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ORIGINAL ARTICLE

Improved outcomes in the non-operative management of liver injuries

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Abstract

Objectives: Non-operative management has become the treatment of choice in the majority of liver injuries. The aim of this study was to assess the changes in primary treatment and outcomes in a single Dutch Level 1 trauma centre with wide experience in angio-embolisation (AE).

Methods: The prospective trauma registry was retrospectively analysed for 7-year periods before (Period 1) and after (Period 2) the introduction of AE. The primary outcome was the failure rate of primary treatment defined as liver injury-related death or re-bleeding requiring radiologic or operative (re)interventions. Secondary outcomes were liver injury-related intra-abdominal complications.

Results: Despite an increase in high-grade liver injuries, the incidence of primary non-operative management more than doubled over the two periods, from 33% (20 of 61 cases) in Period 1 to 72% (84 of 116 cases) in Period 2 ($P < 0.001$). The failure rate of primary treatment in Period 1 was 18% (11/61), compared with 11% (13/116) in Period 2 ($P = 0.21$). Complication rates were 23% (14/61) and 16% (18/116) in Periods 1 and 2, respectively ($P = 0.22$). Liver-related mortality rates were 10% (6/61) and 3% (4/116) in Periods 1 and 2, respectively ($P = 0.095$). The increase in the frequency of non-operative management was even higher in high-grade injuries, in which outcomes were improved. In high-grade injuries in Periods 1 and 2, failure rates decreased from 45% (9/20) to 20% (11/55) ($P = 0.041$), liver-related mortality decreased from 30% (6/20) to 7% (4/55) ($P = 0.019$) and complication rates fell from 60% (12/20) to 27% (15/55) ($P = 0.014$). Liver infarction or necrosis and abscess formation seemed to occur more frequently with AE.

Conclusions: Overall, liver-related mortality, treatment failure and complication rates remained constant despite an increase in non-operative management. However, in high-grade injuries outcomes improved after the introduction of AE.

Keywords

trauma, liver injury, non-operative management, angio-embolisation, outcomes

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Introduction

The liver is the organ most frequently injured in abdominal trauma. Over the last two decades, the management of traumatic liver injuries has changed considerably. Traditionally, surgery was the treatment of choice for most liver injuries. However, with the increasingly fast availability of computed tomography (CT) and modern, minimally invasive, percutaneous interventional techniques such as angio-embolisation (AE), non-operative management has evolved as the treatment of choice in both minor and major liver injuries.[1–3] With non-operative management strategies, approximately 70% of all liver injuries can be treated without increased risk for mortality.[4] Many studies have described decreasing mortality rates using this strategy.[2–7] However, various other

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studies have meanwhile reported an increase in the incidence of major complications, such as hepatic necrosis, abscesses or bile leakage.[8–10]

In 1999, AE was introduced in the Academic Medical Centre (AMC), a designated Level 1 trauma centre in the Netherlands. Since 2002, angiography with or without embolisation has become an accepted method for the evaluation and treatment of liver injuries. The aim of this study was to compare the failure rates of primary treatment before and after the introduction of angiography in patients with liver injury in the AMC. The effects on clinical outcomes and complication rates were also assessed.

Materials and methods

Data collection

All patients with liver injuries admitted to the AMC between January 1995 and December 2008 were identified for review from the hospital's prospective trauma registry, the in-hospital information system or financial administrative registration. The prospective interventional radiology registry was checked to verify that no patients were missed. Patients who were initially treated at other hospitals were excluded from this analysis. Patients who were primarily evaluated elsewhere (without intervention) and referred to the AMC for initial treatment were, however, included.

A chart review was performed to collect demographic data, including age, gender, trauma mechanism and injury severity score (ISS). Data collection was performed according to a preplanned, standardised format. Primary treatment was assessed as non-operative (observation and/or AE) or surgical exploration. Potential liver injury-related complications with subsequent interventions were also recorded. One radiologist (KPvL), with trauma and vascular interventional experience, re-evaluated all available admission CT scans and classified liver injury grades according to American Association for the Surgery of Trauma (AAST) classifications.[11] Grade 1 and 2 injuries were classified as low grade and Grade 3–5 injuries were designated as moderate to high grade. Data on the presence of contrast blushes, haemoperitoneum and the extension of haemoperitoneum were also registered. If no CT scan was available, injuries were graded according to intraoperative findings or ultrasonographic outcome.

Study periods

Data and outcomes in two periods were compared. These periods referred to those before (Period 1, 1995–2001) and after (Period 2, 2002–2008) the introduction of AE in the treatment of liver injuries in the AMC, respectively. A total of 186 patients were eligible for inclusion during the study period. Nine patients were excluded because initial evaluation and stabilising interventions had been performed in other hospitals.

Treatment and imaging protocols

In Period 1, the protocol dictated surgical exploration in patients with a suspicion of moderate to severe liver injury independent of haemodynamic status. In Period 2, according to the changed protocol, haemodynamically unstable patients who did not respond to fluid resuscitation (non-responders) were treated primarily operatively. Operative treatment began with four-quadrant packing before the structural exploration of the abdomen. If necessary, the Pringle manoeuvre was performed to stop extensive haemorrhage and gain an overview. Grade 1–3 injuries were treated with local tamponade, electro-coagulation, local haemostatic materials (i.e. TachoSil®) or several sutures (monofilament). Operative treatment of Grade 4 and 5 injuries was dependent on the stability of the local haemorrhage control measures mentioned above, but usually these injuries were packed with several gauzes for 24–48 h. Resections were preferably not performed in the acute phase.

In haemodynamically stable patients or transient responders, management was primarily non-operative. Non-operative management consisted of observation in the intensive care unit (ICU) with regular (6-hourly) blood tests on the first day. The length of ICU observation depended on the clinical and laboratory findings and varied from 24 h to 72 h. Depending on CT findings (liver injury combined with contrast blush), an angiography was subsequently performed.

In Period 1, a dual-slice, helical CT scanner was used for scanning trauma patients. Slices measuring 5 mm (in increments of 5 mm) were acquired in the arterial (using bolus tracking) and portal (70 s time delay) phases to detect liver laceration and contrast extravasation.

In Period 2, 16-slice and 64-slice CT scanners were available. The scanning protocol was adapted to allow the acquisition of 3-mm slices (in increments of 2 mm) in the arterial and portal phases.

The angiography procedure was performed under local anaesthesia. Subsequently, the common femoral artery was punctured prior to the introduction of a 5-Fr sheath. A 5-Fr cobra catheter or coeliac catheter (Cordis Corp., Johnson & Johnson Co., Miami, FL, USA) was used for selective catheterisation of the coeliac trunk. The lacerated branches of the hepatic artery were identified with digital subtraction angiography. Superselective catheterisation and embolisation were performed using a 3-Fr microcatheter (Renegade™; Boston Scientific Corp., Natick, MA, USA) and 0.018-inch microcoils (Boston Scientific Corp.). Occasionally, a combination of coils and 300–500-μ polyvinyl alcohol particles (Cook Medical, Inc., Bloomington, IN, USA) was used. Contrast blush was defined as contrast extravasation or pseudoaneurysms.

Study endpoints

The primary outcome was the failure rate of primary treatment. Failure was defined as death caused by uncontrollable liver haemorrhage, or re-bleeding after primary intervention requiring radiological or operative (re-)interventions. Preplanned second-look operations to inspect or remove the packing were not considered to represent failure. Secondary operations performed within 24 h because of increased haemodynamic instability were considered to represent failure. Complications were defined as

Table 1 Demographic data, severity of trauma and initial investigations and treatment

	Period 1 (1995–2001)	Period 2 (2002–2008)	*P*-value
Patients, *n*	61	116	
Age, years, median (range)	29 (19–36)	29 (20–41)	0.617
Male, *n* (%)	44 (72%)	78 (67%)	0.609
Blunt trauma, *n* (%)	43 (71%)	91 (78%)	0.241
ISS, median (range)	20 (9–34)	22 (11–34)	0.866
Multi-trauma, *n* (%)	38 (62%)	79 (68%)	0.438
Initial CT scan, *n* (%)	21 (36%)	89 (77%)	<0.001
Injury grade			
Low (Grades 1, 2), *n* (%)	41 (67%)	61 (53%)	0.061
High (Grades 3–5), *n* (%)	20 (33%)	55 (47%)	
Initial treatment			
Observation, *n* (%)	20 (33%)	61 (52%)	<0.001
Operative, *n* (%)	41 (67%)	32 (28%)	
Angio-embolisation, *n* (%)	0 (0%)	23 (20%)	

ISS, injury severity score; CT, computed tomography

liver injury-related or intra-abdominal complications, such as abscess formation, bile leakage, jaundice, liver infarction and liver necrosis, cholecystitis and fistula formation. Wound infections or general complications such as pneumonia were not assessed. Secondary clinical outcome parameters were length of ICU and total hospital stay, transfusion requirements in the first 48 h and overall mortality rate. Mortality was classified according to whether it was caused by liver-related complications or other causes, whether traumatic or non-traumatic.

Statistics

All continuous variables are presented as medians with interquartile ranges (p25–p75) and were compared using the Mann–Whitney *U*-test for two variables or, in contexts with more than two variables, the Kruskal–Wallis test. Categorical variables were calculated as percentages and compared using chi-squared analyses and Fisher's exact test when applicable. Statistical significance was declared at the 0.05 level. All data were collated and analysed using SPSS for Windows, Version 15.0.1 (SPSS, Inc., Chicago, IL, USA).

Table 2 Clinical outcomes

	Period 1 (*n* = 61)	Period 2 (*n* = 116)	*P*-value
Length of hospital stay, days, median (range)	11 (7–20)	10 (4–26)	0.831
ICU stay, days, median (range)	1 (0–6)	2 (0–5)	0.473
PRBC units, median (range)	4 (0–14)	2 (0–8)	0.183
FFP units, median (range)	2 (0–12)	0 (0–4)	0.029
Failure rate, *n* (%)	11 (18%)	13 (11%)	0.207
Overall mortality, *n* (%)	16 (26%)	17 (15%)	0.060
Liver-related mortality, *n* (%)	6 (10%)	4 (3%)	0.095
Uncontrollable haemorrhage, *n* (%)	6 (10%)	3 (3%)	
Liver failure, *n* (%)	0 (0%)	1 (1%)	
Complication, *n* (%)	14 (23%)	18 (16%)	0.222
Two or more complications, *n* (%)	4 (7%)	9 (8%)	

ICU, intensive care unit; FFP, fresh frozen plasma; PRBC, packed red blood cells

Results

Of the 177 patients included in the study, 122 (69%) were male. The median age of study patients was 29 years (range: 19–38 years). A total of 43 (24%) patients had sustained penetrating trauma. Median ISS was 22 (range: 10–34) and median liver AAST Grade was 2 (range: 2–3). The demographic data, severity of trauma and initial investigations and treatment for Periods 1 and 2 are shown in Table 1.

Table 2 presents clinical outcomes for both periods. In Period 2, failure and complication rates and liver-related mortality did not significantly differ from those in Period 1. The only patient in Period 2 to die of liver failure was not eligible for liver transplantation because of abdominal sepsis.

Table 3 shows the liver injury-related, intra-abdominal complications occurring during the two periods. Abscess formation seemed to occur more frequently after AE. In Period 1 more bile leakage was found after operative interventions. Four operative interventions in four patients and nine radiographic interventions in five patients were necessary to resolve complications in Period 1. In Period 2, complications were treated with eight operations in six patients and 22 percutaneous interventions in 14 patients. Two

Table 3 Liver injury-related or intra-abdominal complications

	Period 1		Period 2		
	Observation (*n* = 20)	Operation (*n* = 41)	Observation (*n* = 61)	Operation (*n* = 32)	AE (*n* = 23)
Bile leakage, *n*	–	6	1	–	2
Jaundice/liver failure, *n*	1	–	1	1	–
Necrosis/infarction, *n*	–	1	–	1	3
Abscess, *n*	1	1	1	1	5
Cholecystitis, *n*	–	–	–	–	1
ACS	–	–	–	1	–
Fistula, *n*	–	1	–	–	–
(Re-)bleeding, *n*	2	3	3	8	2
Total, *n*	4	12	6	12	13

AE, angio-embolisation; ACS, abdominal compartment syndrome fistula: biliary pleural fistula

Table 4 Outcomes per period for low- and high-grade injuries

	Low-grade injuries (Grades 1, 2)			High-grade injuries (Grades 3–5)		
	Period 1 (*n* = 41)	Period 2 (*n* = 61)	*P*-value	Period 1 (*n* = 20)	Period 2 (*n* = 55)	*P*-value
AAST grade	1 (1–2)	2 (2–2)	0.003	3 (3–4)	3 (3–4)	0.363
Observation	16/41	40/61	0.008	4/20	21/55	0.173
Operation	25/41	14/61	<0.001	16/20	18/55	<0.001
Angio-embolisation	0/41	7/61	0.040	0/20	16/55	0.040
Liver-related mortality	0/41	0/61	NA	6/20	4/55	0.019
Complication	2/41	3/61	1.000	12/20	15/55	0.014
Failure rate	2/41	2/61	1.000	9/20	11/55	0.041

AAST, American Association for the Surgery of Trauma; NA, not applicable

patients required a complication-related operation after non-operative management in Period 2. Just one patient required a cholecystectomy as a result of liver and gallbladder necrosis after embolisation. Two other patients managed non-operatively in Period 2 experienced temporary liver infarction which resolved completely without further intervention. Six planned re-operations were performed for depacking in Period 1, as were eight in Period 2.

Table 4 shows the injuries divided into low and high AAST grades by period and compared for primary treatment and outcomes. In Period 2, more high-grade injuries were treated non-operatively with equivalent outcomes with respect to liver-related mortality rate, failure and complication rates. An increase in non-operative treatment was also seen in low-grade injuries. Although the complication rates were comparable, the failure rate seemed to decrease, but without reaching statistical significance.

Table 5 shows specific CT findings of all patients evaluated with CT in both periods, classified according to primary treatment and outcomes. Although patients primarily treated with AE had sustained more severe liver injuries with more contrast blushes and haemoperitoneum detected on CT, equal failure rates were detected. However, the patient treated non-operatively received fewer transfusions within the first 24 h compared with the primarily operated group. Thirteen patients were observed despite a visible contrast blush on CT. Two of these patients (15%) suffered re-bleeding which was eventually treated successfully with AE.

Table 6 presents the outcomes of primary treatment by injury grade for both periods. In one of the nine patients with a Grade 3 injury who underwent AE, primary treatment failed, as it did in one of the six patients with a Grade 4 injury who underwent AE in Period 2. The one patient with a Grade 5 injury who was treated non-operatively underwent AE. This patient's course was complicated by temporary hepatic ischaemia and abscess formation, which finally resolved completely with non-operative management.

Discussion

In concordance with recent literature, the present study shows an important shift in the treatment of choice during the two periods

Table 5 Computed tomography (CT) findings, primary treatment and outcomes in the population evaluated with CT

	Population evaluated with CT			
	Observation (n = 59)	Angio-embolisation (n = 22)	Operation (n = 30)	P-value
Injury severity score	17 (9–27)	27 (22–34)	34 (13–37)	0.001
AAST grade	2 (2–3)	3 (2–4)	2 (2–3)	0.005
Blush present	13/59	15/22	7/30	<0.001
Haemoperitoneum, present	29/59	17/22	20/30	0.058
Haemoperitoneum ≥3 quadrants	12/59	11/22	18/30	0.001
PRBC	0 (0–2)	5 (3–7)	10 (4–29)	<0.001
FFP	0 (0–2)	3 (0–4)	8 (1–29)	<0.001
Failure rate	4/59	2/22	6/30	0.158

AAST, American Association for the Surgery of Trauma; FFP, fresh frozen plasma; PRBC, packed red blood cells

Table 6 Failure rate classified according to injury grade

Grade	Period 1				Period 2			
	Non-op, n	Failure, n	Op, n	Failure, n	Non-op, n	Failure, n	Op, n	Failure, n
1	9	0	12	1	11	0	3	1
2	7	1	13	0	36	0	11	1
3	2	0	11	6	28	4	13	3
4	2	1	3	0	8	1	4	3
5	0	NA	2	2	1	0	1	0
Total	20	2	41	9	84	5	32	8

Non-op, non-operative primary management; op, operative primary management; NA, not applicable

studied. In the first period (1995–2001), primary surgical exploration was performed in more than two-thirds of patients. After the introduction of AE and endovascular intervention in the second period (2002–2008), primary operative management was reduced to one-third of patients, whereas non-operative management was successful in the majority of patients. Despite this increase in the non-operative management rate and notwithstanding an increase in the severity of injuries, clinical outcomes did not differ significantly between the two periods. In addition, some improvements in outcomes were found with respect to the failure rate of non-operative management, and liver injury-related mortality and complication rates in high-grade injuries after the introduction of AE. This shift towards non-operative management, especially in higher-grade injuries with better outcomes, reflects the outcomes described in the literature in recent years, during which the majority of liver injuries have been managed successfully with non-operative methods.[2–7] One explanation for the increased success of non-operative management is the continuous evolution and improvement in imaging and endovascular techniques. Modern imaging techniques such as thin-slice, multi-detection CT allow for a detailed overview of the extent of the liver injury and reveal the presence of active haemorrhage. The provision of this information allows a more specific treatment to be devised. Secondly, the introduction of AE allows patients with specific CT findings to potentially be treated in a minimally invasive manner. Given the availability of AE, trauma surgeons are more likely to initiate non-operative treatment, even in higher-grade injuries, because, in the event of failure, intervention in the form of AE is possible and, in the event of AE failure, surgical intervention is possible.

The recent literature reveals that the increased use of AE and decreased mortality rates result in increased frequencies of severe complications, such as liver necrosis, bile leakage and intra-abdominal abscesses.[6,9,12] The present study showed that abscess formation and liver infarction or necrosis were more common in the period after the introduction of AE. However, there was no increase in radiographically confirmed bile leakage. In general in Period 2, few complications emerged after non-operative management. After angiography, two surgical interventions were required in two patients and 16 radiological (re-)interventions were needed in eight patients. The observed re-operation rate of 2% was acceptable, compared with the complication-related, re-operation rates of 21–34% described in the literature.[8,13]

This study has several limitations, most of which relate to the retrospective analysis of data. Firstly, the two periods compared here differ in that not only was AE introduced, but other improvements in trauma care also occurred. After Period 1, the AMC became a dedicated Level 1 trauma centre to which injured patients requiring specialised trauma care were referred. Simultaneously, advances in ICU treatment, transfusion and fluid resuscitation protocols and radiological and surgical techniques during Period 2 may also have contributed to better outcomes. The continuous evolution and improvement of imaging techniques may also cause a bias in the results. Better imaging quality may influence and increase injury gradations because such imaging provides more specific details of the injury. However, we tried to eliminate this bias by re-evaluating all available CT scans. Secondly, injury characteristics, such as blushes and/or large haemoperitoneum, which are suggestive of more severe injury and can be diagnosed with all types of CT scanner, were diagnosed more frequently in the second period.

Secondly, the study design prevented any assessment of the considerations that had led to the decision for non-operative management. Based on these results, neither the grade of liver injury nor other specific CT findings seemed to predict the primary choice of treatment. In the population initially observed, 22% of patients had a contrast blush on CT and 21% had signs of severe haemoperitoneum. By contrast, patients who were treated with AE had more CT findings of severe injury than patients who were primarily operated. In addition, 23% of patients with low-grade injuries received operative treatment in Period 2. Although several studies have described the use of flowcharts based on CT findings to facilitate decision making, the present data on CT findings and primary treatment showed that other clinical signs or injuries must have played an important role in treatment planning. A final limitation of the present study is that the numbers of patients included were relatively low. Although we found an overall increase in non-operative management, we also found a slight but statistically non-significant improvement in clinical outcomes in the period after the introduction of AE. The relatively low number of inclusions provides an explanation for this failure to achieve statistical significance.

Conclusions

Non-operative management of liver injury is currently undertaken more frequently than in the past, with low failure rates, despite an increase in the severity of injuries. After the introduction of AE in the non-operative management protocols in the AMC, liver-related mortality, treatment failure and complication rates remained constant despite the increase in non-operative management. In high-grade injuries, outcomes with respect to liver injury-related mortality, complication rate and failure of primary treatment improved after the introduction of AE. Abscess formation and liver infarction were more common after AE than after laparotomy.

Conflicts of interest

None declared.

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