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Evolution of non-operative management of liver trauma

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ABSTRACT

The management of complex liver injury has changed during the last 30 years. Operative management has evolved into a non-operative management (NOM) approach, with surgery reserved for those who present in extremis or become hemodynamically unstable despite resuscitation. This NOM approach has been associated with improved survival rates in severe liver injury and has been the mainstay of treatment for the last 20 years. Patients that fail NOM and require emergency surgery are associated with increased morbidity and mortality. Better patient selection may have an impact not only on the rate of failure of NOM, but the mortality rate associated with it. The aim of this article is to review the evidence that helped shape the evolution of liver injury management during the last 30 years.

Until the start of the 20th century the management of severe abdominal injury was expectant and this approach was associated with extremely high mortality.[1] Pringle's[2] seminal monograph published in 1908 describes the serious consequences resulting from trauma to the liver, noting that "Rupture of the liver is fortunately an accident not often met with, but one which, when it is seen, may be associated with a condition as serious as anyone can meet within surgical practice." Moore *et al*[3] described a 6-year review of operative results (1972–1978) that showed 9% of their patients with severe liver injuries had been managed with formal hepatic lobectomy, a technique that carried a mortality rate of 70%. High mortality rates for operative intervention stimulated Moore *et al*'s[3] interest in management options other than formal resection and described that throughout the study period there had been a transition away from operative to conservative management. Other authors were also reporting similar devastating rates of operative mortality in the late 1970s and early 1980s.[4–6]

The successful non-operative management (NOM) of liver injuries had already been suggested in the animal experiments performed by Tellman in 1879[7] and the clinical experiences of J William Hinton[8], who in 1929 said: "In ruptures of the liver conservative treatment is more desirable than an exploratory laparotomy, as surgery is of no avail in ruptures of the liver, for usually the haemorrhage has stopped and is started again by the surgical intervention." The first clinical application of NOM in hepatic trauma was described in children in 1986. Oldham *et al*[9] studied 188 consecutive pediatric patients with serious injuries. Liver injuries were identified on CT in 53 of these, with 92% (49 patients) being treated successfully with NOM. The study demonstrated that the vast majority of pediatric blunt liver trauma patients could undergo NOM safely.[9] During the next few years, several authors demonstrated the validity of a NOM approach in pediatric patients.[10–13]

The concept of NOM in adults remained controversial in the 1980s, with concerns being raised regarding the unknown natural history of non-surgically treated hepatic trauma, inaccuracy of CT interpretation, and the inherent delays in examination.[14] One of the first studies to use CT in adult patients for NOM of blunt liver injuries was published by Meyer *et al* in 1985.[15] They studied 24 patients during a 2.5-year period and used CT to assess the degree of injury and whether NOM was suitable. Of the 24 patients, 14 were discharged 4 to 8 days after their injury, with 4 patients discharged within 96 hours. None of the 24 patients required surgery or suffered any complications. The authors concluded that patients with minor injuries could be managed safely with NOM, but that "the treatment of most liver injuries is surgical, and that NOM is not an acceptable alternative." The authors recommended several criteria when considering NOM of liver trauma using CT assessment, including hemodynamic stability, good quality scans with accurate interpretation, senior surgical decision making, appropriate critical care facilities, and the personnel to perform emergency surgery if required.[15]

In agreement with this view, Farnell *et al*[14] described the management of 66 consecutive blunt hepatic trauma patients at the Mayo Clinic between 1981 and 1987. Of the 66 patients, 46 were operated on immediately due to hypovolemic shock, with 20 stable patients undergoing CT scan. A NOM approach was taken in patients with hemodynamic stability and findings on CT of either contained capsular hematoma, unilobar fracture, minimal hemoperitoneum with no other intra-abdominal injuries, and an absence of devitalized liver. Of the 46 patients operated on, 14 died (30%). Of the 20 patients in the NOM group, 3 went on to require surgery due to instability. The other 17 patients all recovered from their injury without complication. The NOM group had significantly shorter length of hospital stay, fewer days in intensive care, and less blood transfusion in the first 24 hours and in total.[14] However, patients in the NOM group also had significantly lower Injury Severity Score than their operative management

counterparts with significantly less deranged clinical parameters on presentation.

In the 1990s several studies began evaluating NOM as the primary treatment strategy in cases of severe liver injury. In 1994, Meredith *et al*[16] examined 126 patients presenting with blunt hepatic trauma to a level 1 trauma center in North Carolina during a 36-month period under a NOM protocol. Of these, 24 required immediate surgery due to hemodynamic instability and 10 died of extra-abdominal injuries. A total of 92 patients underwent CT scanning. Of these, 20 required surgery for subsequent hemodynamic instability and the remaining 72 patients were intentionally treated with NOM, of whom 70 (97%) were successful. None of the 31 patients with American Association for the Surgery of Trauma (AAST) grade III to V liver injuries failed NOM. The overall mortality for grade III, IV, and V injured patients was 16%, 13%, and 29%, respectively. However, the mortality in the 17 patients with grade III to V injuries who were treated surgically for their liver injury was 47%. The authors concluded that NOM was the preferable management option for approximately half of their patients that presented with blunt liver trauma and for the significant majority who had liver injuries that were hemodynamically stable enough to undergo CT scanning.

One of the first prospective studies to evaluate NOM strategies in complex liver trauma was Croce *et al*[17] in 1995. The authors prospectively evaluated 134 patients with blunt hepatic trauma during a 22-month period, with the aim to establish whether NOM was feasible for all grades of blunt hepatic injury and whether there were any physiological or anatomic factors that could predict who would require surgery. Unstable patients underwent immediate laparotomy, as did patients with non-hepatic injuries that required exploration. All patients in the study that were considered hemodynamically stable underwent CT scanning and were managed conservatively in the intensive care unit. The 112 patients who were selected for NOM covered the full spectrum of AAST grading. The NOM group was compared with a group consisting of 168 patients with blunt liver injuries who were previously prospectively studied.[18] Of these, 84 (50%) were matched to the NOM group according to injury severity. Liver injuries were grouped into AAST grade I and II and AAST grade III to V. In the subgroups of patients with minor liver injury, the mortality for the NOM cohort was 10% and for the control cohort 6%. Neither group had any deaths related to liver injury or complications. The authors concluded that 89% of all patients with blunt liver injury that are hemodynamically stable at presentation can be managed without surgery and that NOM should be the treatment of choice. Several single-institution studies reported high success rates of NOM in patients with severe blunt hepatic trauma in the same period.[14 16 19–22]

Moreover, two large studies of NOM were described.[23 24] *Pachter et al*[23] undertook a multicenter study to assess whether the combined experiences at level 1 trauma centers could validate the reported high success rate and low morbidity and mortality associated with NOM. Thirteen level 1 trauma centers accrued 404 adult patients sustaining blunt hepatic injuries treated with NOM during a 5-year period. Hemodynamic stability was the major inclusion criterion for the NOM group. Once this was established, the other criteria consisted of the absence of peritoneal signs in a neurological intact and unimpaired patient, CT scanning and AAST injury assessment, an absence of concurrent intra-abdominal or retroperitoneal injury requiring immediate surgical intervention, and no requirement of ongoing liver-related blood transfusions. There were 27 deaths (7%) in this series, with 16 directly related to head trauma. Only two deaths (0.4%) were attributed to hepatic injury. Twenty-one patients (5%) had complications, with the most common being bleeding, occurring in 14 (3.5%). Overall, six patients required operative intervention: three for hemorrhage, two for missed enteric injuries, and one for persistent sepsis after unsuccessful percutaneous drainage. Overall 98.5% of patients in this study successfully completed NOM. Then, Richardson *et al*[24] published a landmark review in 2000, looking at the evolution in the management of hepatic trauma during a 25-year period, in particularly focusing on the impact of treatment changes on outcomes. The authors conducted a retrospective review of 1842 patients treated at the University of Louisville Trauma Unit between 1975 and 1999. They described that, although there was an increase in the number of liver injuries and a steady number of high-grade injuries seen, the actual number of operations performed for major hepatic venous injuries reduced by over 50% in the final 5 years of the study compared with the previous study periods. This correlated with an improvement in survival from major hepatic venous injuries. The authors contended that many venous injuries heal without surgical intervention due to their low pressure nature, and that manipulation of these is liable to cause massive, uncontrollable bleeding and therefore are better treated with NOM.[24]

Malhotra *et al*[25] published data that compared the outcomes of a cohort of 661 blunt hepatic trauma patients from 1993 to 1998 (NONOP2 group) with a cohort of 168 consecutive patients admitted between November 1985 and October 1990 who underwent surgery (OP group) for their liver injury and a second cohort of 136 consecutive patients admitted between January 1993 and October 1994 who were all treated with NOM (NONOP1 group). In the NONOP2 group, 101 patients required immediate surgery, with the most common indication being hemodynamic instability, and 42 (7.5%) failed NOM, 20 due to liver-related problems. Overall 85% were treated with NOM with a 92.5% success rate. The rate of serious infections and transfusion requirements (both during the first 24 hours and in total) were lower in the NONOP2 group. There was also a significant difference in the length of hospital stay between the groups. The OP cohort had an average length of stay of 20.4 days, with the NONOP1 group and the NONOP2 group having an average of 18.3 days and 12.7 days, respectively. The combined mortality for all three cohorts in this study was 15%, with liver-specific mortality being identical across all three cohorts (4%). Of the 25 deaths from liver injury, 23 occurred in patients with grade IV, V and VI injuries that required immediate emergency surgery. The similar liver-related mortality across all three cohorts gave a strong indication that using NOM to treat even high-grade liver injuries was a safe approach in hemodynamically stable patients.

A 2006 study by Coimbra *et al*[26] described NOM as the "treatment of choice for stable patients sustaining blunt liver injury." The authors produced a 15-year retrospective review of 128 consecutive patients with grade III and IV liver injuries, with 27 being treated conservatively. The study showed that the operative mortality of grade III and grade IV injuries remained unchanged between 1985 and 1993 (33.3%) and between 1994 and 1999 (28.6%), whereas the mortality of patients treated non-operatively was 0%. The authors observed a 23.5% reduction in mortality since the introduction of their NOM protocol. Coimbra *et al*[26] discussed that the key to successful NOM was careful patient selection. They also commented that the classic criteria for choosing NOM of hemodynamic stability, normal neurological status, an absence of a clear indication for laparotomy, low grade (AAST I–II) injury, and the requirement for

no more than two units of blood had been challenged in that no single criterion can predict who will fail NOM, and hemodynamic stability of the only necessity for its use.

Since Richardson *et al*'s[24] review in 2000, advances in CT scanning and access to angiography and embolization techniques undoubtedly have improved the outcome of severely injured trauma patients.[27 28] However, mortality rates for high-grade liver injuries were still significant, invariably due to the fact that the patient frequently presented with profound acidosis, hypothermia, and coagulopathy.[29] In 2007, Asensio *et al*[30] published a 54-month prospective study specifically focusing on the management of 75 patients with AAST grade IV and V liver injuries, and whether a multidisciplinary approach improved outcomes. Of the 75 patients, 52 (69%) had grade IV injuries, with the remaining 23 having grade V injury. In total 23 patients died (31% mortality), of whom 18 died from intraoperative hemorrhage. The mortality rates among patients with grade IV and V injuries were 19% and 57%, respectively. This compared favorably with other series by Cogbill *et al*,[31] who described a 46% mortality rate for grade IV and 80% mortality rate for grade V injuries, and an earlier study by Asensio *et al*[27], where mortality rate for grade IV injuries was 47% and for grade V injuries 77%.

A 2012 study by van der Wilden *et al*[32] retrospectively reviewed the role of hepatic angiography and embolization in 393 high-grade (AAST grade IV and V) liver injuries from 11 level 1 and 2 trauma centers across New England in the USA. The authors' starting hypothesis was that grade IV and V injuries could be safely treated with NOM with angiographic embolization as an adjunct. Of their patient cohort, 133 (33.3%) underwent immediate emergency surgery due to hemodynamic instability, with the other 262 given a trial of NOM. In 23 out of the 262 patients NOM failed (8.8%), with 8.1% of grade IV and 14.3% of grade V patients requiring delayed surgery. Patients who failed NOM had a significantly lower systolic blood pressure at admission, required longer stay in the intensive care unit, and had high rates of morbidity compared with patients who completed NOM. This does question their initial designation as being hemodynamically stable at admission. Of the patients who successfully completed NOM, 79 underwent hepatic angiography (33.1%) and 55 received embolization (23%). The authors reported a success rate of 93.2% (55 out of 59 patients) for patients undergoing angiography and embolization and attributed a high rate of successful NOM to this technique.[32]

However, the need for angiography and embolization might be reduced by improved resuscitation strategies. Gaski *et al*[33] performed a retrospective study of 583 patients with liver injuries cared for at the Oslo University Hospital between 2002 and 2014. Up to 2008 all patients with high-grade injuries underwent angiography, which was then adjusted to angiography only when signs of significant hemorrhage or contrast extravasation were identified on CT. The study therefore compared the period before (P1) and after (P2) 2008. There was an increase in the proportion of patients selected for NOM between P1 (65%) and P2 (76%), with no increase in the NOM failure rate (1% in both periods). Overall mortality fell from 14% in P1 to 7% in P2. As expected, the 46 patients who underwent laparotomy had a high mortality rate (46%), of which 67% were hemorrhage-related. When specifically comparing the grade IV and V injuries, it was noted that the 83 patients in P2 received significantly more plasma in the first 24 hours than the 66 patients in P1, resulting in a more balanced transfusion ratio. Patients in P2 also received significantly lower volume of crystalloid compared with P1. Between P1 and P2 there was no difference between 68% and 70% NOM rates or NOM failure rates (4% and 0%). There was a significant reduction in the number of patients undergoing angiography (68% in P1 compared with 22% in P2), with a similar reduction in angioembolization rates (30% vs. 12%). Mortality rates in the grade IV and V injury group was 17% in P1 and 15% in P2. However, liver-related deaths went from 11% to 4%.

The study concluded that with improved damage control resuscitation (DCR) protocols, NOM is safe in 70% of patients with AAST grade IV and V injuries and normal physiology, and that this strategy has low failure rates and mortality. Shrestha *et al*[34] also showed that improved resuscitation with DCR principles improved survival rates in severe liver trauma. The authors performed a retrospective study of all AAST IV and V injuries, dividing them into a pre-DCR group (between 2005 and 2008) of 108 patients and a DCR group (between 2009 and 2011) of 98 patients. The DCR group had an increased success rate of NOM, from 54% pre-DCR to 74% in the DCR group, as well as significant reduction in transfusion requirements in the first 24 hours and reduction of total crystalloid transfusion during the same time period. The implementation of DCR principles improved survival rates from 74% to 94% during the two time periods.

The increasing diagnostic sensitivity of whole body CT in trauma has reduced the rate of missed injury considerably, with rates reported as low as 2.4%.[35] This has allowed the NOM management of isolated liver injury to be undertaken with increasing confidence. In parallel to this, improvements in interventional radiology techniques mean that many complications of liver trauma related to hemorrhage or bile leaks can be successfully treated radiologically without the need for open surgery.[36] Biliary peritonitis has traditionally been treated with laparotomy; however, percutaneous drainage may be combined with endobiliary stent placement as a safe alternative when necessary.[37] Since even severe liver injuries can undergo NOM with a high degree of safety, contemporary treatment strategies should reflect the importance of patient physiology and associated injuries more than liver injury grade.[38] However, mortality remains obstinately high in patients with grade IV and V injuries who are critically ill at admission, and it is this population that requires further study to improve their outcomes.[33 34]

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