Ústřední vojenská nemocnice - Vojenská fakultní nemocnice Praha
1. lékařská fakulta Univerzity Karlovy
Interní klinika, Oddělení gastroenterologie, hepatologie a metabolismu
Subkatedra gastroenterologie IPVZ v Praze

Vzácná komplikace plánované operace.

J. Csomor, I. Murínová, K. Broulíková, O. Kučerka, P. Sedloň, J. Jarošek, P. Urbánek, M. Zavoral

XXI. Dny Intenzivní medicíny, Kroměříž 2017

Anamnéza

- 57 letá žena

- **RA:** bezvýznamná
- **OA:** arteriální hypertenze, CHOPN, v.s. plicní fibroza
  stp. akutní biliární pankreatitídě, EPST a CHE 2006
  stp. APPE, ovarektomii vlevo 1979
- **Abusus:** kuřák 3-5 cig/den, alkohol minimálně
- **FA:** Lomir, Cynt, Losartan, HCTH, Euphyllin, Letrox
- **AA:** PNC

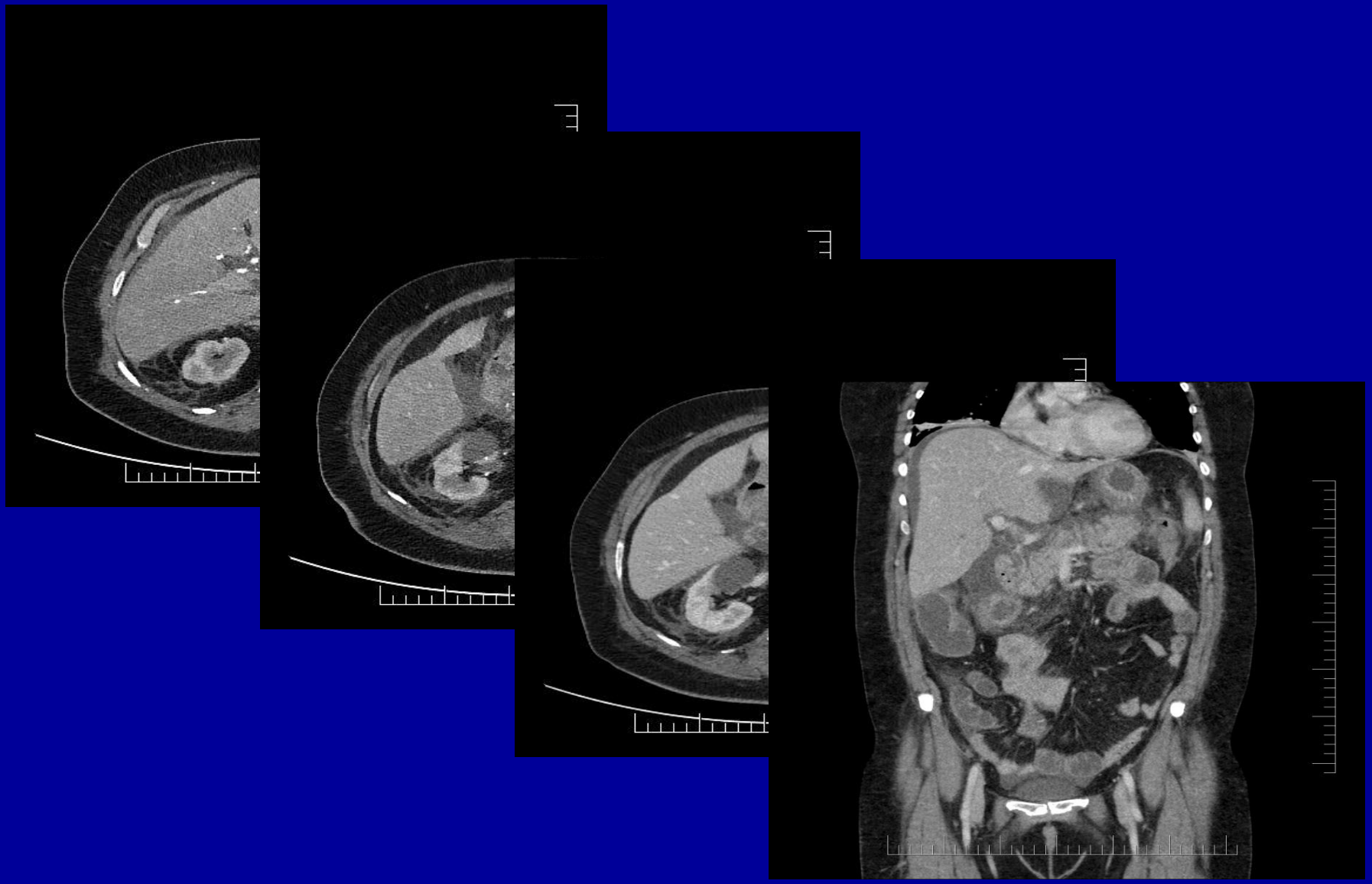
Nynější onemocnění

- přichází plánovaně ke strumektomii pro polynodozní eufunkční strumu, operaci indikoval endokrinolog
- operace provedena bez komplikací
- 12-15 hodin po operaci: bolesti v epigastriu, nauzea, zvracení, zástava pasáže
- podány infuze, analgetika
- nález na břiše: břicho nad niveau, palpačně difuzně bolestivé, bez jasné rezistence, bez peristaltiky
- celkově pacientka schvácena, opocená, tachykardická 100/min, DF 18/min, TK 115/80 torr

Laboratoř

Parameter	Jednotky	Výsledek	Norma
Leukocyty	$x10^9/l$	18.71	4.1 – 10.2
Hemoglobin	g/l	169	135 - 174
Hematokrit	%	48	35 – 44
Urea	mmol/l	14.9	2 – 6.7
Kreatinin	umol/l	136.7	49 - 90
Kalium	mmol/l	3.34	3.8 – 5.0
Calcium	mmol/l	1.89	2.1 – 2.65
Amyláza	umol/l	62	0.47 – 1.67
C reaktivny protein	mg/l	169.9	< 8
Laktát	mmol/l	2.43	0.5 – 1.6
Bilirubin	umol/l	5.9	0 – 21
ALT	ukat/l	0.34	0.1 – 0.83
AST	ukat/l	0.55	0.1 – 0.85
GMT	ukat/l	0.45	0 – 1
LDH	ukat/l	5.57	2.25 – 3.75
Glykémia	mmol/l	6.1	3.3 – 5.6

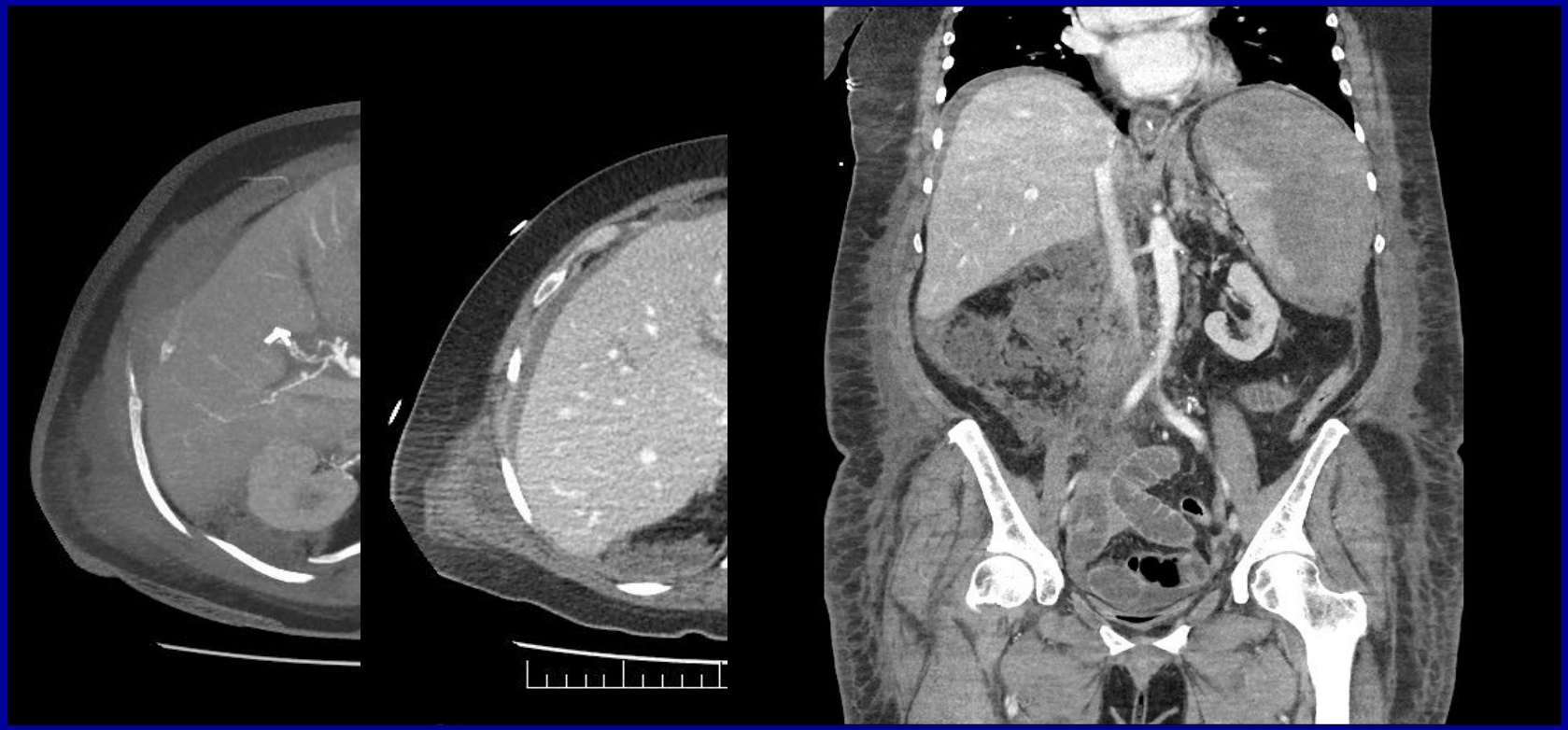
Statim CT břicha



Další průběh

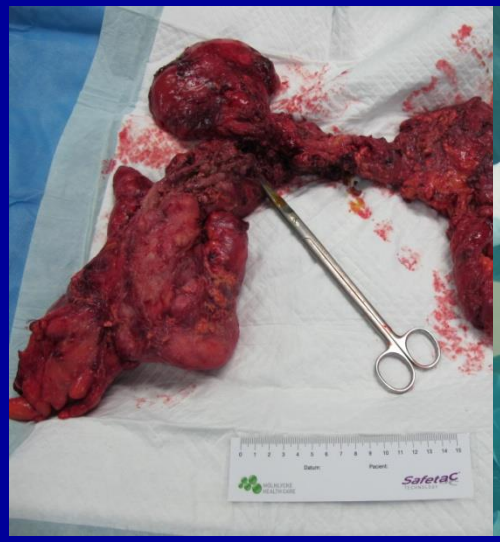
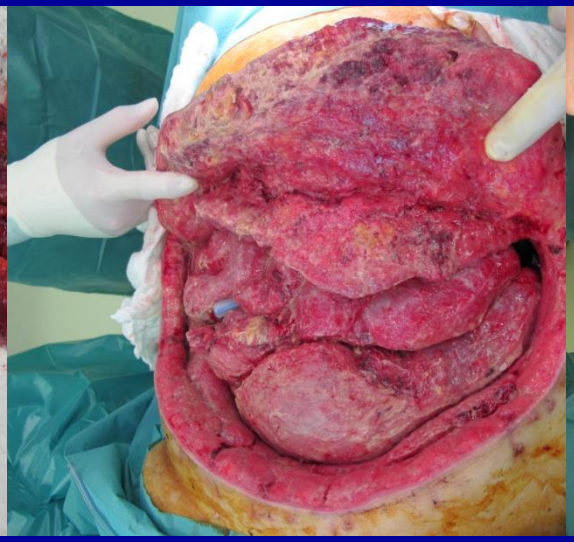
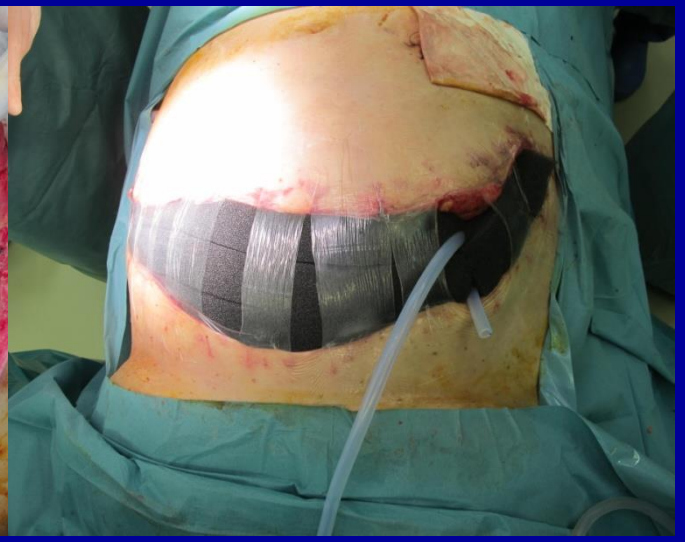
- překlad na JIP IK, předpokládaný těžký průběh
- Ranson skóre 2/6 bodů, BISAP 2 b., APACHE II 13 b.
- tekutinová resuscitace, analgetika, časná enterální výživa via NJS
- do 48 hodin nutnost OTI a UPV pro respirační selhání
- pro peak CRP 550 mg/l zahájena ATB léčba Piperacillin/Tazobactam
- postupná stabilizace stavu, oběhové, ventilační i laboratorní zlepšení
- 20.den hospitalizace náhle zhoršení, obraz šoku

Další průběh



Další průběh

- provedena akutní splenektomie, nekrektomie pankreatu, laváž a drenáž dutiny břišní
- operační revize, nekrektomie pankreatu a retroperitonea
- subtotální kolektomie pro vícečetné perforace střeva
- VAC systém

Další průběh

- komplexní resuscitační péče, kombinovaná nutrice, cílená ATB léčba dle kultivací, EBR, plasmy, opakované operační revize, nekrektomie
- 90 dní po přijetí do nemocnice exitus letalis pacientky na progredující MODS

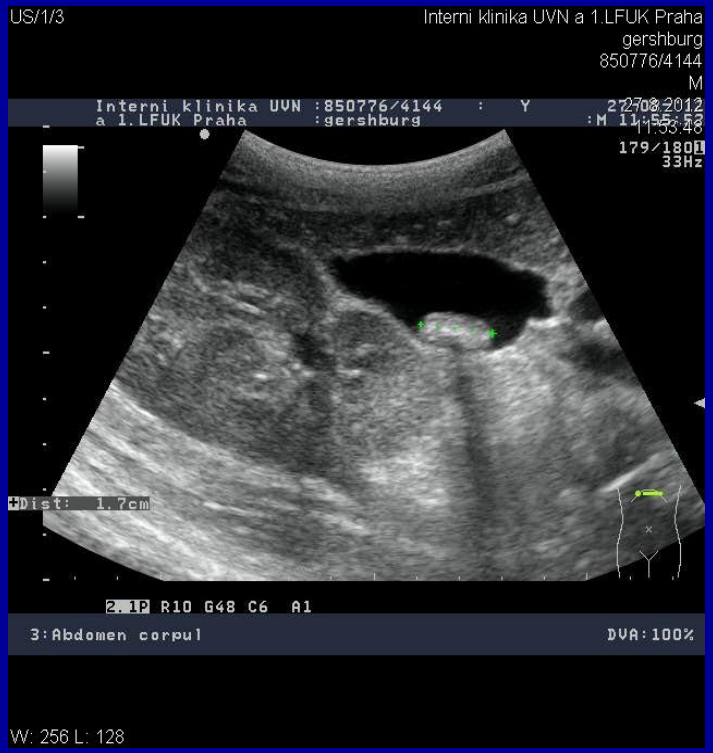
Etiologie pankreatitídy ??

- biliární ?
- etylická ?
- hyperkalcémie ? hyperlipidémie ?
- pancreas divisum ?
- postraumatická ? autoimunní ? parainfekční ?

Repeated Transabdominal Ultrasonography Is a Simple and Accurate Strategy to Diagnose a Biliary Etiology of Acute Pancreatitis

Signoretti, Marianna MD*; Baccini, Flavia MD*; Piciucchi, Matteo MD, PhD*; Iannicelli, Elsa MD†; Valente, Roberto MD*; Zerboni, Giulia MD*; Capurso, Gabriele MD, PhD*; Fave, Gianfranco Delle MD*

- kombinace
  2x USG vyšetření
  a zároveň
  elevace ALT
  = přesnost 87%

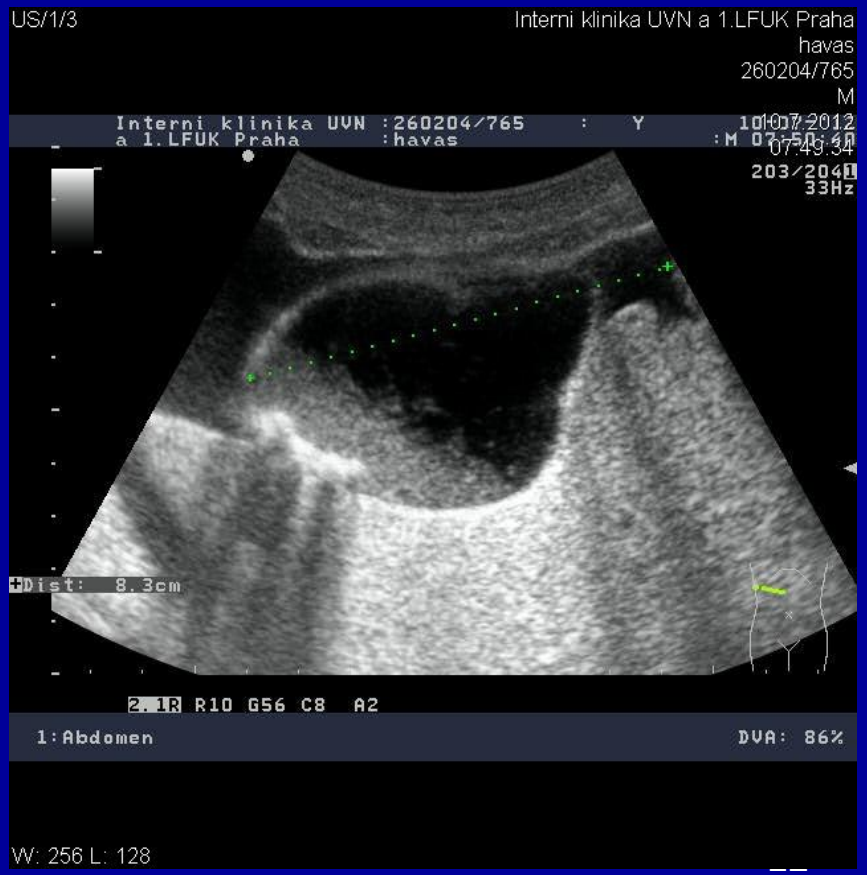


Surg Endosc (2008) 22:1620–1624
DOI 10.1007/s00464-007-9665-2

Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy

Ming-Hsun Yang · Tien-Hua Chen · Shin-E Wang · Yi-Fang Tsai · Cheng-Hsi Su · Chew-Wun Wu · Wing-Yiu Lui · Yi-Ming Shyr

- ALT 3x ⇧ než norma do 48h od začátku symptomů PPV 85%
- normální jaterní testy NPV 97%



Poléková pankreatitída ?

- 0,1 – 2 % všech akutních pankreatitíd

ACE inhibitors	Cyproheptadine	Linagliptin	Liraglutide
Macrolides	Rifapentine	Acetaminophen	Cytosine
Mefenamic acid	Rivastigmine	ACTH	Danazol
6-MP	Ropinirole	Alendronate	Dapsone
Mesalamine	Saw palmetto	Saxagliptin	All-trans-retinoic acid
Alogliptin	DDP-4 inhibitors	Metformin	SSRIs
Alpha-methyldopa	Diazoxide	Methimazole	Sirolimus
Sitagliptin	Aminosalicylates	Diphenoxylate	Methyldopa
Sodium stibogluconate	Amiodarone	Dipyridamole	Divalproex sodium
Metronidazole	Somatropin	Amlodipine	Doxercalciferol
Mirtazapine	Statins	Ampicillin	Doxorubicin
Montelukast	Sulfamethoxazole	Antivirals	Ertapenem
Mycophenolate	Sulfasalazine	Aspirin	Estrogens
Exenatide	Nitrofurantoin	Sumatriptan	Atypical antipsychotics
Fibrates	NSAIDs	Tacrolimus	Azathioprine
Finasteride	Octreotide	Tamoxifen	Bupropion
Fluoroquinolones	Paclitaxel	Tetracyclines	Calcitriol
5-Fluorouracil	Pegaspargase	Thiazide diuretics	Cannabis
Furosemide	Penicillin	Thrombolytic agents	Capecitabine
Gabapentin	Pentamidine	TNF-alpha inhibitors	Carbamazepine
GLP-1 analogs	Pergolide	Topiramate	Ceftriaxone
Gold	Phenolphthalein	Valproic acid	Cimetidine
HAART agents	Pilocarpine	Venlafaxine	Cisplatin
Ifosfamide	Prazosin	Vincristine	Clomiphene
Indomethacin	Procainamide	Voriconazole	Codeine
Interferon/ribavirin	Propofol	Zolmitriptan	Colchicine
Interleukin-2	Propoxyphene	Corticosteroids	Irbesartan
PPIs	Co-trimoxazole	Isoniazid	Quinupristin/dalfopristin
COX-2 inhibitors	Isotretinoin	Ranitidine	Cyclophosphamide
Lamotrigine	Repaglinide	Cyclosporine	L-asparaginase
Rifampin			

6-MP, 6-mercaptopurine; ACE, angiotensin-converting enzyme; ACTH, adrenocorticotropic hormone; COX, cyclooxygenase; DDP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide-1; HAART, highly active antiretroviral therapy; NSAIDs, nonsteroidal antiinflammatory drugs; PPI, proton pump inhibitor; SSRIs, selective serotonin reuptake inhibitors; TNF, tumor necrosis factor.
(Table adapted with permission from Kaurich.[26])

Jones M R et al: Drug-Induced Acute Pancreatitis: A Review. Ochsner J. 2015 Spring; 15(1): 45–51

Propofol ?

- celosvětově 25 případů AP po propofolu do roku 2000
- třída II: > 4 případy v literatuře
  > 75% případů má časovou souvislost s podáním léku, u propofolu do 24 hodin po podání
- sporná úloha preexistující hyperlipidémie
- idiosynkratická reakce

Badalov N, Baradarian R, Iswara K, Li J, Steinberg W, Tenner S. Drug induced acute pancreatitis: an evidence-based review. Clin Gastroenterol Hepatol 2007;5(6):648–661.

Classification System of Drug-Induced Acute Pancreatitis

- Class Ia drugs
- At least 1 case report with positive rechallenge, excluding all other causes, such as alcohol, hypertriglyceridemia, gallstones, and other drugs
- Class Ib drugs
- At least 1 case report with positive rechallenge; however, other causes, such as alcohol, hypertriglyceridemia, gallstones, and other drugs were not ruled out
- Class II drugs
- At least 4 cases in the literature
- Consistent latency (≥75% of cases)
- Class III drugs
- At least 2 cases in the literature
- No consistent latency among cases
- No rechallenge
- Class IV drugs
- Drugs not fitting into the earlier-described classes, single case report published in medical literature

Naranjo skóre

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given? *	-1	+1	0	
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
			Total Score:	

**Question 6 refers to a typical clinical trials situation and is included here for completeness.*

Total Score	Interpretation of Scores
≥ 9	Definite. The reaction (1) followed a reasonable temporal sequence after drug exposure had been established in body fluids or tissues, (2) followed a recognized response to the suspected drug, (3) was confirmed by improvement on withdrawing the drug and (4) reappeared on reexposure.
5 - 8	Probable. The reaction (1) followed a reasonable temporal sequence after a drug exposure, (2) followed a recognized response to the suspected drug, (3) was confirmed by withdrawal but not by exposure to the drug, and (4) could not be reasonably explained by the known characteristics of the patient's clinical state.
1 - 4	Possible. The reaction (1) followed a temporal sequence after a drug exposure, (2) possibly followed a recognized pattern to the suspected drug, and (3) could be explained by characteristics of the patient's disease.
≤ 0	Doubtful. The reaction was likely related to factors other than a drug.

The Naranjo scale is a tool to help clarify how to evaluate a potential causal association. It is not intended to solve all the complex problems of identification and classification of ADRs.

Naranjo CA, Busto U, Sellers EM, et al. (1981). "A method for estimating the probability of adverse drug reactions". Clin. Pharmacol. Ther. ***30*** *(2): 239–45*

Propofol

- bezpečný lék
- dg. „drug - induced“ akutní pankreatitídy je obtížná, spíše vyloučením jiné příčiny
- rizikové: „single-dose“ podání
- u naší pacientky podáno 250 mg 1% propofolu
- riziko recidivy pankreatitídy po opětovném podání

Děkuji za pozornost

Podpořeno z programového projektu Ministerstva zdravotnictví ČR s reg. č. 16-31028A.

Csomor J, Murínová I, Broulíková K. et al. Propofol-induced acute pancreatitis. *J Clin Pharm Ther.* 2017 Apr 10. doi: 10.1111/jcpt.12524.