versus DOR. Overall, 76 and 47 patients received EOR and DOR, respectively. The focus of 1 study (7) was on patients with low-risk CT signs of suspected MBI and that of 2 studies (9, 11) on patients with high-risk CT signs. Considering all studies, there was no statistical heterogeneity between studies (Figure 4B), and in the fixed-effects model, the mortality rate was not significantly different between EOR and DOR (RR=1.05, 95% CI=0.31-3.61, P=0.93). Focusing on the study on patients with low-risk CT signs, the mortality rate was not significantly different between EOR and DOR (RR=1.19, 95% CI=0.13-10.62, P=0.88). Focusing on studies on patients with high-risk CT-signs, there was no statistical heterogeneity between studies, and in the fixed-effects model, the mortality rate was not significantly different between EOR and SOR (RR=0.99, 95% CI=0.22-4.38, P=0.99).

-Complication rate

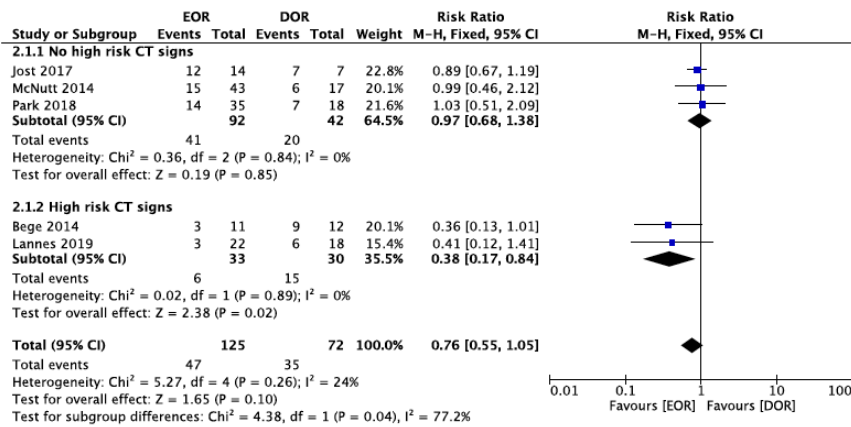
The complication rate was reported in 5 studies (7, 9-12) for EOR versus DOR. Overall, 125 and 72 patients received EOR and DOR, respectively. In 3 studies (7, 10, 12), the focus was on patients with low-risk CT signs of suspected MBI, and in 2 studies (9, 11), on patients with high-risk CT signs. Considering all studies, there was no statistical heterogeneity between studies (Figure 4C), and in the fixed-effects model, the complication rate was not significantly different between EOR and DOR



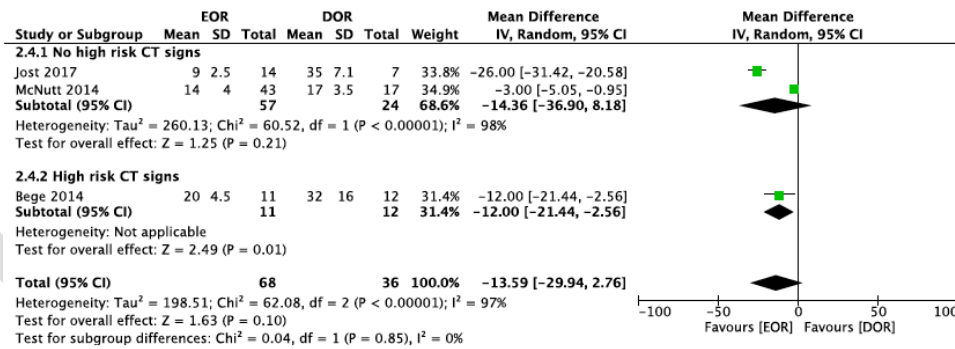
4A. Non-therapeutic surgical intervention



4B. Mortality



4C. Complication rate



4D. Length of stay

Figure 4. Early Operating Room vs Deferred Operating Room in trauma patients undergone surgery for computed tomography signs of suspected Bowel/Mesenteric Injuries (High-risk computed tomography signs: pneumoperitoneum and/or arterial mesenteric vessel contrast extravasation)

(RR=0.76, 95% CI=0.55-1.05, P=0.10). Considering studies on patients with low-risk CT signs, the complication rate was not significantly different between EOR and DOR (RR=0.97, 95% CI=0.68-1.38, P=0.85). Focusing on studies on patients with high-risk CT-signs, there was no statistical heterogeneity between studies, and in the fixed-effects model, the complication rate was significantly lower in EOR, compared to DOR (RR=0.38, 95% CI=0.17-0.84, P=0.02).

-Length of stay

Length of stay was reported in 3 studies (7, 11, 12) for EOR versus DOR. Overall, 68 and 36 patients received EOR and DOR, respectively. In 2 studies (7, 12), the focus was on patients with low-risk CT signs of suspected MBI, and in 1 study (11), on patients with high-risk CT signs. Considering all studies, there was statistical heterogeneity between studies (Figure 4D), and in the random-effects model, LOS was not significantly different between

EOR and DOR (MD=-13.59, 95% CI=-29.94-2.76, P=0.10). Focusing on studies on patients with low-risk CT-signs, there was statistical heterogeneity between studies, and in the random-effects model, LOS was not significantly different between EOR and DOR (MD=-14.36, 95% CI=-36.90-8.18-1.38, P=0.21). Focusing on the study on patients with high-risk CT signs, LOS was significantly lower in EOR, compared to DOR (MD=-12.00, 95% CI=-21.44-2.56, P=0.01).

4. Conclusion

It is well known that in trauma and emergency surgery setting, it is challenging to perform randomized controlled trials and obtain high-quality data. It is even more difficult to focus on a such rare injury as MBI. Available data consist of observational studies and case series and, to the best of our knowledge, the present research was the first meta-analysis trying to collect and analyze the bodies of evidence available. First of all, available literature has not reached a definitive consensus about the influence of the delay in surgical intervention on the outcomes of a patient with proven traumatic MBI.

The results of the present study are consistent with those reported in most studies (24, 29, 30), showing that the delay is not associated with higher mortality. The available evidence is even less clear regarding the effect of delay on morbidity. According to some authors, the delay did not lead to an increased complication rate (24, 31). However, the results of a recent review (29) showed that there were sufficient data to indicate higher morbidity, especially if surgical intervention was delayed for more than 24 h. Morbidity in the early and delayed intervention groups varied from 14.1%-62% and 35%-63.6%, respectively (27, 29, 30, 32).

Based on the findings of the present study, the heterogeneity of available results was probably due to the different delay cut-off points considered in the different studies to distinguish between "early" and "deferred" surgical intervention. To elaborate more, in the subgroup analysis, only considering studies with a delay cut-off lower than 12 h (i.e., 4 h, 6 h, or 8 h), the complication rate of patients with proven MBI was significantly lower in the EOR group. Probably, after 12 h from the patient's arrival, surgical intervention cannot bring the same benefits in terms of complications of an early one. Moreover, LOS was found to be shorter in the EOR group. No difference was revealed about the necessity of bowel resection and stoma formation between EOR and DOR; however, this result might have been obtained due to insufficient data on this topic.

The delay of the surgical intervention in

patients with MBI aggravates patients' outcomes lead to the assumption that it would be advisable to perform surgical exploration in all patients with suspected MBI. Nevertheless, systematic surgical exploration for all hemodynamically stable patients with suspected bowel or mesenteric injury has led to a reported high rate of non-therapeutic laparotomy, up to 44% and 31% for suspected intestinal lesions and suspected mesenteric injuries, respectively (33). It has also resulted in the reported morbidity of a negative laparotomy ranging between 8% and 40% (8, 34).

To compare the risks of EOR in all traumatic patients with CT signs of suspected BMI with the risks of clinical observation and SOR (in patients showing clinical deterioration or radiological signs aggravation), the present research analyzed failure rate, mortality rate, complication rate, and LOS in patients undergoing treatment with EOR vs SOR. Due to the presence of heterogeneity, a subgroup analysis was performed based on the presence or absence of high-risk CT signs, defined as the finding of pneumoperitoneum and/or arterial mesenteric vessel contrast extravasation at CT scan.

Free air is reported as a fairly reliable sign of bowel injury in patients with blunt abdominal trauma, with a specificity of 95%-100% (4, 27); however, the reported sensitivity was only 30%-60% (4, 27). Mesenteric extravasation has a reported sensitivity and specificity for acute mesenteric injury of 26%-77% and 40%-100%, respectively. Other signs of suspected BMI are reported as extraluminal air, bowel wall thickening, arterial vessel extravasation, mesenteric stranding, bowel wall discontinuity, reduced bowel wall enhancement, free fluid without solid organ injuries, and mesenteric hematoma (7-16). Nonetheless, there have been no CT findings reported with both high sensitivity and specificity (28). In one study, multivariate analysis revealed CT findings of free air and mesenteric extravasation as the only risk factors for surgical intervention (P=0.0002 and P=0.02, respectively) (12).

According to the results of the present research, the failure rate (defined as performing a non-therapeutic surgical exploration in patients undergoing treatment with EOR and as the need for delayed surgical exploration in a patient undergoing SOR) and the LOS were not significantly different between EOR and SOR, neither in patients with high-risk CT signs nor in those without them. However, in the group of patients with low-risk CT signs, the complication rate was lower in patients undergoing clinical observation and SOR. Furthermore, the mortality rate seemed to be lower in the SOR group among patients with low-risk CT signs; nevertheless, it was not statistically significant. No differences

were found in complication and mortality rates between EOR and SOR in patients with high-risk CT signs.

An analysis on patients with CT signs of suspected BMI, excluded patients with successful non-operative management and focused on patients undergoing surgical intervention, early (EOR) or deferred (DOR, for non-operative management failure). The non-therapeutic surgical exploration rate and the mortality rate were not significantly different between EOR and DOR, nor in patients with or without high risk CT signs. However, in the subgroup of patients with high risk CT signs, the complication rate and the LOS were lower than in patients undergoing early surgical exploration.

The major limitation of the present study was related to the low-quality of included studies, meaning that they were all observational studies, in almost all studies there were associated abdominal lesions which could be confounding factors, some studies involved both penetrating and blunt trauma patients, and each study considered different CT signs for suspected MBI. Moreover, since the included studies were performed between 1998 and 2019, the diagnostic performance of the CT could vary due to technological progress. Furthermore, the overlap of some patients in different study groups was possible. However, as already mentioned above, in this setting, higher-quality studies are highly difficult to be performed. Further studies are needed to be conducted to establish the role of the explorative laparoscopy and the diagnostic peritoneal lavage in the diagnosis of MBI, and that of novel techniques, such as angioembolization, in patients with arterial mesenteric bleeding.

In the light of previously reported findings, blunt trauma patients with CT signs of pneumoperitoneum and mesenteric active contrast bleeding should receive a surgical exploration as soon as possible, probably, in the authors' opinion, with an exploratory laparoscopy to minimize invasiveness in case of negative exploration or plan for subsequent therapeutic measures in case of injuries. Present data show that complications are reduced with surgical exploration within 12 h. On the other hand, traumatic patients with low-risk CT signs of suspected MBI can receive clinical observation in an appropriate setting with the availability of continuous monitoring, a surgeon, an anesthetist, and an operating room 24 h a day. These patients should receive a clinical and/or radiological re-evaluation within 12 h, and in case of clinical or radiological aggravation, should receive a surgical exploration. This selective approach in patients without high-risk CT signs could reduce the complication rate without increasing mortality

and LOS, compared to a systematic surgical intervention approach for all hemodynamically stable patients with suspected MBI. However, probably it would be better to maintain a low threshold for surgical exploration, possibly with an explorative laparoscopy, to minimize treatment delay.

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None

Footnotes

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