In patients with alcohol-related chronic pancreatitis, what is the safety and efficacy of a) coeliac access block vs medical management b) thoracoscopic splanchnicectomy vs medical management c) coeliac access block vs splanchnicetomy, in improving patient outcomes?
 In patients with alcohol-related chronic pancreatitis, what is the safety and efficacy of a) surgery vs medical management b) endoscopic interventional procedures vs medical management c) surgery vs endoscopic interventional procedures?

3) In patients with alcohol-related chronic pancreatitis, does early versus late a) coeliac access block b) splanchnicetomy c) endoscopic interventional procedures d) surgery improve patient outcomes?

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of	Outcome measures	Source
	level	patiento						funding
Cahen DL,	1++ RCT	N=39	Patients with chronic	Endoscopic	Surgery	Median	Pain	AstraZeneca
Gouma DJ, Nio			pancreatitis	treatment		24	Complications	
Y et al.		Lost to			Operative	months	Exocrine and	
Endoscopic		follow-up:	Inclusion criteria: diagnosis	Endoscopic	pancreaticojejunostomy		endocrine sufficiency	
versus		One	based on clinical symptoms	transampullary			Length of stay	
surgical		patient	and morphologic changes	drainage of the	N=20			
drainage of the		lost at 6	detected by imaging studies;	pancreatic duct				
pancreatic		mths	pancreatic functional		18 underwent a			
duct in chronic		(surgery)	insufficiency; or both	N=19	pancreaticojejunostomy.			
pancreatitis.[s								
ee comment].		Study	Obstruction of the pancreatic	Median number of	1 patient had a Whipple			
New England		terminated	duct as determined by	procedures 5	procedure			
Journal of		early due	imaging					
Medicine.		to interim		Pancreatic-duct	1 patient underwent Frey's			
2007;		analysis	Severe, recurrent pancreatic	obstruction was	procedure for stone			
356(7):676-684.		reporting	pain insufficiency relieved by	caused by a	extraction			
Ref ID: 2024		а	non-narcotic analgesics or	combination of				
		significant	requiring opiates	strictures and stones in	All anastomoses remained			
		difference		15/19 (79%), by stones	patent during follow-up			
		favouring	Exclusion criteria Age < 18 or	alone in 3/19 (16%)	(technical success rate			
		surgery	> 80 yrs	and by strictures alone	100%) as demonstrated by			
			Enlargement of the	in 1/19 (5%)	magnetic resonance			
			pancreatic head > 4 cm		cholangiopancreatography			

	Previous pancreatic surgery	16/18 complete stone	performed three months		
	Suspected pancreatic cancer	extraction (89%), 11/16	after surgery and during		
	Life expectancy < 2 yrs	multiple stones	episodes of pain		
		·			
	Patient population:	N=10 single lithotripsy			
	Endoscopy: mean age 52	session			
	yrs, male sex 58% alcohol				
	abuse 47%, pain-continuous	N=6 multiple session			
	63%, pain-intermittent 37%,				
	Izbicki pain score mean 73	Median number of			
	(range 0 to 100), duration of	session per patient one			
	symptoms 16 mths, SF-36				
	quality of life scores: physical	16/19 (84%)			
	mean 31, mental health	pancreatic-duct			
	mean 33, exocrine	strictures, all of which			
	insufficiency 68%, endocrine	were distally located			
	insufficiency 21%				
		Balloon dilation 15/19			
	Surgery: mean age 46 yrs,				
	male sex 15%, alcohol abuse	Overall rate of			
	60%, pain-continuous 55%,	technical success 53%			
	pain-intermittent 37% Izbicki				
	pain score mean 69, duration	The treatment of four			
	of symptoms 21 mths, SF-36	patients was converted			
	quality of life scores: physical	to surgery because of			
	mean 35, mental health	intractable pain; only			
	mean 37, exocrine	one had relief after			
	insufficiency 80%, endocrine	surgery			
	insufficiency 20%				
	At baseline, there were no				
	significant differences				
	between the two groups				

Effect				
	Endoscopy n-19	Surgery N=20	Endoscopic vs Surgical (95%CI)	P value
Izbicki pain score (0 to 100, 100 severe pain)	51±23	25±15	24 (11 to 36)	<0.001
Pain relief – no. (%)	6 (32%)	15 (75%)	-43 (-72 to -15)	0.007
Technical success	10 %53%)	20 (100%)	-47 (-70 to -25)	<0.001
Complications no. (%)	11 (58)	7 (35)	23 (-8 to 53)	0.15
Major	0	1 (5)		
Minor	11 (58)	6 (30)		
Death no. (%)	1 (5)	0	5 (-5 to 15)	0.49
Hospital stay – median no.	8 (0 to 128)	11 (5 to 59)	-3 (-9 to 4)	0.13
days (range)				
Procedures – median no.	8 (1 to 21)	3 (1 to 9)	5 (2 to 8)	<0.001
(range)				
SF-36 quality of life				
Physical	38±9	47±7	-8 (-13 to -3)	0.003
Mental	40±9	45±9	-3 (-8 to 1)	0.15
Exocrine function Insufficiency persisted no. (%) Insufficiency developed no. (%)	11 (61) 6 (33)	13 (65) 1 (5)		0.05
Insufficiency resolved no. (%)	1 (6)	3 (15)		
Sufficiency persisted no. (%)	0	3 (15)		
Endocrine function				0.48
Insufficiency persisted no. (%)	3 (17)	4 (20)		
Insufficiency developed no. (%)	3 (17)	1 (5)		
Insufficiency resolved no. (%)	1 (6)	0		
Sufficiency persisted no. (%)	11 (60)	15 (75)		

One (1/19, 5%) patient died of a perforated ulcer 4 days after the last shock-wave lithotripsy session. The patient was being treated with a non-steroidal anti-inflammatory drug, which

may have had a role in the development of the ulcer. However, given the interval between the treatment and death, a causative role of lithotripsy cannot be ruled out. There were no reported deaths associated with surgery

### Complications

Endoscopic interventions

18 complications occurred in 11/18 (58%) patients. In one patient, shock-wave lithotripsy caused a skin wound that persisted for four months. Five patients had stent-related complications, all of which were treated by replacement of the stent. Pancreatitis occurred in four patients, and cholecytitis in one; all these patients were treated conservatively Surgery

Seven patients (35%) had complications. One patient required a repeated laparotomy because of leakage of the anastomosis. In two patients, bleeding from the operative site was suspected but not confirmed. In addition, one patient had pneumonia, and three had wound infections

Dite P, Ruzicka	1+ RCT	N=72 (randomised)	Patients with	Endoscopic therapy	Surgery	5 yrs	Mortality	None
M, Zboril V et			painful				Complication	reported
al. A		N=140 (total, including	obstructive	Randomised N=36	Randomised N=36		S	
prospective,		patients who 'chose'	chronic				Pain	
randomized		which treatment they	pancreatitis	Sphincterotomy, dilation	Surgery tailored to the individual		Weight gain	
trial comparing		underwent)		or bougienage of	and included resection		Diabetes	
endoscopic			Inclusion criteria:	strictures excluding	procedures for localised disease		mellitus	
and surgical			age > 18 < 70	extracorporeal shock-	with ductal dilation.			
therapy for			yrs, diagnosis	wave lithotripsy				
chronic			established by		In patients in whom chronic			
pancreatitis.[s			imaging, pain	Total N=64	pancreatitis was limited			
ee comment].			score of more		predominately to the pancreatic			
Endoscopy.			than 3 on	All patients underwent	head, either the duodenum and/or			
2003;			Melzack's score,	sphincterotomy and	bile duct were also involved and			
35(7):553-558.			failure of	33/64 (52%) received	stenosed – Whipple's resection			
Ref ID: 226			conservative	additional stenting.	was performed. Chronic			
			management	Stone extraction was	pancreatitis predominately			
			during three	carried out in 15/64	affecting the pancreatic tail was			
			previous years,	(23.4%), six of whom	treated surgically by left			
			duration of	had stents placed due to	pancreatic resection. A drainage			
			clinical illness	concomitant strictures	procedure was used in patients			
			over five yrs	and stones. Additional	with absence of focal pancreatic			
			-	bile duct stenting was	enlargement, grossly dilated			
			Exclusion	performed in 8/64	pancreatic duct, and chronic			
			criteria: Previous	(12.5%)	pancreatic pseudocysts if present			
			interventional					

				procedure for chronic pancreatitis including ce access bloc endotherapy surgery Patient population: ( N=140): 11 (85% male), mean age 4 yrs, alcohol- related 123/ (87.8%), rati- diabetes at s of study 31/ (22.1%)	liac k, y or (Total 9/140 , 1.7 '140 e of start 140			Total popula N=76 61/76 (80%) including 33 preserving p resection, 23 hemipancre and five dist In 15/76 (15 procedure w	ation underwent resection, duodenum pancreatic head 3 atoduodenectomies, al pancreatectomies. %) a drainage vas carried out			
	Total g	group N=140	_			Randomised group N=72		=72				
	Endot	nerapy n=64	Surgery	n=76 (%)	P va	lue	Endothe	erapy n=36	Surgery n=36 (%)	P value		
Mortolity	(%)		0		NIA		(%)		0	ΝΙΔ		
	62/64	(07%)	NR		NR		NR		NR			
	02/04	(31/0)										
Complications	5 (8%)	)	6 (8%)		NR		NR		NR	NR		
Abdominal pain												
Complete absence	14.3		36.9		0.00	2	15		33.8	0.002		
Partial relief	50.8		49.3		ns		46.4		52.1	ns		
No success	34.9		13.8		ns		38.2		14.1	ns		
Body weight												
Increase	26.9		52.1		0.00	2	28.6		47.2	0.003		
Unchanged	23.9		19.1		ns		25.7		25.0	ns		
Decrease	49.2		28.8		ns		45.7		27.8	ns		

Diabetes mellitus	s 35.9		43.4	ns	34.2 (n=	:12)	38.8 (n=14)	ns		
Technical success	S									
A mean of two sea	ssions of initia	l treatment (rang	ge one to four) was requ	ired to achieve	technical succes	s'. In the stent	ed patients, the mean	duration of s	tent treatment	was `6 months
(range 12 to 27) v	vith a mean of	six stent exchar	nges (range four to nine	).						
Prevention of acu	te exacerbatic	ons								
During follow-up,	three patients	were hospitalise	ed due to an acute exac	erbations, one ii	n the opoid group	and one in the	e non-opioid use group			
Alexakis N,	Prospective	N=112	Patients with	Surgery		Surgery		Non-	Mortality	None
Connor S,	case series		chronic	Previou	s opioid use	No previous	s opioid use	opioid 12	Pain	reported
Ghaneh P et al.	3		pancreatitis		•	-	•	mths (3	Complication	
Influence of			(N=231) who	N=46		N=66		to 60)	s	
opioid use on			underwent					· ·	Work status	
surgical and			surgery	Opioid u	se was defined	Surgery inclu	ided: Beger	Opioid	Steatorrhea	
long-term			(112/231, 76	%) as daily	regular use of	procedure 24	1/46, pylorus-	24 mths	Activity	
outcome after				morphin	e salts,	preserving		(3 to 60)	-	
resection for			Alcohol etiol	ogy: including	slow-release	pancreatodu	odenectomy 0/46	· · · ·		
chronic			With opioid u	ise preparat	ions eg	and duodenu	im-preserving and			
pancreatitis.			27/46 (59%)	morphin	e, for at least 3	spleen prese	erving total			
Surgery. 2004;			Without opio	id months		pancreactom	iy 15/46			
136(3):600-608.			use 31/66 (4	7%)						
Ref ID: 2025			,	Surgery	included: Beger					
			Alcoholic chi	onic procedu	re 23/66,					
			pancreatitis:	A pylorus-	preserving					
			typical histor	y pancreat	toduodenectom					
			(recurrent	v 25/66 a	and duodenum-					
			episodes of	preservi	ng and spleen					
			acute	preservi	ng total					
			pancreatitis)	and pancrea	ctomy 6/66					
			a history of		<b>,</b>					
			excessive							
			alcohol intak	e						
			(usuallv > 80)	a/d						
			for some vea	ars in						
			males, less i	n						

one or more of the following: calcification of the pancreas, moderate to marked ductal lesions, marked exocrine
the following: calcification of the pancreas, moderate to marked ductal lesions, marked exocrine insufficiencev
calcification of the pancreas, moderate to marked ductal lesions, marked exocrine insufficiencev
the pancreas, moderate to marked ductal lesions, marked exocrine insufficiency
moderate to marked ductal lesions, marked exocrine
marked ductal lesions, marked exocrine
lesions, marked exocrine
exocrine
insufficiency
Patient
population:
Opioid use:
median age 48
vr. male:female
46:20, alcohol
47%, age at first
symptoms 43
vrs, no. of
hospitalisations
median 3, mean
duration of
symptoms 2 yrs,
median weight
65 kg
No previous
opioid use:
median age 42
yr, male:female
31:15, age at first
symptoms 35
vrs**alcohol
59%, no. of

hospitalisations median 10**, mean duration of symptoms 5.9 yrs**, median weight 74 kg		
**denotes significant difference (see effect)		

Effect

- With the exception of an enlarged head of pancreas (opioid use vs no opioid use 44 vs 24%; p=0.19) there were no significant differences between the two groups with respect
  to preoperative CT findings
- Patients not on opioids compared to those who were on opioids prior to surgery:
- Were significantly older (median 48 (18 to 79) vs 42 (21 to 63); p=0.001)
- Were significantly older when the first symptoms appeared (median 43 (9 to 77) vs 35 (8 to 59); p=0.004)
- Had significantly fewer hospitalisations (median 3 (0 to 42) vs 10 (1 to 30); p=0.001)
- Had a significantly shorter duration longer duration of symptoms (2 (0 to 40.5) vs 5.9 (0.1 to 22.1; p=0.038)
- Significantly more patients in the opioid compared to the non-opioid group underwent one or more types of total pancreatectomy (21 (46%) vs 19 (14%); p=0.0002)

#### Pain

- There was a significant difference in the non-opioid and opioid groups on the VAS score:
- Preoperatively (median 7 (0 to 10) vs 9 (7 to 10); p=0.001)
- 3 months (median 2 (0 to 7) vs 3 (0 to 9); p=0.030)
- There were no significant differences at 12 (no data) or 24 months (no pain 57 vs 49%; ns)

	Non-opioid group n=53	Opioid group n=35
Analgesia	36 (68%)	14 (40%)
Steatorrhea	17	9
Activity – normal	29 (55%)	16 (45%)
Working	18 (34%)	8 (23%)

			Patients without opioid us	se n=66	Patients with opioid use n=	-46	р			
Patients with cor	nplications		34		27		0.56	0.56		
Deaths			1		4					
Pulmonary comp	olications		8		12		0.079	0.079		
Cardiovascular c	Cardiovascular complications 6				3	0.73				
Gastrointestinal	fistula		12		10		0.63			
Abscess/collection	on		6		8		0.24			
Delayed gastric	emptying		4		2		0.99			
Haemorrhage			2		8		0.015			
Early reoperation	1		3		11		0.003			
Other complication	ons		6		2		0.46			
Hospital stay		•	20 (19 to 38)		24 (23 to 47)		0.34			
Basinski A,	2+ Non-	N=48	Patients with small duct	Patients chose	Controls		8 weeks	Pain (VAS)	None	
Stefaniak T,	randomised		chronic pancreatitis	the procedure				EORTC, QUALITY	reported	
Vingerhoets A	case			according to the	fr Conservative treatment	nt		OF LIFE QLQ C-30,		
et al. Effect of	control (two		Inclusion criteria: chronic	needs				functional		
NCPB and	studies)		pancreatitis diagnosed by		N=32			assessment of		
vSPL on pain			CT scan and endoscopic	Neurolytic coella				thereps (FACIT)		
life in chronic			reliograde	(NCDP) = 20				(FACIT)		
nancreatitis			persistent pain for three	(NCPD) 11=30						
nationts			months or more and	Videothorasconi	c					
World J			scoring at least 66 7% on	splanchnicetom						
Gastroenterol.			the pain visual analogue	(VSPL) n=18						
2005:			scale	(1012)						
11(32):5010-										
5014. Ref ID:			Exclusion criteria: Patients							
2070			with pancreatic							
			inflammatory tumours or							
			pseudocysts							
			-							

No patient had structural			
lesions			
Patient population: Coeliac plexus block: mean age 50 yrs, male:female 3:1, etiology (alcohol vs other ratio) 6.5, period from the symptomatic onset of the disease 6 yrs, 17/30 (58%)			
Splanchnicectomy: mean age 48 yrs, male:female 3.51, etiology 8.0, onset 11.5 yrs, opioid use 11/18 (61%)			
Control: mean age 52 yrs, male: female 3.34, etiology 7.0, onset 7 yrs, opioid use 18/32 (56%)			

Effect

Opioid use

There was no statistical difference when comparing the proportion of patients who underwent NCPB and VSPL for:

• Opioid withdrawal (47 vs 36%; ns)

• Reduction in opioid dose (53 vs 45%; ns)

Mortality and morbidity

• There were no cases reported

Orthostatic hypertension was observed for three days in 9/30 (30%) from the NCPB group and in 1/18 (5.5%) patients in the VSPL group Intermittent intercostals pain was treated with paracetamol for two weeks in 4/18 (22%) patients in the VSPL group. In one of these, an intercostals nerve block was performed and in one patient a classic thoracotomy was performed due to massive adhesions (excluded from study)

Outcome			VSPL (n=18) mea	n effect (95%CI)		NCPL (n=30) mean effe	ect (95%CI)		
Pain (VAS) 0 to	100% severe p	pain	15.82 (14.68 to 16	6.96)		8.89 (8.30 to 9.48)			
Physical well-bei	ing		1.81 (1.57 to 2.06)			2.19 (2.96 to 2.42)			
Emotional well-being			0.08 (-0.11 to 0.29)			3.55 (3.27 to 3.84)			
Fatigue			2.52 (2.25 to 2.79)	2.52 (2.25 to 2.79)					
Ailments typical	for the illness		0.05 (-0.14 to 0.26	, 6)		0.64 (0.45 to 0.83)			
Nealon WH.	2+	N=85	Patients with	Surgery	No surge	rv	Operated	Mortality	National
Townsend CM.	Prospective		chronic		je	.,	mean	Complication	Institute for
Jr., Thompson	cohort	N=68 follow-up	pancreatitis	N=41	N=44		14.8	S	Health
JC. Operative			parioreanner	N=30 (follow-up)			months	Clinical	American
drainage of the		Lost to follow-up N=3	79/85 (93%)		N=38 (foll	ow-up)	(10 to 15	features	Cancer
pancreatic			alcohol-related			• •F)	months)	Weight	Society
duct delays		Data not available		Puestow 44% Puestow	Reasons f	for not operating: 18/44	Non-		
functional		(appropriate follow-up	Grading system	plus pseudocyst 20%	non disab	ling pain, small main	operated		
impairment in		time not reached	based on ERCP.	Puestow plus biliary	duct 17/44	4. patient refusal 7/44.	14.1		
patients with		N=14	two exocrine and	two exocrine and hypass 17% Puestow cirrhosis 2/44			Months		
chronic			two endocrine plus pseudocyst plus			-/	(9 to 15		
pancreatitis. A			tests Score 0 to	biliary bypass 20%	Grade: 26	(44 (59%) mild to	months)		
prospective			$5  \Omega = \text{mild} \cdot 1 \text{ to}$	Sindly Sypace 2070	moderate	and 18/44 (41%)	internatio)		
analysis.			2 moderate: 3 to	Grade: 25/41 (61%) mild	severe				
Annals of			5 severe	to moderate: 16/41	001010				
Surgery, 1988:				(39%) severe					
208(3):321-329.									
Ref ID: 514									
Effect		l	1	1	1		1		1
Surgery (N=41)									
Mortality									
No deaths occurre	ed								
Complications.									
Three patient had	Three patient had wound infections								
Grade changes	Grade changes								
Surgery vs non su	irgery								
At follow-up There	e was a signific	cant difference between t	he surgery and no su	urgery groups for the propo	rtion of patie	ents who remained at the	same grade	of mild to mode	rate

At follow-up There was a significant difference between the surgery and no surgery groups for the proportion of patients who remained a (sustained pancreatic function) (16/19 (84%) vs 7/24 (29%); p<0.05) or who progressed to 'severe' (3/19 (16%) s 17/24 (71%); p<0.05)

### **Clinical features**

Surgery vs no surgery

There was no significant difference between the surgery and no surgery group for:

- Disabling abdominal pain (28/44 (64%) vs 41/41 (100%); ns)
- Weight loss (32/44 (73%) vs 34/41 (83%); ns)
- Steatorrhea (10/44 (23%) vs 11/41 (27%); ns)
- Insulin-dependent diabetes mellitus (9/44 (20%) vs 8/41 (19%); ns)

### Weight gain

Surgery vs no surgery

There was no significant difference between the surgery and no surgery group for:

• the proportion of patients with a history of weight loss 23/30 (77%) vs 31/38 (82%)

A significantly higher proportion of patients who underwent surgery compared with those who did not:

• gained weight (25/30 (87%) vs 5/38 (13%); p<0.05) and the mean weight gained was significantly higher (4.2 kg (1.4 to 12.7) vs 0.50 kg (-3.6 to 2.7); p<0.05)

Lankisch PG,	2+	N=335	Patients with	Surgery	No surgery	Mean	Pain	None
Lohr HA, Otto	Prospective		chronic			11.3 yrs		reported
J et al. Natural	cohort		pancreatitis	90/335 (27%)	245/335 (73%)			
course in			(based on clinical					
chronic			history and at	70/90 (78%) alcoholic	No further details reported			
pancreatitis.			least one	pancreatitis				
Pain, exocrine			abnormal					
and endocrine			secreting-	Surgical procedures				
pancreatic			pancreozymin	included: 68% drainage				
insufficiency			test. Faecal fat	procedures				
and prognosis			analysis was also					
of the disease.			used)					
Digestion.								
1993;			Excluded:					
54(3):148-155.			patients with					
Ref ID: 474			painless chronic					
			pancreatitis (7%)					
			Alcoholic					

	pancreatitis was defined as admitted regular drinking of more than 2 liters of beer a day or 80 g pure alcohol a	
	than 2 yrs	
	230/335 alcoholic pancreatitis (69%)	
	Excluded: 8/230	
	with painless	
	chronic	
	pancreatitis	
Mortality		

### wortality

Three patients died within 8 weeks of surgery. Three further patients died of hypoglycaemia.

Pain

Surgery vs no surgery

Pain disappeared or distinctly subsided immediately after operation in 62 (89%) of 70 patients with full documentation of the postoperative course: 40 had pain relief for mean 6.3 ( $\pm$  4.5 yrs), but pain relapse occurred in 22 (36%) patients 1.6  $\pm$  2 yrs after operation. There was no significant difference in the pain course between operated and non-operated patients (p=0.6096)