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Journal: The journal of trauma and acute care surgery

Year: 2015 Sep

Issue: 79

Volume: 3

Pages: 468-74

DOI: 10.1097/TA.0000000000000724

Management of severe blunt hepatic injury in the era of computed tomography and transarterial embolization:

A systematic review and critical appraisal of the literature

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The authors of this manuscript declare no conflicts of interest.

This study was presented at the 101st Annual Congress of the Swiss Society of Surgery in Berne in 2014.

Abstract

Background: During the last decade, the management of blunt hepatic injury (BHI) has considerably changed. Three options are available: non-operative management (NOM), transarterial embolization (TAE), and surgery. We aimed to evaluate in a systematic review the current practice and outcomes in the management of grade III to V BHI.

Method: MEDLINE database was searched using PubMed to identify English-language citations published after 2000 using the key words *blunt, hepatic injury, severe, and grade III to V* in different combinations. Liver injury was graded according to the AAST classification on computed tomography (CT). Primary outcome analyzed was success rate in intention to treat. Critical appraisal of the literature was performed using the validated NICE " Quality Assessment for Case series" system.

Results: Twelve articles were selected for critical appraisal (n=4946 patients). The median quality score of articles was 4/8 (range 2-6). Overall, the median ISS score at admission was 26 (range 0.6-75). A median of 66% (range 0-100%) of patients was managed with NOM with a success rate of 94% (range 86-100). TAE was used in only 3% of cases (range 0-72%) due to contrast extravasation on CT with a success rate of 93% (range 81-100%), however 9 to 30% of patients required a laparotomy. Thirty-one percent (range 17-100%) of patients were managed with surgery due to hemodynamic instability in most cases, with 12- 28% requiring secondary TAE to control recurrent hepatic bleeding. Mortality was 5% (range 0-8%) after NOM and 51% (range 30-68%) after surgery.

Conclusions: NOM of grade III to V blunt hepatic injury is the first treatment option to manage hemodynamic stable patients. TAE and surgery are considered in a highly selective group of patients with contrast extravasation on CT or shock at admission, respectively. Additional standardization of the reports is necessary to allow accurate comparisons of the various management strategies.

Level of evidence: Systematic review Level IV

Key words: blunt; hepatic; injury; management

The management of blunt hepatic injury (BHI) has changed since the last century, from observation in the early 1900s, to operative interventions, and to the current practice of non-operative management (NOM), selective surgery or transarterial embolization. The Eastern Association for the Surgery of Trauma (EAST) first addressed these issues in the Practice management Guidelines for Non-operative management of blunt injury to the liver and spleen published in 2003 and updated in 2012 (1, 2). The improved outcome in patients with severe liver injury (grade III to V according to the American Association for the Surgery of Trauma Organ Injury scale (3)) seen during the last decade has been attributed mainly to the increased use of NOM in hemodynamic stable patients, and early use of perihepatic packing in severely bleeding patients, including those with juxtahepatic veins injury (4). According to the most recent series, 60 to 100% of patients with blunt hepatic injury are currently managed non-operatively, even in the most severe form with venous injury (5-7).

While the outcome of patients with severe blunt hepatic injury is closely related to the concomitant injuries (6), the primary management of hepatic injury is still debated. Three options are available today: transarterial embolization (TAE), non-operative management (NOM), or surgery. Since the majority of studies assessing these 3 different management strategies included low-grade blunt hepatic injury (grade I and II) with a mixture of blunt and penetrating liver injuries, it is difficult to extrapolate those results to patients with only high-grade blunt liver injury. The aim of this study was to assess in a systematic review the current practice and outcome of the various treatments used in the management of grade III to V blunt hepatic injuries.

METHODS

Search strategy

A systematic literature review on the management of Grade III to V BHI was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (8). MEDLINE database in the Medical library of the University Hospital of Lausanne was searched using PubMed (www.pubmed.gov). We considered only articles written in English published after 2000 including randomized control trials (RCTs), and retrospective cases or cohort studies using the following Medical Subject Headings (MeSH) terms:

Blunt [All Fields] AND hepatic [All Fields] AND ("wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields] OR "injury"[All Fields])

The end of search strategy was December 2013 and last update was in June 2014.

Study inclusion and exclusion criteria

Only studies reporting data on the management of Grade III to V BHI confirmed by angiographic computed tomography (CT) and classified according to the AAST at admission were included (3). For patients who underwent surgery, we recorded the intraoperative grade or the grade assigned by the CT after surgery. Studies including penetrating trauma were excluded. In addition, series including exclusively juxtahepatic venous injury, case reports and series of less than 10 patients or pediatrics patients (less than 16 years) were also excluded.

Method for quality appraisal

Critical appraisal of the studies was considered by study type and data collected and potential source of bias were considered. The available published data on the management of grade III to V BHI included non-randomized case-comparison series and case series. Therefore, those series were assessed using the validated National Institute for Health and Care Excellence (NICE) " Quality Assessment for Case series" system, which assesses characteristics of methodology, outcomes and interpretation from a possible score of 8 (9)(**SDC 1**).

Data collection process and data analysis

The first author reviewed the full text reprints of all potentially appropriate articles. The following data, where available was extracted from each article: number of participants included in the study, demographics data (age, gender), injury severity score (ISS), and the presence of concomitant abdominal or extra-abdominal injuries. The grade of liver injury was defined according to the American Association for the Surgery of Trauma Organ Injury scale (AAST) (3). Where available, the hemodynamic status of patients at admission was also recorded. This included the presence of shock at admission (defined as hemodynamic instability despite fluid resuscitation or patients requiring catecholamine support to maintain adequate blood pressure) or hemodynamic instability responding to initial fluid resuscitation. In series that also included low-grade injury (i.e. grade I and II), only the available data on grade III to V liver trauma patients were collected.

Patients were divided into 3 groups according to the management of the hepatic injury at admission: (1) non-operative management (NOM), (2) transarterial embolization (TAE), and (3) surgery. The TAE group was subdivided into 2 groups. Primary TAE when performed at admission due to hepatic arterial contrast leak on CT scan. Secondary TAE after failure of NOM

or surgery to control bleeding. NOM patients did not undergo operative intervention or interventional radiology for hepatic injury within the first 24 hours. NOM was considered a failure in patients who needed delayed laparotomy or secondary TAE (more than 24 hours after admission) to control liver bleeding. In patients who underwent surgery, the type of hepatic procedure was recorded (where available), including the need for minor or major liver resection (i.e. < or > than 3 Couinaud's segment), liver packing, and hepatic veins hemostasis. In addition, abdominal compartment syndrome (ACS) requiring laparotomy/laparoscopy, and biliary complications requiring surgery or interventional radiology were also recorded in the three groups. As the studies were heterogeneous in terms of design and methodology, data pooling and meta-analysis was not performed.

Outcomes analysis

The primary outcome analyzed was the success rate of NOM, TAE and surgery to control hepatic bleeding. Secondary outcome analyzed included the in-hospital mortality rate related to the management strategy. Where available, this outcome was divided into liver- or non- liver-related death. In addition, the morbidity related to NOM, TAE, and surgery were assessed. In particular, biliary complications requiring surgery or interventional radiology were analyzed.

RESULTS

The primary search identified 29 articles published between January 2000 and June 2014 that were screened (**Figure 1**) (10, 11). A further 17 articles were excluded: 9 that amalgamated penetrating and blunt hepatic injury (4, 12-19), 6 where the demographics characteristics and outcome of grade III to V blunt hepatic injury was not comprehensively depicted (20-24), and 2 included exclusively patients with juxtahepatic venous injury (25, 26).

Overall characteristics of studies included

Twelve grades III to V blunt hepatic injury management articles including 4946 patients (735 male, 656 female, 3555 not specified) were analyzed (**Table 1**). Median age was 33 (range 16-95) years. There was 299 grade III, 555 grade IV, 181 grade V, and 3911 grades III to V not further specified blunt hepatic injury. The primary management of blunt hepatic injury at admission was performed by NOM, TAE, and laparotomy in a median of 66% (range 0-100%), 3% (range 0-72%), and 31% (range 0-100%) of patients, respectively (**Table 1**). The median ISS score at admission was 26 (range 0.6-75) and was missing in 4 studies (6, 27-29). Twenty two to 90% of patients were admitted in hemorrhagic shock. However, hemorrhagic shock at admission was clearly defined in only half of the series (6, 29-33).

Two studies included pure hepatic blunt injury with no concomitant intra- or extra-abdominal lesions (34, 35). The presence of concomitant abdominal or extra-abdominal injury was clearly described in 5 other studies (**SDC 2**) and ranged from 22 to 55% and 35 to 81%, respectively (30) (31, 33, 36, 37).

Non-operative management

A total of 8 studies included hemodynamic stable patients managed with NOM (5, 6, 27, 31) (34-37). As shown in **Table 2**, the median success rate of NOM was 92% (range 86-100%). Overall, 1 to 5% of NOM treated patients required TAE due to recurrent bleeding more than 24 hours after admission. The median rate of biliary complications secondary to the hepatic trauma was 4% (range 1-8%) with 2 to 5% of patients requiring a laparotomy or laparoscopy for abdominal lavage and drainage. The overall 90-day mortality rate after NOM was 5% (range 0-8%), and the liver-related death was 1% (range 0-4%).

Transarterial embolization

A total of 5 studies included patients with TAE due to contrast extravasation on the angiographic CT at admission (5) (27, 32, 34, 37). In this group, the hemodynamic profile of patients at the time of TAE was not clearly defined. Only 3 studies reported the rate of angiogram at admission, which ranged from 24 to 100% of patients (32, 34, 37). In the later series, 51 to 100% of patients underwent TAE due to contrast extravasation at angiography. As shown in **Table 3**, the success rate of primary TAE to control bleeding was 93% (range 81-100%). Biliary complications in this group were described in only one study (sample size n=14) and were of 60% (32). ACS after TAE was described in two studies and ranged from 4 to 10% (32, 34). Overall, 9 to 30% of patients treated with TAE required a laparotomy for ACS or biliary complications. Liver-related mortality after TAE ranged from 0 to 10%.

Operative management

A total of 7 studies included patients treated with surgery at admission (**Table 4**) (6, 30-33, 35, 37). Two studies included patients only treated with surgery (30, 33). Indication for surgery was hepatic injury in 4 studies (29, 32, 33, 35) and hepatic injury with concomitant abdominal injuries in 3 (6, 30) (31). In two series including only patients treated with surgery, shock at admission was reported in 81% and 90% of cases, respectively (30, 33). The type of hepatic procedure consisted mainly of damaged control surgery with peri-hepatic packing. Other intraoperative hepatic procedures recorded included hepatorraphy, segmentectomy, and right/left hemi-hepatectomy. According to two studies, the rate of juxtahepatic venous injury observed at laparotomy in grade III to V BHI ranges from 12 (5/41 patients) to 84% (37/44 patients) (30, 31). In the latter series, the mortality rate related to juxtahepatic venous injury was 12 (5/41 patients) and 57% (25/44 patients), respectively (Table 4). Twelve to 28% of patients required TAE after surgery to control either persistant bleeding despite perihepatic packing or recurrent hepatic bleeding secondary to hepatic artery pseudoaneurysm (32, 33). The overall complication rate after primary hepatic surgery was 58% (range 15-100), mainly related to bile leakage, liver failure, abscess formation, pulmonary complications, and severe head injuries. Biliary complications after surgical management were clearly described in 3 studies (30, 32, 33). In the first study, 1 patient over 14 survivors (7%) developed a bile leak and the mean number of resected segments was 2.2 (range 0 to 59), while in total 8 patients required a lobectomy or extended lobectomy and 9 a hepatorrhaphy (30). In the second study, 4 patients underwent a packing procedure and all of them developed a postoperative bile leak (32). Finally in the third study, 1 biliary leak occurred among 28 survivors (4%) (33). In the latter study, all patients underwent perihepatic packing procedure during surgery. Thirty three percent of the

laparotomies were associated with hepatorrhaphy and 19% with selective hepatic artery ligation. The overall mortality rate after surgery was 51% (range 30-68), and the liver-related mortality was 31% (range 14-50).

Quality appraisal of included studies

The studies included in the systematic review were associated with significant bias in term of data reporting, selection criteria and follow-up. Due to the heterogeneity of these studies, the critical appraisal of the literature precluded the use of meta-analytical assessment. According to the NICE quality assessment system, a median score of 4/8 (range 2-6) was attributed to the 12 publications included in this systematic review (**Figure 2**). All studies were case series. Of note, one author performed two studies, but one originates from two different centers (5) and the second included seven level-one trauma centers (27). All studies were conducted using data extracted from clinical notes, and only one was based on national administrative data (35). There were 5 multicenter studies (i.e. two or more centers) (5, 27, 31, 35, 37) and the data were collected prospectively in only one study (34).

Discussion

This systematic review highlights that NOM can be used in most of the hemodynamic stable patients with grade III to V blunt hepatic injury. Selective TAE is indicated in cases of contrast extravasation on the angiographic CT scan, while up to 30% of patients admitted will require emergency surgery because of either hemodynamic instability or suspicion of concomitant intra-abdominal injuries.

The non-operative management of blunt hepatic injury is currently the standard of care in hemodynamic stable patients in the majority of level-one trauma centers with reported success rate ranging from 82% to 100%, particularly in cases of low-grade liver injury (i.e. grade I and II) (23, 38-40). However, the data in high-grade liver injury (i.e. grade III to V according to the AAST) are scarce. Most series amalgamate blunt and penetrating trauma with a mixture of grade I to V injuries, leaving 12 retrospective studies during the last decade that analyzed pure high-grade blunt hepatic injury with relative comprehensive results on outcome. The analysis of these studies showed that high grade liver injury does not preclude the use of NOM providing the patient is hemodynamic stable; the overall mortality risk in these patients ranged from 0 to 8%, with a median liver related death of 1%. Interestingly, only 1 to 5% of NOM patients required transarterial embolization due to secondary liver bleeding after admission. Those results are obtained by the careful assessment of the patients at admission, in particular the use of angiographic CT scan in all hemodynamic stable patients. Indeed, it is now well accepted that the integration of CT in early trauma-room management with the use of NOM in hemodynamic stable patients results in improved survival after liver trauma (18). In addition, contrast extravasation on angiographic CT scan, a sign of active bleeding, has been reported as a risk

factor for NOM failure (41). However, contrast leakage after blunt hepatic injury is not always a definite sign of NOM failure, since others have shown that early transarterial embolization is an effective adjunct of NOM, even in cases with contrast leakage in the peritoneum (20). Finally, NOM is associated with a low rate of biliary complications (4%) with only 2 to 5% of patients requiring a laparotomy or laparoscopy for abdominal lavage and drainage. Therefore, it seems that NOM should be the first choice to treat hemodynamic stable patients admitted with grade III to V blunt hepatic injury. However, a close follow-up of these patients is mandatory due to a risk as high as 5% of late bleeding after NOM (i.e. more than 24 hours after admission) that can be managed successfully with TAE.

Overall, a median of 3% of patients underwent TAE at admission due to contrast extravasations in the liver or in the peritoneum at angiographic CT scan, with a success rate ranging from 81 to 100% (5, 27, 32, 34, 37). Of note, only 3 studies reported the rate of angiogram at admission, which ranged from 24 to 100% of patients (32, 34, 37). In the latter series, 51 to 100% of patients underwent TAE due to contrast extravasations at angiogram. Although CT scan next to trauma room may be of obvious benefit, it was not possible to find any convincing data to support this statement. One study describes biliary complication up to 60% in the group of TAE (32). Overall, 9 to 30% of patients in this group required laparotomy for abdominal compartment syndrome, biliary complications, or concomitant abdominal injuries.

The analysis of the studies dealing with operative management should be considered with caution since patients included had higher ISS score with hemodynamic shock in up to 90% of cases (30, 33). Those studies advocate early laparotomy to control bleeding and possible concomitant intraabdominal injuries. Most complications after operative management were related to bile leakage, abscess, and pulmonary infection (6, 30). In addition, 12 to 28% of

patients required TAE after surgery to control either persistant bleeding immediately after perihepatic packing or recurrent bleeding up to 3 weeks after surgery (due to hepatic artery pseudoaneurysm) (32, 33). Of note, there is insufficient data to establish a clear association between surgical strategy and postoperative bile leak. The operative management of severe blunt hepatic injury is then indicated in a highly selected group of patients who are admitted in the trauma-room with hemodynamic instability and possibly associated other abdominal injuries. Of note, mortality rate increased considerably in patients with concomitant cerebral injury (31). Juxtahepatic venous injury is also a strong factor to liver-related death after blunt hepatic trauma. According to series including grade III to V hepatic trauma, juxtahepatic venous injury occurs in up to 12% of patients. In one single series including grade V trauma, it occurs in 84% of patients (30). This life threatening complication has to be recognized promptly as even with early operative management, mortality ranges from 50 to 100% (25, 31). Interestingly, the right hepatic vein is most commonly injured in these patients (25). This high mortality could be explained by the location of the right hepatic vein in the thickest and least mobile portion of the liver, making its access more challenging than on the left side, especially in shock situation. The Western Trauma Association has recently proposed an algorithm for the surgical management of blunt hepatic trauma (42). This algorithm includes different strategies for minor and major bleeding, including packing with or without Pringle maneuver. Vascular isolation with shunting procedure or selective hepatic artery ligation may be used in severe cases with juxtahepatic venous injury or uncontrolled arterial bleeding, respectively.

The present study has obviously several limitations that need to be addressed. The study was based on data collection from several heterogeneous retrospective series, precluding the use of metaanalytic material. However, randomized control trials in the setting of severe trauma

patients can hardly be performed for ethical reasons. Since the first guidelines published in 2003 by the Eastern Association for the Surgery of Trauma (EAST) in the practice management guidelines for non-operative management of blunt hepatic injury (1), a large volume of literature on this topic has been published. This study confirms that NOM can be used safely as standard treatment even in high-grade liver trauma, provided hemodynamic stability of patients at admission and the availability of angiogram with TAE at any time. Surgery is limited to patients with hemodynamic instability or concomitant abdominal injuries. However, the critical appraisal of the literature published the last decade demonstrates the low quality in reporting outcomes after management of grade III to V blunt hepatic injury. According to the NICE "Quality Assessment for Case series" system, inclusion and exclusion criteria are poorly reported in the different series included in this systematic review. In addition, the definition of shock at admission is multiple and lacks standardization. Future studies should aim to mention the rate of angiogram performed at admission that did not end with TAE. A clear description of venous versus arterial hepatic injuries should be addressed since the management of those vascular injuries is different. Finally, more studies with homogeneity in patients' characteristics at admission are needed in order to assess with more accuracy the different treatment options.

In conclusion, the non-operative management of grade III to V blunt hepatic injury should be considered as the first treatment to manage hemodynamic stable patients. TAE is indicated in patients with contrast extravasations on the angiographic CT at admission, or in patients who failed NOM. Surgery has to be considered in a highly selected group of patients with shock at admission and/or suspicion of other abdominal organ injuries, because there is no other option available. Additional standardization of the reports on this topic is recommended to allow accurate comparisons of the various management strategies in the future. There is then an urgent need for an international consensus on reporting results after severe blunt hepatic trauma that should be endorsed by the AAST and ESTES.

Authors' contribution

E.M. designed the study, performed the systematic review, analyzed the data, and wrote the manuscript.

A.D. reviewed and evaluated the data, and edited the manuscript.

N.D. reviewed the data and edited the manuscript.

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Figures legend

Figure 1: PRISMA diagram showing selection of articles for the review.

Figure 2: Items addressed according to the National Institute for Health and Care Excellence (NICE) " Quality Assessment for Case series" system, which assesses characteristics of methodology, outcomes and interpretation from a possible score of 8 (one point is attributed for each question addressed).

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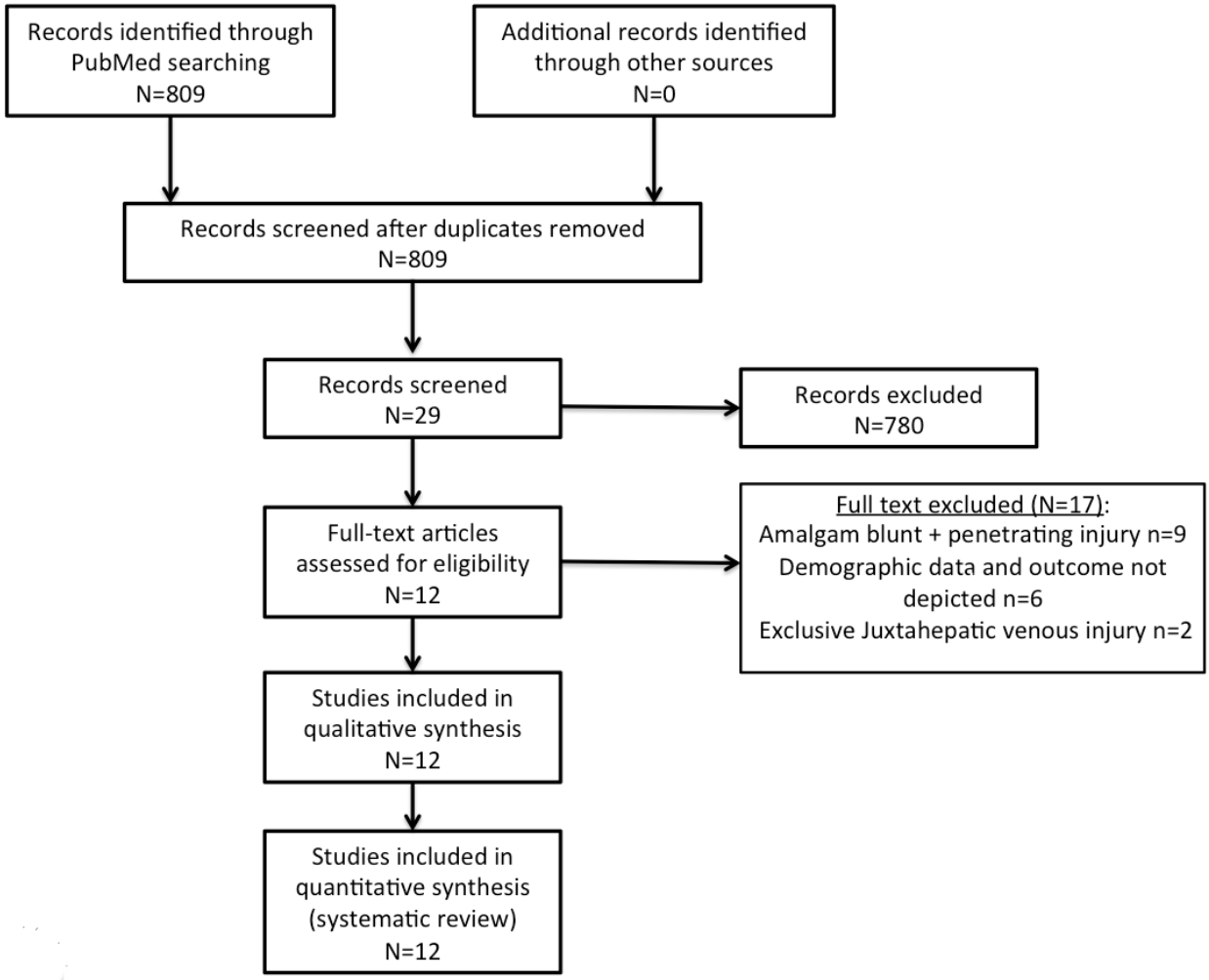

Figure 2: Items addressed according to the National Institute for Health and Care Excellence (NICE) " Quality Assessment for Case series" system, which assesses characteristics of methodology, outcomes and interpretation from a possible score of 8 (one point is attributed for each question addressed).

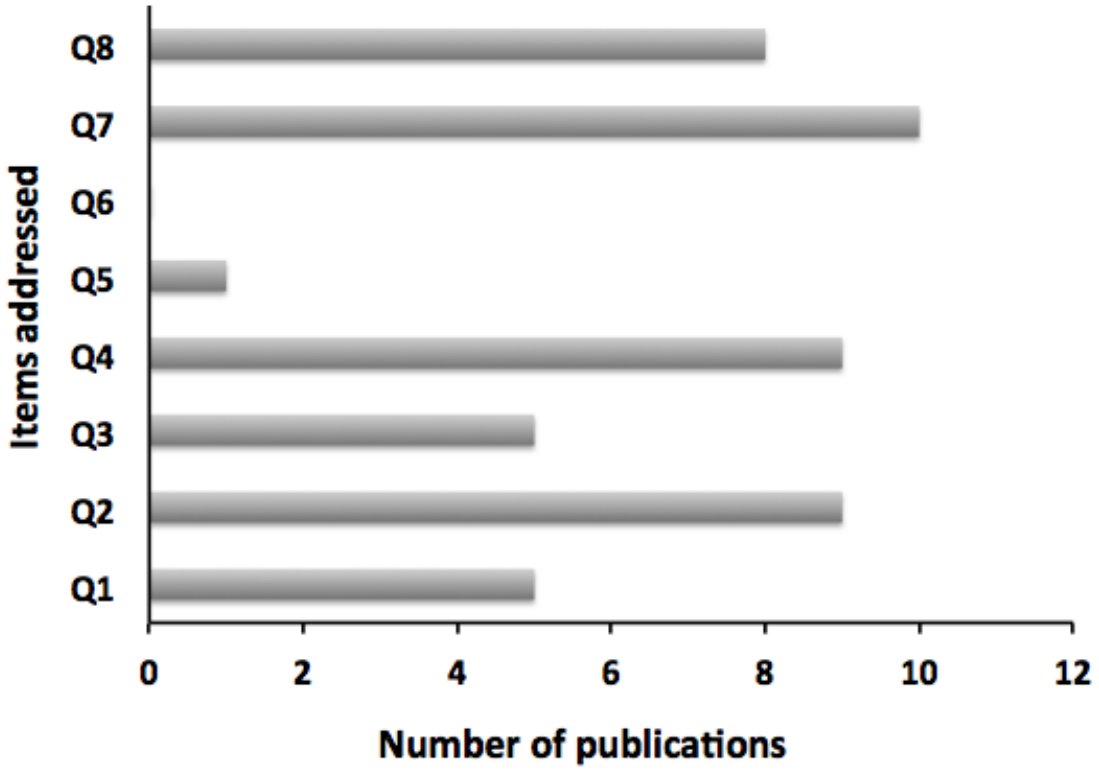

Table 1: Characteristics of the studies

	Year of publication		N	Grade III (N)	Grade IV (N)	Grade V (N)	Primary NOM (%)	Primary laparotomy (%)	Primary TAE (%)	Shock at admission (%)	ISS score (mean)	Only liver injury (%)
Chen et al. (30)	2000	Retrospective	44	0	0	44	0	100	0	81	38	11
Hagiwara et al. (34)	2002	Retrospective	51	37	13	1	35	14	51	23	25	100
Kozar et al. (5)	2005	Retrospective (two centers)	230	130	92	8	95	0	5		24	
Kozar et al. (27)	2006	Retrospective (multicenter)	453				93	0	7			
Monnin et al. (32)	2008	Retrospective	14	2	9	3	0	28	72		12	
Schnüriger et al. (6)	2009	Retrospective	81				78	22	0	22		
Leppäniemi et al. (31)	2011	Retrospective	144	58	66	20	65	35		39	31	45
Zago et al. (36)	2012	Retrospective	18	0	18	0	100	0	0		24	78
Letoublon et al. (29)	2011	Retrospective	83	52	20	11	49	51				
Van der Wilden et al. (37)	2012	Retrospective (multicenter)	393	0	313	80	67	17	16	33	32	56
Polanco et al. (15)	2013	Retrospective (national)	3377				75	22	3		29	100
Lin et al. (33)	2013	Retrospective	58	20	24	14	0	100	0	90	26	

Table 2: Outcome after non-operative management (NOM)

	Patients (N)	Primary NOM (%)	NOM success rate (%)	TAE after NOM (%)	Biliary complication after NOM (%)	Laparotomy/scopy for bile leak (%)	Overall 90-day mortality NOM (%)	Liver related death NOM (%)
Hagiwara et al. (34)	51	35	86		4.5	0	4	4
Kozar et al. (5)	230	100	94	5	3.5	3	4.3	
Kozar et al. (27)	453	100	92	3	4	2	5	0.4
Schnüriger et al. (6)	81	63	100	0	8	5	3	3
Leppäniemi et al. (31)	144	65	91	1	1	3	6	2
Zago et al. (36)	18	100	94	0			0	0
Van der Wilden et al. (37)	393	67	91		6		6	0
Polanco et al. (15)	3377	78	93	3			8	

Table 3: Outcome of patient after primary transarterial embolization (TAE)

	Patients (N)	Primary TAE (%)	Primary TAE success rate (%)	Biliary complications after TAE (%)	Abdominal compartment syndrome after TAE (%)	Laparotomy after TAE (%)	Laparotomy/scopy for bile leak (%)
Hagiwara et al. (34)	51	51	81		4	14	
Kozar et al. (5)	230	5				25	
Kozar et al. (27)	453	4	91			9	
Monnin et al. (32)	14	72	100	60	10	30	50
Van der Wilden et al. (37)	393	16	93				

Table 4: Outcome of patient after operative management

	Patients (N)	Primary laparotomy for hepatic injury (%)	Juxtahepatic venous injury N(%)	TAE after surgery (%)	Overall complications after surgery (%)	Overall 90-day mortality (%)	Liver related death (%)	Death related to Juxtahepatic venous injury (%)
Chen et al. (30)	44	100	37(84)	0	72	68	50	57
Monnin et al. (32)	14	28		28	100			
Schnüriger et al. (6)	81	18			39	39	39	
Leppäniemi et al. (31)	144	30	5(12)		58	30	14	12
Van der Wilden et al. (37)	393	27				53		
Polanco et al. (15)	3377	22				50		
Lin et al. (33)	58	100		12	15	52		