Outcomes and complications of angioembolization for hepatic trauma: A systematic review of the literature

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BACKGROUND: The liver is one of the most frequently injured abdominal organs. Hepatic hemorrhage is a complex and challenging complication following hepatic trauma. Significant shifts in the treatment of hepatic hemorrhage, including the increasing use of angioembolization, are believed to have improved patient outcomes. We aimed to describe the efficacy of angioembolization in the setting of acute hepatic arterial hemorrhage as well as the complications associated with this treatment modality.

METHODS: A systematic review of published literature (MEDLINE, SCOPUS, and Cochrane Library) describing hepatic angioembolization in the setting of trauma was performed. Articles that fulfilled the predetermined inclusion and exclusion criteria were included. We analyzed the efficacy rate of angioembolization in the setting of traumatic hepatic hemorrhage as well as the complications associated with hepatic angioembolization.

RESULTS: Four hundred fifty-nine articles were identified in the literature search. Of these, 10 retrospective studies and 1 prospective study met inclusion and exclusion criteria. Efficacy rate of angioembolization was 93%. The most frequently reported complications following hepatic angioembolization included hepatic necrosis (15%), abscess formation (7.5%), and bile leaks.

CONCLUSION: Although the outcomes of hepatic angioembolization were generally favorable with a high success rate, the treatment modality is not without associated morbidity. The most frequently associated major complication was hepatic necrosis. Rates of complications were affected by study heterogeneity and should be better defined in future studies. (*J Trauma Acute Care Surg*. 2016;80: 529–537. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Systematic review, level III.

KEY WORDS: Angioembolization; liver; trauma.

The management of hepatic trauma is a dynamic field with significant paradigm shifts during the past several decades. The liver's size and location make it one of the most commonly injured organs in the abdomen. The vast majority of hepatic injuries are secondary to blunt trauma sustained during motor vehicle collisions.[1] The possibility of uncontrolled hemorrhage and a myriad of delayed complications contribute to a high morbidity and mortality rate associated with hepatic trauma. Historically, operative management was the treatment option of choice for patients with hepatic injuries. In the 1980s, rapidly improving imaging with computed tomography (CT) allowed for noninvasive assessment of trauma patients and their associated injuries. The arrival of transarterial angioembolization (AE) of acute hemorrhage in the early 1970s[2,3] and the advances in catheter and microcatheter design coupled with widespread interventional training have created a viable option for acute arterial hepatic hemorrhage. By the mid 1990s, endovascular techniques became an integral part of the care of trauma patients. At the same time, a push for nonoperative management of hepatic trauma patients began, in part fueled by the success of nonsurgical treatment of pediatric patients and the high rate of nontherapeutic operations.[4,5] These advances in nonsurgical intervention, combined with the contemporary use of AE, are believed to have played a decisive role in decreasing overall morbidity and mortality.[6] Today, algorithms for the operative and nonoperative management of adult blunt hepatic trauma consider interventional radiologists and their support staff as integral team members in the treatment of hepatic trauma.[7,8] Nonoperative management for hepatic trauma is regarded as the standard of care in hemodynamically stable patients, regardless of the grade of the injury,[9] and the majority of hepatic injuries are now managed nonsurgically. Such is true even for higher-grade injuries where the operation rate remains less than 40%.[1] Success rates of nonoperative management, defined as no surgical intervention required, are generally greater than 90%.[10]

Although there is a large body of literature supporting the use of AE in the setting of hepatic trauma, the expected efficacy and complication rates of this treatment are not well characterized, and the majority of reports consist of small numbers (<100) of patients. There have been several reports questioning its efficacy when combined with additional operative measures.[11–13] Other investigators have raised concern over the seemingly high rate of liver necrosis following hepatic embolization[14] as well as the possibility of gallbladder infarction following occlusion of the right hepatic artery.[15] Furthermore, the ideal timing of AE in the setting of hepatic trauma remains unanswered.

We conducted a systematic review of the literature to define the value of AE as a resuscitative measure in patients with hepatic lacerations secondary to trauma. The primary objective of this study was to determine the efficacy of AE in the setting of hepatic hemorrhage secondary to trauma. A secondary objective was to establish reported complication rates following AE of the liver.

PATIENTS AND METHODS

Search Strategy

The MEDLINE, SCOPUS, and Cochrane Library databases were electronically searched for published articles on the use of AE in trauma patients with hepatic injuries. The search was conducted using the following search terms and BOOLEAN operators: "hepatic" OR "liver" AND "trauma" AND "embolization." Before the search, inclusion and exclusion criteria were defined. Articles were considered eligible for inclusion if they met the following criteria: (1) The study population consisted of patients with traumatic causes (blunt or penetrating) of hepatic hemorrhage. (2) AE was considered as an intervention for the treatment of hepatic hemorrhage. (3) At least one outcome of interest was described. (4) A liver injury grade range was provided for embolized patients. The principle outcome of interest was the efficacy rate of AE in obtaining control of arterial hepatic hemorrhage. Secondary outcomes of interest included mortality rate, liver-related mortality rate, and frequency of both AE-specific and non–AE-specific complications. Exclusion criteria included: (1) case reports, (2) case series with fewer than 10 consecutive patients, (3) articles describing the treatment of only iatrogenic causes of hepatic hemorrhage or articles in which patients experiencing iatrogenic causes of hemorrhage could not be separated from those experiencing traumatic causes of liver injury, and (4) articles limited to pediatric patients only. Search results were limited to humans, English language, and articles published after 1990. Two reviewers (C.S.G., S.W.K.) independently scrutinized the titles and abstracts of the articles retrieved. Most of the search results could be excluded based on the title and abstract alone. The full-length articles of the remaining articles were reviewed for eligibility criteria. The references of these articles were also searched for additional relevant articles. Any discrepancy between the two reviewers was resolved by review of a self-made quality assessment form. The quality assessment form included the following questions: (1) Is the embolization technique clearly described? (2) Was the description of the outcomes of interest complete? (3) Was there an adequate description of other clinical factors that may impact the primary and secondary outcomes, such as description of additional injuries in polytrauma patients or review of the patient population Injury Severity Score (ISS)? (4) Were additional clinical factors detailed such as transfusion requirements? (5) Can missing data be reliably obtained? (6) Can liver injury grade be determined for each embolized patient. A protocol does not exist for this systematic review.

Data Extraction and Synthesis

Data extraction from the eligible articles was performed with a predefined template. The data extracted included year of publication, study period, study type (prospective, retrospective), and both minor and major complications following embolization. Weighted means and ranges were calculated for variables of interest. Because of the heterogeneity of the data, meta-analysis was not performed.

RESULTS

A total of 459 unique articles were identified in the search process. Of those, 402 articles were excluded through title and abstract filtering. No randomized controlled trials were identified. After review of the full texts of the 57 remaining articles, 46 were excluded, leaving a total of 11 articles in the study (Fig. 1).[14–24] A manual review of references did not identify any additional articles that met the inclusion criteria. All but one of the included articles was a retrospective case series.[24] The publication dates ranged from 2002 to 2014, with eight studies published in the last decade. The included studies are summarized in Table 1.

Patient Demographics

A total of 998 patients were included in the patient study populations. The study population age range was 3 years to 84 years. The median ISS for the study populations was 24 (range, 16.9–36.9). Six studies did not record ISSs.[15,16,18–20,22] A total of 347 patients with hepatic hemorrhage were embolized from 1992 to 2012, accounting for 34.8% of the total study patients. The mean age (SD) of embolized patients per study was 31 (21.9) years, with a range of 12–71 years. Seven studies recorded the number of patients undergoing angiography.[14,15,18,19,22–24] More than two thirds of patients (72%) undergoing angiography proceeded to embolization. A total of 10 articles reported individual liver injury grade scores for patients.[14–20,22–24] Embolized patients had an average injury grade of score of 3.73 with range of I to V. One study recorded only injury grade range for embolized patients.[21] Blunt trauma accounted for 92% of injuries, with motor vehicle collision as the most common cause.

Indications for Embolization

A total of six studies reported the indications for embolization.[14–16,19,20,24] A contrast blush on CT was the most common indication. The next most common indications included failure of nonoperative management and control of continued hemorrhage following damage-control laparotomy.

Technique

Of the articles describing the embolization protocol, all reported use of microcatheter systems with selective and superselective embolization techniques. Gelatin sponge and microcoils were the most commonly used embolization materials.

Efficacy

The AE success rate ranged from 77% to 100%. The weighted average efficacy rate was 93%. Two studies reported a failure to embolize three patients secondary to technical factors such as stenotic arteries or sharp branching limiting cannulation of the bleeding vessel.[23,24] One patient's neurologic status declined before embolization attempts, and the procedure was terminated.[23] Three studies including 51 patients reported on the impact of embolization timing with respect to transfusion requirements.[15,20,23] A total of 26 patients underwent immediate embolization following CT, while 25 were embolized following failure of conservative management, following damage-control laparotomy, or for hemobilia. Among the early embolizations, an average of 5.8 U of packed red blood cells were required in the first 24 hours. An average of 11.1 U of packed red blood cells were used in the late embolization group.

Mortality

Details regarding deaths among embolized patients were obtained from all but one study and are summarized in Table 2.[19] There were a total of 31 deaths accounting for a death rate of 9.6% among patients undergoing embolization (range, 0–27%). There were 18 liver-related deaths, for a total liver-related death rate among embolized patients of 5.6% (range, 0–19.2%).

Morbidity

The most commonly reported complication was hepatic necrosis (Table 3). There were a total of 48 cases of hepatic necrosis accounting for 14.9% of embolized patients (range, 0–43%). A single study accounted for 30 cases (63%) of hepatic necrosis.[14] Details on abscess formation were obtained from nine studies.[14–18,20,21,23,24] A total of 23 patients (7.5%) developed hepatic abscesses or infected hepatic collections after embolization. There were 17 cases of gallbladder infarction following embolization and 37 reported bile leaks/bilomas. There was only one reported groin hematoma following embolization.[15] Although complications were reported in the studies by Li et al.[19] and Tzeng et al.,[22] these complications could not be definitively assigned specifically to

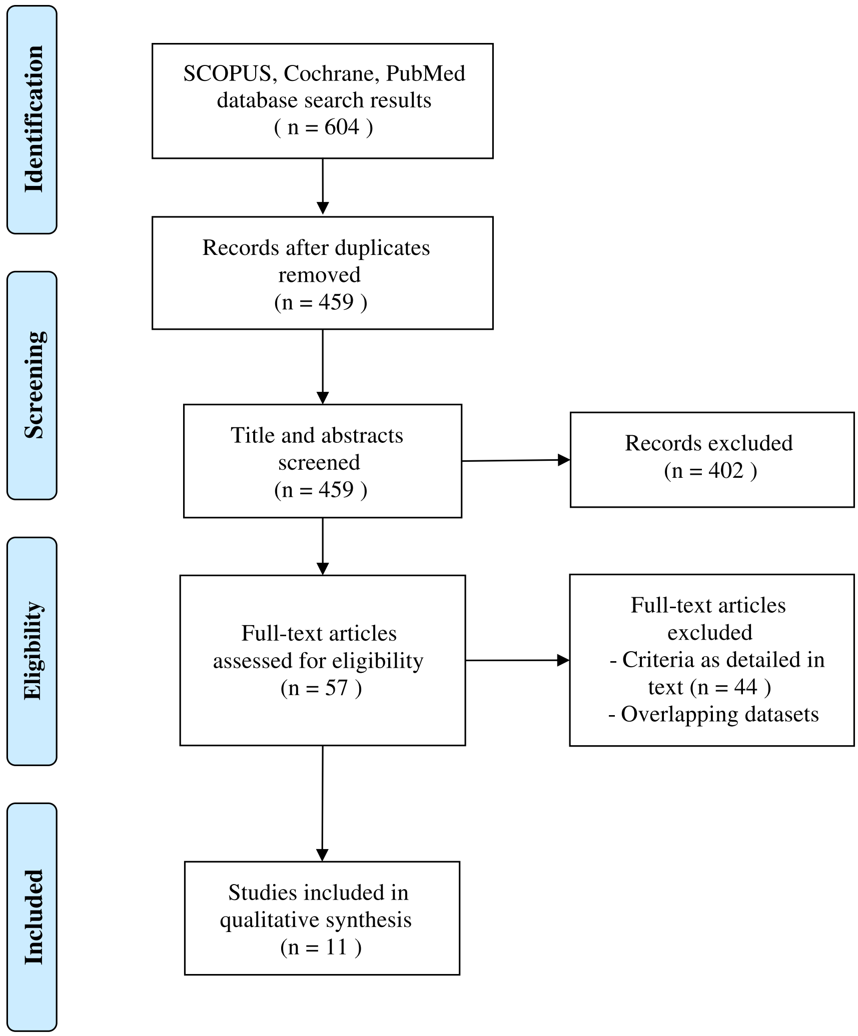

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram showing the selection of articles for inclusion.

patients who underwent AE, and therefore, these complications were not included in the calculations.

DISCUSSION

The management of traumatic hepatic injuries has benefited from a significant paradigm shift during the past four decades. Advances in diagnosis, management, and treatment have lead to a multidisciplinary approach to the treatment of complex hepatic hemorrhage. Currently, there is substantial body of evidence in support of nonoperative management of hemodynamically stable patients with hepatic injuries.[5,25–28] Success with nonoperative management of patients has led to significant decreases in mortality rates.[6] As a result of the compelling improvements in patient outcomes, nonoperative management is the standard of care in hemodynamically stable patients with traumatic liver injuries. Angiography and AE are essential components of successful nonoperative management of hepatic trauma patients as well as a critical component of hemorrhage control following laparotomy.[9,13,29–33] Indications for conventional hepatic angiography include active extravasation identified by CT, evidence of ongoing bleeding despite conservative resuscitative measures, hemobilia, and high-grade liver injuries.

The demographics of this study's patient population are similar to those of multiple published large retrospective reviews, with a mean patient age in the early 30s and a significant male predominance. Like other studies, blunt hepatic injury was more common than penetrating, with motor vehicle collisions as the most common cause of hepatic injury.[34] Although only three studies recorded the ISS for embolized patients, the ISS range was consistent with major traumatic and multisystem injuries.[14,15,23]

Hepatic transarterial embolization was 93% effective in stopping arterial hemorrhage. Lee et al.[18] reported 11 cases of incomplete embolization. Ten of these cases were secondary to a persistent contrast blush without an identifiable vessel or a blush supplied by multiple collaterals that could not be embolized. There was one reported failure secondary to a stenotic celiac artery. Both Lee et al. and Hagiwara et al.[24]

TABLE 1. Characteristics of Included Studies, Patient Demographics, and Embolic Agents Used

Article	Publication Year	Study Type	Study Period	No. Patients With AE (Noniatrogenic)	M/F Ratio for AE Patients	Age Range for AE Patients (Noniatrogenic)	AAST Average	AAST Grade I	AAST Grade II	AAST Grade III	AAST Grade IV	AAST Grade IV	Embolization Agents Used
Dabbs et al.[14]	2009	Retrospective	2002–2007	71	2.4	34 ± 14	3.9	0	0	16	44	11	Coils, gelatin sponge
Hagiwara et al.[24]	2002	Prospective	1996–2000	32	nr	nr	3.5	0	0	18	13	1	Coils, gelatin sponge, PVA particles
Kong et al.[16]	2014	Retrospective	2002–2011	70	2.9	36.3 (16–62)	3.4	0	13	25	23	9	Coils
Kozar et al.[17]	2005	Retrospective	2000–2003	12	nr	nr	4.3	0	0	0	8	4	nr
Lee et al.[18]	2014	Retrospective	2009–2012	48	1.6	31.5 (8–64)	3.6	0	5	14	25	4	Coils, gelatin sponge
Li et al.[19]	2014	Retrospective	2007–2012	24	3.2	35.9 ± 10.8 (17–69)	3.9	0	1	5	13	5	nr
Mohr et al.[15]	2003	Retrospective	1995–2002	26	nr	33 (16–85)	3.9	0	0	6	17	3	Coils, gelatin sponge, PVA particles
Monnin et al.[20]	2008	Retrospective	2000–2005	14	6	37 (7–77)	4.1	0	0	2	9	3	Coils, Gelatin sponge, PVA particles
Saltzherr et al.[21]	2011	Retrospective	1995–2008	23	nr	nr	nr	nr	nr	nr	nr	nr	Coils, PVA particles
Tzeng et al.[22]	2005	Retrospective	1996–2003	15	2.6	nr	3.9	1	0	3	6	5	Coils, tissue adhesive
Wahl et al.[23]	2002	Retrospective	1997–2001	12	nr	47	3.7	0	0	5	6	1	nr

nr, not reported; PVA, polyvinyl alcohol.

TABLE 2. Outcomes of AE

Article	No. Patients With AE (Noniatrogenic)	Immediate Rebleeding	Efficacy Rate	Death	Liver-Related Death
Dabbs et al.	71	2	97.2%	10	8
Hagiwara et al.	32	2	93.8%	2	2
Kong et al.	70	0	100.0%	0	0
Kozar et al.	12	0	100.0%	0	0
Lee et al.	48	11	77.1%	5	0
Li et al.	24	2	91.7%	nr	nr
Mohr et al.	26	2	92.3%	7	5
Monnin et al.	14	0	100.0%	1	0
Saltzherr et al.	23	2	91.3%	0	0
Tzeng et al.	15	2	86.7%	0	0
Wahl et al.	12	1	91.7%	6	3

nr, not reported.

reported failures of nonoperative management despite technically successful embolization. Many of the patients who failed conservative management despite successful embolization were found to have significant juxatahepatic venous injuries. These types of injuries can be difficult to identify during angiography; however, they should be suspected in patients with high-grade liver lacerations who require ongoing fluid resuscitation despite successful embolization. Cross-sectional imaging can aid in the detection of retrohepatic caval and juxtahepatic venous injuries, and ongoing venous hemorrhage may require operative packing. Failure to identify these types of injuries is an important explanation for the failure of nonoperative treatment. Despite successful embolization, delayed hemorrhage can still occur and has been documented in 5% to 12% of patients.[35–37] More recent advent of hybrid operating suites may allow for near-simultaneous treatment of arterial hemorrhage with AE and juxtahepatic venous injuries with laparotomy.

Several articles have suggested that early angiography and embolization improve outcomes in patients with high-grade hepatic injuries.[12,13,30,31,38–40] Similar improved outcomes with earlier embolization have also been documented with both traumatic pelvic and splenic injuries.[41–45] Only three articles in this study sufficiently separated outcomes for early versus late embolization patients.[15,20,23] In each study, there was a trend toward reduced transfusion requirements for those patients undergoing early AE. However, higher transfusion requirements in the late AE could be confounded by greater severity of injury in this group, as these patients could have been more likely to require damage-control laparotomy. Given the small and heterogeneous patient samples, no definitive conclusions could be drawn about mortality and morbidity rates.

One of the principal advantages of AE is that it is generally well tolerated, even among critically ill patients. In this study, the average liver injury grade of patients undergoing embolization was 3.73, which is consistent with a major traumatic event. Not surprisingly, high-grade hepatic injuries are frequently associated with polytrauma and elevated ISSs, complicating a patient's hospital course. Despite impressively high injury grades and ISS ranges among the study populations, the overall mortality rate for embolized patients remained just less than 10%, and the liver-related mortality rate was less than 6%. There were no reported procedure-related mortalities. The overall mortality rate is within the range of previously published data evaluating patients with high-grade liver injuries and less than that of the National Trauma Data Bank, despite an overall higher weighted average organ injury score.[1]

Complications are common following significant hepatic injuries. Not surprisingly, the number of complications increases with a higher degree of liver injury.[17,36,46] One of the major criticisms of AE in the setting of hepatic trauma is the apparent high morbidity rate. A major concern is hepatic necrosis following embolization, as it can be associated with longer hospital stays, increased transfusion requirements, and the need for multiple operations in what was otherwise a planned nonoperative treatment course. Hepatic necrosis occurs following the death of a large number of contiguous hepatocytes. In the setting of trauma, hepatic necrosis is caused by major devascularization of a portion of the liver through a traumatic insult, therapeutic embolization, or a combination of the two. The liver's dual arterial and portal venous blood supply confers protection against ischemic insults. However, despite

TABLE 3. Complications Following AE

Article	No. Patients With AE (Noniatrogenic)	Hepatic Necrosis	Abscess	Gall Bladder Infarction	Bile Leak/Biloma
Dabbs et al.	71	30	12	5	14
Hagiwara et al.	32	None reported	None reported	None reported	None reported
Kong et al.	70	11	None reported	5	6
Kozar et al.	12	None reported	None reported	None reported	1
Lee et al.	48	None reported	None reported	None reported	None reported
Li et al.	24	None reported	Not reported for AE patients	None reported	Not reported for AE patients
Mohr et al.	26	4	2	4	7
Monnin et al.	14	1	2	2	6
Saltzherr et al.	23	2	5	1	2
Tzeng et al.	15	0	Not reported for AE patients	0	0
Wahl et al.	12	0	2	0	1

this robust dual supply, the combined insult of trauma and embolization has been shown to cause significant hepatic necrosis. The included studies report a hepatic necrosis rate that ranged from 0% to 42%, with a weighted mean rate of 15%. However, nearly two thirds of cases of hepatic necrosis were documented in a single study by Dabbs et al.,[14] which had a notably high rate of necrosis compared with the other studies (42% vs. 0–16%). The degree of arterial selectivity during embolization in this study was not clear, but it is generally thought that reduced necrosis rates may be achieved by the use of microcatheter systems and superselective embolization. In addition, the high rate of necrosis may be secondary to the higher injury grade and ISSs for the patients in that study. This in turn may further exacerbate injury to the liver because of higher rates of damage-control laparotomy. It is notable that in the study by Dabbs et al., nearly 97% of patients with major hepatic necrosis underwent operative management including perihepatic packing. If this study is excluded as an outlier, the mean hepatic necrosis rate falls to 6.2%.

Similar to previous studies, abscess formation and bile leak/biloma were the next two most common complications.[17,47] These complications are not AE specific and have been documented following both operative and nonoperative management of liver trauma.[48–50] These complications can often be managed through minimally invasive techniques such as percutaneous drainage with a nominal impact on the patient's hospital course. Identification of biliary injuries is important because bile leaks may be an important contributor to delayed bleeding. Gallbladder infarction is an important complication that is generally identified following nontarget embolization of the cystic artery during embolization of the right hepatic artery.

The current study is limited by the quality of the available published studies. Most of the included articles were retrospective without comparative groups. There is currently no standardization for patient selection or reporting, resulting in heterogeneity in the data. If incomplete embolization was described, it was considered an AE failure. If the details of rebleeding following AE were not sufficiently described, it was considered embolization failure. If a complication was not reported, then a complication was assumed to not occur; this assumption could have impacted our results. Lee et al. reported no AE-related complications but did not describe non–AE-specific complications such as abscess formation or bile leak.[18] It seems unlikely that none of these complications occurred in the third largest study population. Similarly, the available published studies could be affected by publication bias, although this could have had either positive or negative impacts on AE outcomes. When not specifically stated, organ injury scoring was assumed reported using the American Association for the Surgery of Trauma (AAST) classification. One study reported organ injury grade using the Mirvis scoring system.[51] The numerical values from this study were included in the average orange injury grade.

To date, there are no consensus guidelines on appropriate patient selection criteria for those who would benefit from angiography and AE. For patients who are hemodynamically stable, contrast-enhanced CT has been shown to identify those at risk for impending failure of nonoperative management, with high risk seen in those with intraperitoneal contrast extravasation in the peritoneum, hemoperitoneum involving multiple abdominal compartments, or contrast extravasation into ruptured liver parenchyma.[52–54] However, low-grade hepatic injuries with contained, intraparenchymal contrast pooling may benefit from observation alone.[54] After laparotomy, persistent transfusion requirements usually suggest need for angiography and embolization. In this setting, additional imaging can be helpful, as early postoperative CT has been found to determine which patients would require postlaparotomy AE with high sensitivity and specificity.[55]

In summary, the present review demonstrates that hepatic AE is an effective and important component in the management of traumatic hepatic hemorrhage. However, serious complications such as hepatic necrosis can occur following embolization, and the rates of these complications should be better defined in future studies. The poor quality of currently available studies limits establishment of additional clinically relevant conclusions. Questions remain regarding patient selection and the ideal timing of embolization.

AUTHORSHIP

C.S.G. contributed in the study design, literature search, data collection, data analysis, data interpretation, writing, and critical revision. E.M.B. contributed in the data interpretation, writing, and critical revision. S.W.K. contributed in the study design, literature search, data collection, data analysis, data interpretation, writing, and critical revision.

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