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Is necrosectomy obsolete for infected necrotizing pancreatitis? Is a paradigm shift needed?

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Abstract

In 1886, Senn stated that removing necrotic pancreatic and peripancreatic tissue would benefit patients with severe acute pancreatitis. Since then, necrosectomy has been a mainstay of surgical procedures for infected necrotizing pancreatitis (NP). No published report has successfully questioned the role of necrosectomy. Recently, however, increasing evidence shows good outcomes when treating walled-off necrotizing pancreatitis without a necrosectomy. The literature concerning NP published primarily after 2000 was reviewed; it demonstrates the feasibility of a paradigm shift. The majority (75%) of minimally invasive necrosectomies show higher completion rates: between 80% and 100%. Transluminal endoscopic necrosectomy has shown remarkable results when combined with percutaneous drainage or a metallic stent. Related morbidities range from 40% to 92%. Single-digit mortality rates have been achieved with transluminal endoscopic necrosectomy, but not with video-assisted retroperitoneal necrosectomy series. Drainage procedures without necrosectomy have evolved from percutaneous drainage to transluminal endoscopic drainage with or without percutaneous endoscopic gastrostomy access for laparoscopic in-

struments. Most series have reached higher success rates of 79%-93%, and even 100%, using transcystic multiple drainage methods. It is becoming evident that transluminal endoscopic drainage treatment of walled-off NP without a necrosectomy is feasible. With further refinement of the drainage procedures, a paradigm shift from necrosectomy to drainage is inevitable.

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Key words: Delay until liquefaction; Infected necrotizing pancreatitis; Minimally invasive treatment; Transluminal endoscopic drainage/necrosectomy; Walled-off pancreatic necrosis

Core tip: A shift from early, prompt surgical necrosectomy to delay until liquefaction has become the global consensus for treatment of infected necrotizing pancreatitis, which allows drainage procedures and minimally invasive techniques to play a more important role before definitive surgery. Success rates of 80% and single-digit mortality rates are reported with transluminal endoscopic drainage and irrigation with a percutaneous gastrostomy access route. Zero mortality using transluminal endoscopic drainage without a necrosectomy can be achieved. A paradigm shift from necrosectomy to drainage for the treatment of walled-off necrotizing pancreatitis should be considered.

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INTRODUCTION

Bradley^[1] described the original 19th-century dispute

between Senn and Fitz concerning the value of necrosectomy for necrotizing pancreatitis (NP). In 1886, Senn^[2] claimed that removing necrotic pancreatic and peripancreatic tissue would be beneficial for patients with severe acute pancreatitis (AP). Fitz^[3], however, was convinced that the prognosis of an individual episode of AP was determined only by the pathologic findings and not based on whether surgical debridement had been performed. But even Fitz^[4], who initially considered the operation useless and hazardous, later suggested that the “the sooner the operation was carried out, the better for patients with AP”. Until about 1925, Senn’s views held sway, and debridement was common practice before AP surgery. Moynihan^[5] expressed the prevailing surgical opinion of the time: “Recovery from the disease, apart from operation, is so rare that no case should be left (surgically) untreated. However, few survived surgical intervention. After the development of an amylase assay, the therapeutic pendulum swung away from surgery toward nonsurgical management and surgical intervention was contraindicated. Even though this conservative approach spared the majority of patients with mild or moderate AP surgical intervention, many patients with severe AP still died. In an attempt to confront persistent high mortality rates from nonsurgical management of severe AP, the concepts of surgical approaches were advocated and surgical mortality often exceeded 50%”.

Since then, the rationale of AP surgery evolved from exploratory laparotomy to total pancreatectomy in severe AP in the late 1960s and 1970s, to early immediate surgical intervention in the 1980s when the pancreas was proved to be infected, to the notion, in 1993, of 100% mortality if AP was treated non-operatively^[6], to the present concept, expressed in 2007, that patients with severe NP complicated with infection benefit from delayed necrosectomy and drainage^[7].

Surgical necrosectomy was the mainstay of NP treatment a decade ago, especially when non-surgical approaches failed. However, from serendipitous antibiotic treatment for infected NP^[8], non-surgical therapy for sterile NP^[11], and no debridement with minimally invasive left-flank drainage^[9], to the dual drainage of endoluminal and percutaneous approaches^[10], more evidence has been reported for successful treatment of infected NP (INP) without a necrosectomy. This resurrects the same question 125 years later by the author and by Smadja and Bismuth: Is necrosectomy a “useless and hazardous approach” for AP^[11]? The same dispute occurred between Bradley^[12] and Warshaw^[13] over sterile NP but not INP. Bradley concluded: “However, surgical debridement and drainage remains the preferred approach for infected pancreatic necrosis despite occasional anecdotal reports of successful management by transcutaneous or endoscopic means”.

Currently, the management of NP has undergone a paradigm shift toward minimally invasive techniques for necrosectomy, obviating the need for open necrosectomy in most cases^[14]. There is increasing evidence that mini-

minally invasive approaches, including a step-up approach that incorporates percutaneous catheter or endoscopic transluminal drainage followed by video-assisted retroperitoneal or endoscopic debridement^[15], are associated with improved outcomes over traditional open necrosectomy for patients with INP. A recent international multidisciplinary consensus conference emphasized the superiority of minimally invasive approaches over standard surgical approaches^[16]. A minimally invasive necrosectomy is still used, according to most reports. Recently, increasing evidence on the efficacy of endoscopic technique includes reports of successes without a necrosectomy when treating NP, which raises the same old question of whether necrosectomy is obsolete.

Purpose: Author’s questions

Is necrosectomy mandatory for treating NP? Can we avoid it? If necrosectomy can be avoided, then a paradigm shift may allow us to move toward minimally invasive drainage procedures. Our aim is the same as Traverso and Kozarek^[17], who stated that the word “necrosis” induces a “knee-jerk” response to perform necrosectomy. They claimed that, given time, the necrosis would dissolve (“necrolyse”) or become infected. Even though INP indicates surgical debridement in most medical centers worldwide, they first perform percutaneous drainage, which, they say, has “drastically lowered the need for pancreatic necrosectomy to less than 10%” and the mortality rate to “single digits”.

Data collection

The outcomes of NP, primarily INP, treated using conservative treatment, open necrosectomy, interventional drainage, and minimally invasive methods that were reported after 2000 were reviewed. Morbidity, mortality, reoperation rate, pancreatic fistula rate (for surgery), endoscopic sessions, completion rate for endoscopic methods, and the success rate for drainage methods were compared to see whether there has been a paradigm shift from surgery to minimal invasive-especially drainage-alternatives.

Outcomes

Even for INP, completely conservative treatment (Table 1) with antibiotics without mortality was possible in three reports^[8,18,19]. Surgery could be avoided in 67.0%-87.5% of cases. For sterile NP, the mortality of conservative treatment remained between 0% and 15.3% (Table 1), which is the same as reported before 2000.

Despite some studies’ reports of single-digit mortality using surgical necrosectomy^[20-23], high mortality (20.0%-63.9%) is reported in the majority of series (Table 2). Except in a few centers, surgical outcome has not changed much, and the surgical risk is high. A nationwide study in the United States of 1783 patients from 1998 to 2010 indicated that the incidence of pancreatic debridement significantly decreased from 0.44% to 0.25% and that in-hospital mortality (overall 22.0%) significantly de-

Table 1 Results of nonsurgical or conservative treatment for necrotizing pancreatitis published mainly after 2000

Ref.	Year	Cases (n)	Type (Intend)	Morbidity (%)	Reoperation rate (%)	Mortality (%)	Remark
Sterile							
Bradley ^[1]	1991	40	Nonsurgical			10.0	
Uomo <i>et al</i> ^[61]	1996	146	Nonsurgical			9.5	1984-1993
Baril <i>et al</i> ^[20]	2000	26	Antibiotics		0	7.0	1993-1997
Büchler <i>et al</i> ^[62]	2000	56	Conservative			1.8	Two false negatives excluded
Zerem <i>et al</i> ^[41]	2009	20	Conservative		15.0	0.0	Randomized controlled study
Garg <i>et al</i> ^[54]	2010	137	Conservative			15.3	1997-2008
van Santvoort <i>et al</i> ^[18]	2011	386	Conservative			7.3	21 Dutch hospitals
Babu <i>et al</i> ^[46]	2013	14	Conservative			7.0	Step-up; one INP
Infected							
Dubner <i>et al</i> ^[8]	1996	3	Antibiotics	0	0	0.0	Unstable or refused surgery
Baril <i>et al</i> ^[20]	2000	6	Antibiotics		0	33.0	1993-1997
Runzi <i>et al</i> ^[63]	2005	16	Antibiotics	62		12.5	
Lee <i>et al</i> ^[19]	2007 ¹	8	Antibiotics	0	0	0.0	
Garg <i>et al</i> ^[54]	2010 ¹	71	Conservative or PCD			25.4	1997-2008
van Santvoort <i>et al</i> ^[18]	2011	11	Antibiotics	0	0	0.0	21 Dutch hospitals
Sterile + infected							
Büchler <i>et al</i> ^[62]	2000	58	Conservative			5.0	Two false negatives
Garg <i>et al</i> ^[54]	2010 ¹	208	Medical			18.8	1997-2008

¹Non-randomized controlled study. INP: Infected necrotizing pancreatitis; PCD: Percutaneous drainage.

creased from 29.0% to 15%^[24].

In the majority (75%) of the included series on minimally invasive necrosectomy report higher completion rates between 80%-100%^[10,25-38] (Table 3). Minimally invasive necrosectomy, mainly transluminal endoscopic necrosectomy (TEN) with drainage, has shown remarkable results combined with percutaneous drainage (PCD)^[10,26,29,34] or using a metallic stent^[28,32]. Related morbidities ranged from 40% to 92%^[11,26,30,33,34,36,39,40]. Single-digit mortality rates have been achieved in the majority of the TEN groups, but not in the video-assisted retroperitoneal drainage group. The percutaneous endoscopic gastrostomy access route was used in three series^[25,32,34] (Table 3).

The success rate of PCD varies (Table 4). Some series^[41-43] report that it remains unchanged at 35%-49%, but most^[17,19,20,41] have reached a higher success rate of 76%-93%. The transluminal endoscopic drainage (TED) rates are about 80%^[19,44], and even 100%^[45] when using single transluminal gateway transcystic multiple drainage methods. Single-digit mortality was reported in most series^[19,20,41,44-47], and zero mortality is a reality^[19,20,41,45,47].

DISCUSSION

The pathophysiology of AP is usually divided into three phases. In phase one, trypsin is prematurely activated pancreatic acinar cells, which synthesize, store, and secrete digestive enzymes. Once trypsin is activated, it activates a variety of harmful pancreatic digestive enzymes. In phase two, intrapancreatic inflammation occurs through a variety of mechanisms and pathways. In phase three, extrapancreatic inflammation, including acute respiratory distress syndrome occurs, which is often fatal. In about 80% of patients, AP is mild; however, in 10%-20%, the pathways that contribute to increased intrapancreatic and extrapancreatic inflammation lead to

systemic inflammatory response syndrome, a complex response to infection, trauma, burns, pancreatitis, and a variety of other injuries. In some instances, systemic inflammatory response syndrome predisposes a patient to multi-organ dysfunction, pancreatic necrosis, or both^[7]. The following precepts have been proposed over the past 130 years: (1) 1886, removing necrotic pancreatic and peripancreatic tissue is beneficial for patients with severe AP^[2]; (2) 1889, the sooner surgery is done, the better for patients with AP^[3]; (3) 1925, recovering from AP without surgery is rare; thus, no patient with AP should be surgically untreated^[5]; (4) 1993, the mortality in non-operatively treated patients approaches 100%^[6]; (5) when the pancreas is infected, surgery is mandatory; (6) when the pancreas is infected, early necrosectomy and drainage are recommended; (7) delay until demarcation (used for the era of open necrosectomy to delay the operation timing and to spare the viable pancreatic tissue from being sacrificed during debridement); and (8) 1996, surgical debridement is rarely necessary in sterile pancreatic necrosis^[1].

There is no reason to use immediate surgery for patients with mild AP. Infected pancreatic necrosis, however, is an indication for surgical intervention. Approximately 20% of patients develop NP, which has a mortality rate of 15%. The major cause of death, in addition to early organ failure, is extrapancreatic infection or infectious pancreatic necrosis, which leads to sepsis and multi-organ failure. Secondary infection of pancreatic necrosis develops in approximately 30% of patients with necrosis, which increases the mortality rate to approximately 39%. Infected necrosis is virtually always an indication for intervention^[48]. Surgery within the first 14 d of the onset of INP should be avoided because early surgery is associated with increased mortality^[49]. The conventional management of INP is open surgical debridement. Other surgical approaches have been used,

Table 2 Results of surgical necrosectomy for necrotizing pancreatitis published mainly after 2000

Ref.	Year	Cases (n)	Type (Intend)	PF (%)	Morbidity (%)	Reoperation rate (%) or n/patient	Mortality (%)	Remark
Sterile								
Baril <i>et al</i> ^[20]	2000	1	Open	0.0	0.0	0.0	0.0	1993-1997
Büchler <i>et al</i> ^[62]	2000	1	Closed+irrigation	?		?	100.0	
Rau <i>et al</i> ^[64]	2005	142	Closed+irrigation	23.0	61.0	43.0	23.0	1992-2001
Howard <i>et al</i> ^[21]	2007	23	Planned re-lap		78.0	30.0	9.0	Symptomatic
Garg <i>et al</i> ^[54]	2010	9	Closed+irrigation	> 30.0			55.5	1997-2008
Infected								
Baril <i>et al</i> ^[20]	2000	11	Open	NA	91.0	45.5	9.0	1993-1997
Büchler <i>et al</i> ^[62]	2000	27	Closed+irrigation	29.0		22.0	18.5	two un-OP excluded
Rau <i>et al</i> ^[64]	2005	140	Closed+irrigation	30.0	78.0	27.0	27.0	1992-2001
Howard <i>et al</i> ^[21]	2007	66	Surgery		86.0	33.0	15.0	
Garg <i>et al</i> ^[54]	2010	36	Closed+irrigation		63.0		63.9	1997-2008
van Santvoort <i>et al</i> ^[15]	2010	45	Closed+irrigation	38.0	69.0	31.0	16.0	RCT; one operation, 42%; 33% need PCD
		24	VARD		65.0		17.0	
van Santvoort <i>et al</i> ^[18]	2011	78	VARD/TEN/OP		64.0		18.0	21 Dutch hospitals
Babu <i>et al</i> ^[46]	2013	27	Closed+irrigation	22.2	51.9	22.2	40.7	Step-up
Sterile + infected								
Smadja and Bismuth ^[11]	1986	12	Surgery, early				100.0	
		15	Surgery, late				27.0	
		11	Surgery, elective				0.0	
Connor <i>et al</i> ^[39]	2005	47	Closed+irrigation		95.0		39.0	81% infected
Olakowski <i>et al</i> ^[65]	2006	144	Open packing		43.0	3-8/patient	21.0	83% infected
Nieuwenhuijs <i>et al</i> ^[66]	2003	38	Open packing	21.0	89.0	3-70/patient	47.0	
		21	Closed+irrigation	14.0	44.0	0-3/patient	33.0	
Reddy <i>et al</i> ^[40]	2006	118	Closed+irrigation	36.0	58.0		38.1	65.3% infected
Howard <i>et al</i> ^[21]	2007	102	Planned re-lap					
	(1993-2001)	59		49.0	89.0	67.0	18.0	76% infected
	(2002-2005)	43		60.0	72.0	68.0	4.0	72% infected
Rodriguez <i>et al</i> ^[67]	2008	167	Closed packing	50.0		11.0	11.0	72% infected
Garg <i>et al</i> ^[54]	2010	45	Closed+irrigation				48.9	1997-2008
Babu <i>et al</i> ^[68]	2010	28	PCD + surgery				22.0	2000-2008
Doctor <i>et al</i> ^[22]	2011	61	Open + laparoscopy (re-OP 8%)	50.8			9.8	1998-2009; 83.6% INP
Bausch <i>et al</i> ^[50]	2012	30	Closed+irrigation	16.7	90.0	73.3	63.3	83.3% infected
Madenci <i>et al</i> ^[23]	2014	68	Closed packing	74.2	> 74.2	14.7	8.8	2006-2009; 63% infected
Wormer <i>et al</i> ^[24]	2014	1783	Surgical debridement				22.0	1998-2010; nationwide

INP: Infected necrotizing pancreatitis; OP: Operation; PCD: Percutaneous drainage; PF: Pancreatic fistula; RCT: Randomized control study; Re-lap: Re-laparotomy; TEN: Transluminal endoscopic necrosectomy; un-OP: Not operated on; VARD: Video assisted retroperitoneal debridement.

including single-stage and multistage methods with a variety of drainage and closure techniques. Necrosectomy is a relatively standardized technique used with a variety of methods to control drainage, for example, marsupialization of the lesser sac, wide closed-suction drainage, continuous lavage of the septic cavity, and a planned repeat necrosectomy with a delayed primary closure. Less invasive methods have also been reported, namely, using laparoscopic techniques and equipment along the track of existing percutaneous drains^[49].

The term and concept of “delay until liquefaction” was developed by the author^[9] for minimally invasive drainage from the left flank without debridement. Typically, at least three weeks is needed for liquefaction of the retroperitoneal and peripancreatic tissue to reach the left flank. This permits a sump drain to be inserted from the left flank to the pancreatic head area without opening the abdomen. This strategy is currently commonly used for the timing of delayed management with open or

minimally invasive approaches for drainage and necrosectomy^[7]. Walling-off the liquefied necrotic tissue that has formed a secure attachment to the gastric or duodenal wall enables endoscopic drainage with or without a necrosectomy from the stomach, duodenum, or left retroperitoneum. A prolonged delay may cause unnecessary adverse events.

Consensus ON NP

Several important points were established at a one-day meeting held in conjunction with the annual meeting of the American Pancreatic Association in 2010^[16]: (1) sterile acute necrotic collections almost never require intervention early in the course of disease, and in the later phase (*i.e.*, after several weeks), only if there are disabling symptoms, such as abdominal pain, significant mechanical obstruction (*e.g.*, a gastric or biliary outlet), or both; (2) infected acute necrotic collections may occasionally require early intervention, but because early open surgery is

Table 3 Results of minimal invasive necrosectomy for walled-off necrotizing pancreatitis published after 2000

Ref.	Year	Cases (n)	Type (Intend)	Sessions ¹	Completion rate (%)	Morbidity (%)	Reoperation rate (%)	Mortality (%)	Remark
Infected									
Raczynski <i>et al</i> ^[25]	2006	2	TEND + irrigation	3	100.0	0.0	0.0	0.0	2 PEG (1st report?)
Escourrou <i>et al</i> ^[26]	2008	13	TEND + irrigation	1-3	100.0	46.0	0.0	0.0	+ PCD × 2
Bala <i>et al</i> ^[27]	2009	8	Lt RPD + N+ irrigation	3-17	87.5	25.0		12.5	Stepped
Antillon <i>et al</i> ^[28]	2009	1	TEN + stent		100.0	0.0	0.0	0.0	Transgastrostomy; Foley irrigation
Will <i>et al</i> ^[29]	2012	18	TEN ± PCD	3-8	100.0	16.6	0.0	0.0	One unrelated death
Bakker <i>et al</i> ^[30]	2012	10	TEND	2-6	100.0	20.0	0.0	10.0	RCT; 10% PF
		10	VARD/Lap	1-2	40.0	80.0	60.0	40.0	70% PF
Castellanos <i>et al</i> ^[31]	2013	32	VARD	1.0	100.0	9.3	0.0	15.6	
Sarkaria <i>et al</i> ^[32]	2014	17	TEN + Stent ± PEG-J + irrigation	5.3	88.0	5.9	11.8	0.0	8 PEG-J
Sterile + infected									
Connor <i>et al</i> ^[39]	2005	47 (NS)	Lt. RPD + N	1-9		92.0		19.0	81% INP
Voermans <i>et al</i> ^[33]	2007	25	TEND + irrigation	NA	92.0	40.0	4.0	0.0	76% NP
Papachristou <i>et al</i> ^[34]	2007	53	TEND ± PCD ± PEG + irrigation	3	81.0	49.0	22.6	6.0	49% INP
Seifert <i>et al</i> ^[35]	2009	93 (NS)	TEND	6	80.0	26.0	11.8	7.5	1999-2005
Raraty <i>et al</i> ^[36]	2010	137 (NS)	VARD			75.0		19.0	64% INP
van Santvoort <i>et al</i> ^[15]	2010	43 (NS)	Lt. RPD + N (Step-up)	1-7	35.0	40.0	60.0	19.0	RCT
Gardner <i>et al</i> ^[37]	2011	104	TEND	1-14	91.0	14.0	2.0	2.0	39% INP
Bausch <i>et al</i> ^[50]	2012	30	PCD + N		57.0	43.0	21.0	21.0	93% INP
		18	TEND		50.0	44.0	28.0	6.0	72% INP
Ross <i>et al</i> ^[10]	2014	117	TEND + PCD	NA	100.0	4.2	0.0	3.4	Dual modality
van Brunschot <i>et al</i> ^[38]	2014	455 (NS)	TEN ± PCD	4 (1-23)	81.0	36.0	10.0	6.0	Systematic review; 57% INP

¹Values are mean or range. INP: Infected necrotizing pancreatitis; Lap: Laparotomy; N: Necrosectomy; NA: Not available; NS: Walled-off necrosis was not specified; PF: Pancreatic fistula; PCD: Percutaneous drainage; PEG-J: Percutaneous endoscopic gastrostomy-jejunal arm; RCT: Randomized control study; RPD: Retroperitoneum percutaneous endoscopic gastrostomy; TEN: Transluminal endoscopic necrosectomy; TEND: Transluminal endoscopic necrosectomy with drainage; VARD: Video assisted retroperitoneal debridement; WON: Walled-off necrosis.

associated with high morbidity and mortality, it should be avoided whenever possible. Instead, radiologic or endoscopic drainage should be used before surgery to treat the infection and to postpone or obviate the need for surgical debridement; (3) intervention by any method is optimal when infected necrosis is walled-off and demarcated with at least partial liquefaction and discrete encapsulation. This typically requires a delay of four to six weeks; (4) asymptomatic walled-off necrosis (WON) does not require intervention regardless of the size and extension of the collection; it may eventually resolve spontaneously, even in rare cases of infected necrosis; and (5) symptomatic WON generally requires intervention late in the course (*i.e.*, after four weeks) if there is intractable pain, visceral obstruction (*e.g.*, the stomach or bile duct), or infection.

2013 updated guideline

The optimal management of NP continues to evolve. A 2013 guideline published by the American College of Gastroenterology regarding debridement of necrosis and minimally invasive management of pancreatic necrosis states that the mortality of infected necrosis was falsely believed to be almost 100% in patients with INP not

given immediate surgery^[48]. There is ample evidence that antibiotic treatment alone can resolve the infection and, in some patients, preclude surgery. Therefore, the notion that immediate surgery is necessary for patients with INP is no longer valid. Asymptomatic pancreatic and extra-pancreatic necrosis do not require intervention regardless of size, location, and extension, because they are likely to spontaneously resolve, even if infected^[16]. Unstable patients with infected necrosis should undergo urgent debridement. However, the current conventional wisdom is that INP in clinically stable patients should be managed with antibiotics before surgery^[16]. If the infected necrosis does not resolve, minimally invasive necrosectomy or open surgery is recommended once the necrosis is walled-off. Currently, a multidisciplinary consensus favors minimally invasive methods over open surgery to manage NP^[16]. A randomized controlled trial clearly showed that endoscopic debridement is a better strategy than surgery^[30]. Despite advances in surgical, radiologic, and endoscopic techniques, it is necessary to know that many patients with sterile pancreatic necrosis, and some patients with infected pancreatic necrosis, clinically improve sufficiently that they need no surgical intervention.

Table 4 Results of drainage without minimal invasive necrosectomy for necrotizing pancreatitis published mainly after 2000

Ref.	Year	Cases (n)	Type (Intend)	Sessions ¹	Success rate (%)	Morbidity (%)	Reoperation rate (%)	Mortality (%)	Remark
Sterile									
Baril <i>et al</i> ^[20]	2000	13	PCD		92.3		7.7	0.0	
Zerem <i>et al</i> ^[41]	2009	20	Conservative	1.5			15.0	0.0	RCT
		20	PCD	1.4	85.0		15.0	5.0	
Infected									
Freeny <i>et al</i> ^[52]	1998	34	PCD	3.3	47.0	26.0	53.0	12.0	
Baril <i>et al</i> ^[20]	2000	25	PCD	1.4	76.0	8.0	18.0	8.0	
Baron <i>et al</i> ^[44]	2002	38	TED + irrigation	2.0 (1-6)	79.0	NA	18.0	5.0	
Lee <i>et al</i> ^[19]	2007	18	WON PCD + irrigation		83.3	11.0	16.7	5.6	Non-RCT; 32% PF
		5	TED		80.0		20.0	0.0	6% PF
Bruennler <i>et al</i> ^[42]	2008	80	PCD	(1-14)	43.0	29.0	25.0	34.0	1999-2004; 10 + PCN
Mortelé <i>et al</i> ^[43]	2009	35	PCD	3.3	49.0	11.0	37.0	17.0	
van Santvoort <i>et al</i> ^[18]	2011	130	PCD	NA	35.0	42.0	58.0	20.0	21 Dutch hospitals
Mukai <i>et al</i> ^[45]	2014	5	WON SGTMD		100.0	0.0	0.0	0.0	
Sterile + infected									
Traverso <i>et al</i> ^[17]	2005	73	PCD	NA	79.0			11.0	
Chang <i>et al</i> ^[9]	2006	19	WON MIS Lt. flank	1.0	84.2	10.5	5.2	15.8	80% INP
Babu <i>et al</i> ^[46]	2013	29	PCD; step-up			20.0		6.8	86% INP
Varadarajulu <i>et al</i> ^[47]	2011	48	WON TED		52.1	10.4	35.4	6.5	
		12	WON MTGT		91.7	0.0	0.0	0.0	

¹Values are mean or range. INP: Infected necrotizing pancreatitis; MIS: Minimal invasive surgery; MTGT: Multiple transluminal gateway technique; NA: Not available; PCD: Percutaneous drainage; PCN: Percutaneous necrosectomy; PF: Pancreatic fistula; RCT: Randomized control study; SGTMD: Single transluminal gateway transcystic multiple drainage; TED: Transluminal endoscopic drainage; WON: Walled-off necrosis.

Minimally invasive necrosectomy

Although minimally invasive approaches are currently advocated, they still have some related morbidity and mortality^[30,50]. Bausch *et al*^[50] compared the outcomes of minimally invasive retroperitoneal necrosectomy ($n = 14$) and endoscopic transgastric necrosectomy ($n = 18$) with the outcomes of open necrosectomy ($n = 30$). Postoperative problems were ongoing sepsis (29%, 11%, and 73%, respectively) and bleeding that required intervention (21%, 17%, and 26%, respectively). A specific complication of endoscopic transgastric necrosectomy was gastric perforation into the peritoneal cavity during the procedure (28%), which required an immediate open pseudocystogastrotomy. A laparotomy was necessary in 21% of the patients after minimally invasive retroperitoneal necrosectomy and 28% after endoscopic transgastric necrosectomy because of specific complications or a persistent infection. The overall mortality rates were 21% and 6% after minimally invasive retroperitoneal and endoscopic transgastric necrosectomy, respectively, and significantly higher at 63% after open necrosectomy. Bausch *et al*^[50] concluded that morbidity and mortality remained high in acute NP, and that surgery should be delayed as long as possible to reduce them. Minimally invasive procedures can preclude laparotomy, but they can also cause specific complications that require immediate or secondary open surgery.

Bausch *et al*^[50] also found a lower mortality in the TEN group than in the minimally invasive retroperitoneal necrosectomy group, which is similar to what is shown in Table 3. Bakker *et al*^[30] reported that the TEN group had significantly reduced proinflammatory responses, complications (20% *vs* 80%), new-onset multiple organ failure (0% *vs* 50%) and pancreatic fistulas (10% *vs* 70%)

compared to the video-assisted retroperitoneal drainage group. One gastric and one large intestine perforation occurred after video-assisted retroperitoneal drainage.

Ross *et al*^[10] stated that “each treatment modality described for this application is a variation on a common theme—drainage of liquefied necrosis and debridement of necrotic tissue, either mechanically or by flushing and the passage of time”. The key to complete evacuation of necrotic material is creating a large access opening to the cavity^[33]. However, related complications such as bleeding, perforation, fistula, and embolism are inevitable^[26,33,53,57,58]. TEN needs to be used with caution, ideally in an interdisciplinary approach and within clinical trials.

Drain first, but do it better

Earlier results of open or percutaneous drainage were not comparable with the open surgical necrosectomy with drainage procedure, and did not become the standard treatment of choice for INP.

In 2011, Windsor proposed “drain first, but do it better” for INP^[51]. He pointed out that open necrosectomy is not the standard of care in many leading centers and is not an absolute requirement for INP. He concluded that PCD can be the only treatment for some patients with INP, which avoids an unnecessary necrosectomy. However, it has not yet been determined whether PCD is best used when infection is suspected or confirmed, nor has it been established when PCD can be delayed. Some interventional radiologists have long advocated primary PCD, but it has not been widely adopted^[52]. This might soon change, however: 56% of patients—those with sterile NP and those with INP—did not require a surgical necrosectomy after PCD, according to one review^[53]. The role

of PCD as the only treatment for INP needs additional evaluation so that it can be done better.

Ross *et al*^[10] discussed a key point of “how to do it better”, which is “the entry of the catheter into the collection was directed toward the dependent portion of the collection so that gravity could assist in drainage”. The entry is therefore the left flank. Another key point is a large caliber drain and a big skin outlet. The author^[9] used a 3-5 cm left-flank incision to enable the one-time insertion of a large-caliber sump drain directly through a liquefied route to the pancreatic head area where the drain was fixed on one side of the skin but the wound was kept open to enable the liquefied discharge to freely flow along the drain in case the drain lumen was obliterated by the debris. The open wound was pouched using a colostomy bag.

Garg *et al*^[54] concluded that with medical management (conservative + PCD), surgery could be avoided in 76.6% patients. Other studies gave an even higher estimate (approximately 83%; Table 4). However, PCD alone failed in a significant proportion of patients^[18,42,43,52] and a higher mortality rate has been reported^[42].

TED and necrosectomy have been enormously pivotal in complementing the complete management of NP during this paradigm shift of intervention timing from prompt surgical debridement to delay until liquefaction. Promising results have been published. A step-up technique after a PCD failure is, it seems, the best way to “do it better.” Repeated TEN^[33] or TEN + TED showed an 80%-100% success rate (Tables 3 and 4); however TED is preferred because it avoids some complications of TEN.

Drainage with minimally invasive necrosectomy from transluminal endoscopy with or without a stent or from a trans-PCD sinus tract has its specific morbidities. The old important question of whether the necrosectomy is required^[5,11] still remains unanswered. Can a “drain only” strategy further reduce these morbidities but maintain the same outcomes? With the progressive evolution of a multiple transluminal gateway technique for TED^[47], single transluminal gateway transcystic multiple drainages^[45], or dual modality drainage^[10], albeit in only a few case series, allow 100% success when drainage without a necrosectomy is used to treat NP^[10,43].

A transgastrostomy endoscopic procedure reported in 1993^[55] (Table 3^[25,28,32,34]) provides another feasible and easier access to further simplify the treatment. A double percutaneous endoscopic gastrostomy technique developed by Raczynski *et al*^[25] was demonstrated as an inspiring tool. The author suggests a “one or two double-lumen transgastrostomy tube with jejunal arm method^[32,56]” to offer jejunal feeding using a nasogastric tube, if needed, before the “delay until liquefaction” period, and an endoscopic or endoscopically assisted route for drainage later during the walled-off period. Creating a large access opening to the cavity to complete evacuation of necrotic material is essential^[32]. One Foley tied with Penrose drains or two Foley drains keep the access open and offer irrigation.

Surgery: A last resort

Within the last decade, TEN and TED have probably replaced most surgical roles in the treatments of walled-off NP except for the disconnected pancreatic duct syndrome (DPDS)^[17]. DPDS is characterized by evidence of a main pancreatic duct cutoff, an inability to access the upstream pancreatic duct during an endoscopic retrograde cholangiopancreatogram, and computed tomography evidence of viable pancreatic tissue upstream (toward the spleen), in association with a persistent non-healing pancreatic fistula or pancreatic-fluid collection, despite a course of conservative medical management^[57]. DPDS is an increasingly recognized complication of severe AP and abdominal trauma, with reported prevalence rates that range from 10% to 31%. However, these figures are most representative of highly select populations of severe AP in tertiary hospitals; the prevalence in all cases of AP remains unknown^[58]. Although surgical management had been the consensus^[59], there have been reports of success with initial endoscopic treatment^[57]; 19/26 patients showed long-term improvement, seven required surgery after treatment failed, the other five underwent immediate surgery: mortality was 0%. Sarkaria *et al*^[32] included four DPDS patients for a series in which they used esophageal stents to treat walled-off pancreatic necrosis. Complete resolution was achieved in 15/17 patients (88%). Two patients not specified as having DPDS required surgical intervention after endoscopic treatment failed. At least two of their patients did not need surgical rescue for DPDS. More effort should be focused on DPDS in the era of transluminal endoscopic treatment.

Necrosectomy: Obsolete

The answer to “will necrosectomy be obsolete?” is now much more positive. A paradigm-shift from a surgical to a non-surgical approach, or to drainage as proposed by Windsor^[57], whether the necrosis is infected or sterile, is waiting for additional randomized studies. Although not significantly different, endocrine (diabetes) and exocrine insufficiency were lower in the endoscopic drainage group than in the surgery group^[60]. Unnecessary necrosectomy procedures for the risky disease of NP should be prevented^[5,17] and surgical management should be used as a last resort.

CONCLUSION

With the recent successful outcomes of pure endoscopic and complementary endoscopic treatments for failed PCD, it is clear that drainage without a necrosectomy is feasible and should be the first choice of treatment for symptomatic sterile or infected walled-off NP and peripancreatic fluid collection. A paradigm shift from necrosectomy to drainage for the treating NP should be considered to eliminate potential complications.

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