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Operative or Non-Operative Management for High-Grade Pediatric Pancreatic Trauma? A Systematic Review Still Leaves the Question Unanswered

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Abstract

Background: Management of high-grade pancreatic injures in children remains controversial. As in adults, AAST grades I and II injuries are generally managed non-operatively and the very rare grade IV and V injuries that involve the pancreatic head are managed on an individual basis. Grade III injuries, involving pancreatic duct transection within the pancreatic body, are commonly seen in children due to handlebar trauma. These are universally managed with distal pancreatectomy in adults; however, some pediatric surgeons prefer to manage them non-operatively. There have been multiple retrospective studies comparing outcomes between operative management (OM) and non-operative management (NOM), with mixed results. We performed a systematic review to determine whether the current literature supports one management strategy over the other.

Methods: A systematic review of all published English literature was performed. Meta-analysis was performed for fistula and pseudocyst formation as these were the only outcomes for which complete data was attainable. Other outcomes studied were: days on total parenteral nutrition (TPN), days to full enteral feeds, and hospital length of stay (LOS).

Results: Twenty-five multicenter studies were included. Of 1014 pancreatic injuries, 732 (72.2%) were managed with NOM and 267 (26.3%) by OM. Given the heterogeneity of the data, metanalysis could only be performed for the outcomes of pseudocyst and fistula formation. Pseudocyst formation was higher following NOM than OM (pooled odds ratio 2.05, 95% CI 1.04 to 4.07; p<0.001), and fistula rates were similar among the groups (pooled odds ratio 0.60, 95% CI 0.18 to 2.01; p=0.3115). Metanalysis could not be performed on the other outcomes, and mixed results were demonstrated for every outcome.

Conclusion: In children with high-grade pancreatic trauma, NOM leads to higher pseudocyst formation than OM, which is expected. While fistula rates are similar, there is not enough good quality evidence to make definite conclusions about other outcomes or to determine a superior management strategy. A prospective trial is needed to determine the best approach to managing these injuries.

Keywords: Blunt pancreatic trauma; Pancreatic trauma; Pancreatic injury; Level of evidence: III

Introduction

Pancreatic injury in children is rare, comprising less than 10% of cases of blunt abdominal trauma, in which the pancreas is the least commonly injured solid organ following the spleen, liver and kidney [1-3]. The majority of pancreatic injuries in children occur as a result of motor vehicle accidents and direct epigastric force due to a bicycle handlebar [4,5]. The latter commonly cause a laceration of the pancreas at the body overlying the spine, and injury to the pancreatic duct can occur within a deep laceration or complete pancreatic transection.

When possible, non-operative management (NOM) of other solid organ injuries in the pediatric population is now commonly accepted and practiced; however, the management of pancreatic injuries remains a topic of debate among pediatric surgeons. In general, NOM is the standard of care in both adults and children for low-grade (AAST I and II) pancreatic injuries, which only involve the parenchyma without involvement of the pancreatic duct [6]. When duct integrity has been compromised, however, as in grade III pancreatic body injuries, the standard of care in the adult population is to perform a distal pancreatectomy and occlude the proximal end of the duct in order to prevent complications from leakage of pancreatic enzymes [7,8].

In children, success with NOM of these injuries has been published in multiple reports [9-12], and the strategy has gained popularity among some pediatric surgeons, but many still remain skeptical and follow the adult guidelines of OM.

Multiple studies have compared the outcomes of NOM and OM, but these studies are all retrospective, have small sample sizes, and the results are mixed [3,13-17]. To date, there is no consensus on the management of these injuries. We therefore sought to perform a systematic review and meta-analysis of these studies to determine whether the evidence that we currently have is sufficient to demonstrate a clearly superior management strategy for high-grade pancreatic injuries in the pediatric population.

Methods

An electronic search using the MEDLINE, SCOPUS and EMBASE databases from 1970 to 2013 was performed. The search terms "pancreatic trauma", "pancreatic injury", "pediatric pancreatic trauma", "pediatric trauma" and "children" were used in combination with the Boolean term "AND". Only articles written in English were included. Two authors reviewed the abstracts independently. Abstracts that were identified were then reviewed for inclusion into the meta-analysis. Studies were included if they evaluated pediatric patients (age 0 to 18 years) with blunt pancreatic injuries who had been managed either with non-operative or operative management and were available in the English language. Publications were excluded if they were case reports or case series. The outcomes of interest were length of hospital stay, days to full enteral feeds, days on total parenteral nutrition (TPN), pseudocyst formation, and fistula formation. Data obtained from eligible studies was entered into a Microsoft Excel Spreadsheet. Meta- analysis was carried out using R Meta package (Version 3.2-1). Weighted treatment effect was calculated using both the fixed and random effects models. Overall effect was tested using Cochran-Mantel-Haenszel (CMH) test. Treatment effect sizes were calculated as relative risk (RR) for dichotomous along with 95% confidence intervals. Statistical heterogeneity was assessed using a Chi-square test, a between-study variance τ2 and I2 statistic. Funnel plots were used to check the existence of publication bias.

Results

There were 25 publications that met inclusion criteria for systematic review [3,10-34]. Table 1 provides a summary pf the studies included in the review. All publications were retrospective in nature. Nineteen were from a single institution and 6 were multi-institutional reviews. Figure 1 illustrates the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow. In total, there were 1014 pancreatic injuries of which 732 were managed with NOM, 15 with drain placement only and 267 with OM. Of the 18 studies with reported injuries, 190 were grade ≥ III (146 NOM and 46 OM). Meta-analysis could only be performed on the outcomes of pseudocyst and fistula formation due to inconsistent reporting of parameters for the other outcomes.

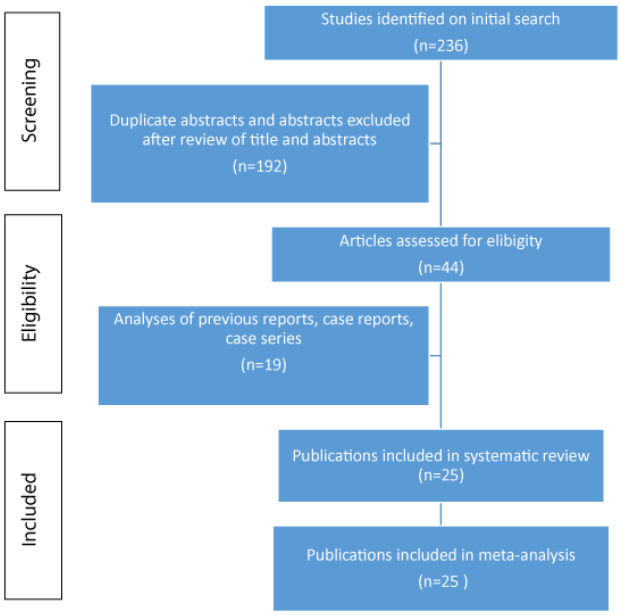

Figure 1 Flow diagram illustrating publication selection.

Table 1 Summary of studies included in systematic review and meta-analysis of management strategies in pediatric blunt pancreatic trauma.

Author	Patients (n)	AAST Grade	Age (years)	Management	LOS	TPN days	Fistula	Pseudocyst	Summary
Multi-center reviews									
Iqbal et al. [17]	167	II & III	9.1 ± 0.4	NOM: 95 OM: 57 Drain:15	NOM: 13.4 ± 12.7 OM: 11.9 ± 7.5	n/a	n/a	NOM: 17 OM: 0	NOM was associated with higher pseudocyst formation NOM was associated with shorter time to initial and goal feeds
Beres et al. [16]	79	I&II: 40 III&IV: 39	NOM: 8.9 ± 3.9 OM: 9.6 ± 4.1	NOM: 24 OM: 15	NOM: 27.5 ± 19.8 OM: 15.1 ± 8.4	NOM: 21.8 ± 18.9 OM: 7.9 ± 7.6	NOM: 1 OM: 1	NOM: 13 OM: 0	NOM associated with longer hospital stay, more days on TPN, more complications

Cuenca et al. [15]	79	I: 32 II: 22 III-V: 24	8.6 ± 5.4	NOM: 47 OM: 32	n/a	n/a	n/a	NOM: 3	NOM appears safe in children with pancreatic injuries
Paul et al. [14]	131	II and III	NOM: 9.1 ± 5.1 OM: 9.6 ± 4.3	NOM: 45 OM:20	NOM: 14.2 ± 12.8 OM: 16 ± 13.4	n/a	NOM: 3 OM: 2	NOM: 8 OM: 3	NOM associated with higher rate of pseudocyst formation
Mattix et al. [3]	173	III to V	0.08-17	NOM: 128 OM:43	NOM: 9.56 ± 19.8 OM: 12.08 ± 12.0	NOM: 4.6(3-31) OM: 13.2(3-66)	NOM: 2 OM: 1	NOM:12 OM: 4	NOM associated with higher pseudocyst formation.
Keller et al. [13]	154	I &II: 123 III-V: 31	<15	NOM: 112 OM: 42	n/a	n/a	n/a	NOM: 15 OM: 10	No difference in mortality between patients managed with NOM and those managed with OM
Single-center reviews									
Abbo et al. [30]	36	I to IV	1-15	NOM: 36	n/a	23.5 (7-67)	n/a	11	NOM is a safe management strategy for blunt pancreatic injury
Cigdem et al. [21]	31	I to IV	3-16	NOM: 25 OM:6	n/a	n/a	n/a	NOM: 11 OM: 1	NOM is associated with higher pseudocyst formation
Klin et al. [24]	10	I to III	3.9 -17	NOM: 7 OM: 3	NOM: 8.33 ± 6.71 OM: 10.5 ± 3.5	n/a	n/a	NOM:3 OM: 0	NOM is associated with higher pseudocyst formation rate
Wood et al. [18]	43	I: 18 II: 6 III: 17 IV: 2	1-17	NOM: 29 OM: 14	NOM: 17 (9-25) OM: 13 (8-34)	n/a	n/a	NOM: 73% OM: 21%	OM associated with decreased pseudocyst formation rate but does not affect hospital length of stay
Juric et al. [29]	7	I: 4 II: 3	5-13	NOM:7	n/a	n/a	n/a	NOM: 3	Major determinants of management for pancreatic trauma are grade and clinical status of patient
Vane et al. [28]	14	II: 5 III: 4 IV: 4 V: 1	2-16	NOM: 5 OM: 9	n/a	n/a	n/a	0	Early drainage in high-grade pancreatic injury decreases hospital length of stay
de Blaauw et al. [12]	34	Not reported	3-14	NOM: 31 OM: 3	24 (2-70) vs. 29(15-69)	n/a	n/a	NOM:14 OM: 2	NOM was associated with higher pseudocyst formation
Snajdauf et al. [33]	13	II: 4 III: 5 IV: 4	3-16	NOM: 0 OM:13	n/a	n/a	n/a	OM: 8	Early diagnosis of pancreatic ductal injury can lead to prompt surgical management
Houben et al. [34]	15	II: 2 III:4 IV: 9	7-16	NOM: 14 OM:1	n/a	n/a	n/a	NOM: 6	Most pancreatic injuries can be managed non-operatively
Stringer et al. [31]	9	I:1 II: 2 III:5 IV:1	3-13	NOM: 8 OM:1	n/a	n/a	NOM: 4	NOM:5	Management of pancreatic injury in children depends on location of injury

Wales et al. [11]	9	III: 2 IV : 7	4-16	NOM:9	n/a	n/a	n/a	n/a	44% of patients developed pseudocysts
Meier et al. [22]	11	Not reported	3-13	NOM: 2 OM:9	n/a	n/a	n/a	NOM: 2	Early NOM allows for earlier return of function and decreased hospitalization
Canty et al. [23]	18	II & III	2 months to 13 years	NOM: 10 OM: 8	n/a	n/a	n/a	NOM: 5	Acute ERCP may provide definitive management of ductal injuries. Distal injuries should be treated with distal pancreatectomy and proximal injuries with NOM if stenting cannot be performed
Firstenberg et al. [26]	9	I to IV	8.7 ± 1.2	NOM: 8 OM: 1	n/a	n/a	n/a	NOM: 5	The majority of blunt pancreatic trauma can be be managed non-operatively
Jobst et al. [32]	56	Not reported	2 months – 14 years	NOM: 26 OM: 30	n/a	n/a	NOM: 1	NOM: 7	The majority of pancreatic injuries can be managed with NOM
Kouchi et al. [27]	20	I: 9 II: 6 III: 5	2-10	NOM: 19 OM: 1	n/a	n/a	n/a	NOM: 10	NOM is effective in children
Shilyansky et al. [25]	35	Not reported	1-16	NOM: 28 OM: 7	NOM: 21	n/a	n/a	NOM: 10	NOM is safe and effective in children
Sjovall et al. [20]	10	Not reported		NOM: 8 OM: 2	n/a	n/a	n/a	NOM: 4 OM: 0	NOM associated with higher pseudocyst formation
Rescorla et al. [19]	6	Not reported	Not reported	NOM: 0 OM: 6	n/a	n/a	n/a	n/a	Recommended early operative intervention for patients found to have ductal injury
Haller et al. [10]	7	Not reported		NOM:4 OM:3	n/a	n/a	n/a	n/a	NOM of solid organ injury is safe and appropriate in patients who are appropriately selected and monitored

Pseudocyst formation

The incidence of pseudocyst formation was recorded in 24 studies [3,10-17,20-34]. There were 318 managed with NOM and 716 injuries managed with OM. Pseudocyst development was reported in 171 patients managed with NOM (53.8%) and 32 patients managed with OM (4.5%). Metaanalysis demonstrated a statistically significant higher risk of pseudocyst formation in the NOM group (pooled odds ratio 2.05, 95% CI 1.04 to 4.07; p<0.001) (Figure 2). There was substantial heterogeneity between groups (I2=68.8%).

Fistula formation

The incidence of pancreatic fistula formation was recorded 6 studies [3,10,12,14,16,32]. There were 269 injuries managed with NOM and 124 managed with OM. There were 11 fistulas reported in the NOM group (4.1%) and 5 in the OM group (4%). Meta-analysis using the fixed-effect model demonstrated no statistically significant difference between groups (pooled odds ratio 0.60, 95% CI 0.18 to 2.01; p=0.3115) (Figure 3). There was no evidence of statistical heterogeneity (I2=16.2%).

Length of hospital stay

There were 10 studies in which the hospital length of stay (LOS) was recorded. Table 2 summarizes the mean and median LOS in these studies. There were 420 injuries managed with NOM and 183 injuries managed with OM. Given the heterogeneity of reported data, a metaanalysis could not be performed. In 4 of the studies reviewed, there was no difference in LOS between the groups [3,12,14,18]. Two of the studies however showed that patients managed with NOM had a longer LOS [16,17].

Days on total parenteral nutrition

There were 4 studies in which the length of time on total parenteral nutrition (TPN) was evaluated. One-hundred and seventy-nine patients were managed with NOM and 80 were managed with OM.

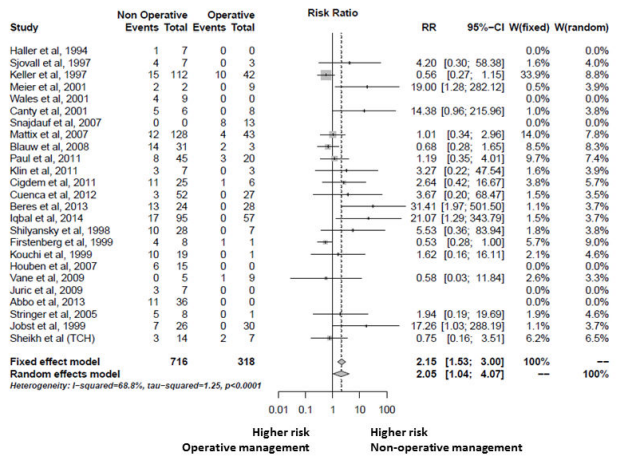

Figure 2 Forest plot comparing the incidence of pseudocyst formation between non-operative and operative management of pancreatic trauma.

A meta-analysis could not be performed giving the heterogeneity of the data. Table 3 summarizes the comparison between the groups. In two studies, patients in the NOM group had more days on TPN compared to those in the OM group [16,22]. However, Mattix et al. found the opposite in which patients undergoing NOM had shorter durations on TPN than those who were managed with OM [3].

Days to oral diet

There was only one study in which the time to full enteral diet was evaluated.

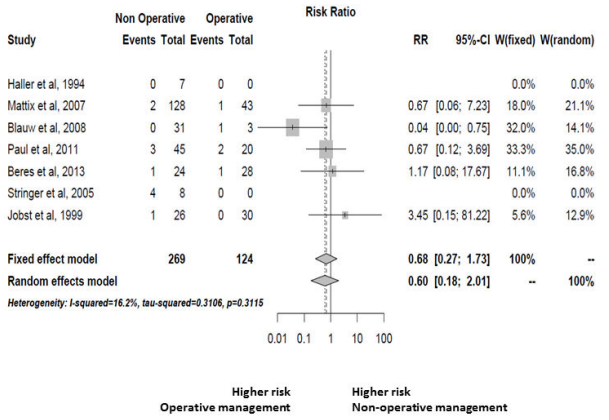

Figure 3 Forest Plot comparing the incidence of pancreatic fistula formation between no operative and operative management of pancreatic injuries in children.

In this study by Iqbal et al., 57 patients treated with OM achieved goal feeds faster than the 95 managed with NOM (7.8 ± 0.7 vs. 15.1 ± 2.5 days; p=0.001) [17].

Table 2 Comparison of length of stay between non-operative and operative management of pancreatic injuries in children.

	Non-operative				Operative			
Study	**Mean (days)**	**SD (days)**	**Median (days)**	**Total**	**Mean (days)**	**SD (days)**	**Median**	**Total**
Meier et al. [22]	6.00			2			11	9
Wales et al. [11]			24	9				0
Mattix et al. [3]	9.56	19.80		128	12.08	12.00		43
de Blaauw et al. [12]			24	31			29	3
Wood et al. [18]			17	29			13	14
Paul et al. [14]	14.20	12.80		45	16.00	13.40		20
Klin et al. [24]	8.33	6.71		7	10.50	3.50		3
Beres et al. [16]	27.50	19.80		49	15.10	8.40		28
Iqbal et al. [17]	15.10	24.40		95	11.90	7.50		57
Cigdem et al. [21]	26.50			25				6

Other complications

Four studies reported complications associated with the primary management of these patients [12,14,22,28]. Overall, there were more reported complications associated with OM compared to NOM. Patients who were treated with NOM had complications including central line infection (n=4) and venous thrombosis (n=1).

Patients managed with OM had complications including small bowel obstruction necessitating enterolysis (n=2), fascial dehiscence (n=1), superficial wound infection (n=1), pneumonia (n=1), pancreatic fistula (n=1) and prolonged ileus

(n=1). In the most recent multicenter retrospective review by Iqbal et al. "morbidity" was reported as higher in patients with high-grade injuries who underwent NOM; however, specific complications or morbidity measures were not defined [17].

Table 3 Comparison of days on total parenteral nutrition between non-operative and operative management of pancreatic injuries in children

Non-operative					Operative			
Study	Mean (days)	SD (days)	Median (days)	Total	Mean (days)	SD (days)	Median	Total
Meier et al. [22]	32.5	17.7		2	8.3			9
Wales et al. [11]			14					
Beres et al. [16]	21.8	18.9		49	7.9	7.6		28
Mattix et al. [3]	4.6			128	13.2			43

Discussion

Blunt pancreatic injury occurs when high-energy force is applied to the upper abdomen, crushing the retroperitoneal structures against the vertebral bodies and causing a spectrum of injury from minor contusion to complete transection. Computed tomography (CT) scan is the most common modality to identify a pancreatic injury, although grading can be challenging (especially in young children) as duct disruption is often unclear [35,36]. Other methods of evaluating ductal integrity are magnetic resonance cholangio pancreatography (MRCP) or endoscopic retrograde cholangio pancreatography (ERCP) [12,19]. Ductal integrity is so important because leakage of pancreatic enzymes can increase complications such as pancreatic ascites, persistent fluid collections called pseudocysts, and fistula formation [8]. Traditional teaching has always been to control duct leakage when possible. Injuries involving the pancreatic head (grades IV and V) may involve duct injury, but these injuries require complex operative management as there may be concomitant duodenal injury, and pancreatic resection requires a pancreatoduodenectomy, which not an ideal operation in the emergent is setting [8]. In children, as in adults, a variety of strategies are employed for these injuries, ranging from observation, drain placement, endoscopic stent placement and pancreatoduodenectomy, but these injuries are variable and are extremely rare [8]. In contrast, ductal transection from pancreatic body injuries (grade III) is more commonly seen in children as a result of direct epigastric force such from a handlebar or a hockey stick [4]. The pancreas is usually disrupted in a similar location overlying the spine and distal pancreatectomy with control of the proximal duct can be fairly easily performed.

In adults, distal pancreatectomy is the standard of care for grade III injuries [7,8]. In children, however, NOM was first described in the 1980s, which avoids a painful operation as well as a concomitant splenectomy (inadvertent or planned) [9], and since then there have been many reports of success with this strategy. Still, many pediatric surgeons prefer the operative approach, and differences of opinion commonly exist even among surgeons within the same practice. NOM of pancreatic trauma has not become as widely accepted as for spleen, liver and kidney trauma, as there are no known clear advantages to saving a portion of the pancreas, and complications can arise from observation. However, pancreatic endocrine function impairment following distal pancreatectomy in adults has recently been reported, which may translate to children, and serves to strengthen the argument of those who favor NOM [37].

Pediatric surgeons have attempted to compare outcomes among both approaches, but these have all been retrospective studies, and, as we have shown in this study, the results are mixed. Furthermore, the multicenter studies combined and compared outcomes from different institutions, but the way that patients for whom NOM are clinically managed varies widely; for instance, some surgeons keep the patients on parenteral nutrition for a prolonged period of time, others use jejunal feeds, and some use ERCP for stent placement. Furthermore, the way that pseudocysts are managed also varies, as some surgeons choose to percutaneously or endoscopically drain them whereas others withhold enteral feeds until spontaneous pseudocyst resolution. We recently demonstrated from a survey of pediatric surgeons that practice variability regarding NOM does exist (publication submitted). The outcomes reported in the majority of the multicenter study such hospital LOS and time on TPN is directly related to the clinical management for the patients managed with NOM. Therefore, the current evidence is difficult to interpret, and pediatric surgeons are still undecided about how to best manage these injuries. A Cochrane review on this same topic concluded that given the lack of randomized trials, there is no firm evidence to support either treatment strategy [38].

In this systematic review, we attempted to combine the reported outcomes from both approaches, but the reported parameters were so variable among the various studies that unfortunately metaanalysis could only be performed for two of the outcomes: pseudocyst and fistula development. We demonstrated that the risk of fistula formation following NOM and OM is similar, and the incidence is actually lower than expected based on the adult literature following distal pancreatectomy [8]. The risk of pseudocyst development is almost two-fold higher from NOM. This is not unexpected, as duct leakage often collects in a peripancreatic collection that can persist into a pseudocyst. Rates of pseudocyst formation

as high as 35% -44% in patients managed with NOM have been reported [14,20,21,24,25]. However, it should be noted that in all except one study [17], the definition of what was reported as a pseudocyst was not provided. Therefore, acute peripancreatic fluid collections identified via repeat imaging soon after pancreatic injury may have been labeled "pseudocysts", but may actually have resolved spontaneously within a short period of time and caused no adverse consequences to the patient.

The most obvious disadvantage of pseudocyst formation is increased length of time on enteral feeds, hospital stay, and time lost from school. However, no consistent correlation was noted between these outcomes and higher pseudocyst development among the studies we reviewed. Some studies showed no difference in LOS between both management strategies and others suggested that NOM is associated with longer LOS [16,17]. The studies also showed mixed results regarding the duration on TPN between those managed with NOM versus those managed with OM. In the only study that examined days to full oral feeds, patients managed with OM returned to oral feeds quicker than their NOM counterparts [17]. Time lost from school and quality of life following OM versus NOM has not been reported.

The main limitation of this systematic review is that all 25 of the included studies are retrospective. Furthermore, 7 did not include the grades of the pancreatic injuries that were being evaluated, and 11 included outcomes from grade I injuries. As such, it is likely that outcomes were compared between groups with mixed severity of pancreatic injury.

To our knowledge, this study is the first to systematically review the current literature on outcomes following NOM or OM of high-grade blunt pancreatic trauma in children. Although NOM is associated with greater risk of pseudocyst formation, current evidence does not suggest a difference in fistula formation, and the data from other adverse outcomes is too variable to compile. Simply a higher incidence of pseudocyst formation may not be worth the benefit of avoiding an operation. Therefore, we are unable to clearly demonstrate a clear advantage of either management strategy, or to affirm that there is no major clinical difference among the two. In essence, in children with grade III pancreatic injuries, pediatric surgeons are still left unsure about how to best manage these patients and how to counsel their parents. The results of this study highlight the necessity for a prospective, randomized trial to definitively establish guidelines regarding the optimal management of these injuries.

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