

Mehmet İLHAN
Yiğit SOYTAŞ
Ali Fuat Kaan GÖK
Süleyman BADEMLER
Recep GÜLOĞLU
Cemalettin ERTEKİN

Correspondance

Mehmet İLHAN
İstanbul University, İstanbul Faculty of Medicine,
Department of General Surgery, İSTANBUL

Phone: 0212 531 09 39
e-mail: op.dr.mehmetilhan@gmail.com

Received: 26/05/2016

Accepted: 19/07/2016

İstanbul University, İstanbul Faculty of Medicine,
Department of General Surgery, İSTANBUL



RESEARCH

TIMING OF LAPAROSCOPIC CHOLECYSTECTOMY IN ELDERLY PATIENTS WITH MILD ACUTE BILIARY PANCREATITIS

ABSTRACT

Introduction: Age-related diseases have increased with the increase in average life expectancy. Biliary pancreatitis is one such disease, and its incidence increases with age. This study aimed to evaluate treatment outcomes for patients aged >65 years who were hospitalized for biliary pancreatitis and underwent cholecystectomy during initial hospitalization.

Materials and Method: A retrospective study was designed for patients aged >65 years who underwent early cholecystectomy for acute biliary pancreatitis at İstanbul Faculty of Medicine, Department of General Surgery, between January 2010 and December 2015. Patients were divided into group A (aged 65-74 years) and group B (aged ≥75 years). Patients' demographics, comorbidities, American Society of Anesthesiology (ASA) scores, history of previous abdominal operations, operation duration, postoperative morbidity and mortality, and length of hospital stay were analyzed.

Results: In total, 192 geriatric patients with acute biliary pancreatitis were analyzed. Seventy-nine (45 women, 34 men) of them underwent early LC for acute biliary pancreatitis during initial hospitalization. There was no significant difference in operation duration and length of hospital stay between the two groups. Postoperative oral intake started within 8 h. No significant difference was found in mortality and morbidity rates between the two groups.

Conclusion: Old age and accompanying comorbidities are fundamental predictors of surgical outcomes. Early LC should be suggested in elderly patients with the regression of mild pancreatitis before hospital discharge, with acceptable morbidity and mortality. It is feasible and safe for older patients to undergo LC. Cholecystectomy could be the definitive treatment for gallstone disease to prevent recurrent pancreatitis.

Key Words: Geriatrics; Aged; Cholecystectomy, Laparoscopic; Gallstone.



ARAŞTIRMA

HAFİF AKUT BİLİYER PANKREATİT GEÇİREN YAŞLI HASTALARDA LAPAROSKOPİK KOLESİSTEKTOMİ NE ZAMAN YAPILMALI?

Öz

Giriş: Ortalama insan ömrü arttıkça yaşla ilişkili hastalıkların sıklığı artmaktadır. Safra taşına bağlı pankreatit, yaşla ilişkili hastalıklardan biridir ve yaşlanma ile birlikte sıklığı artmaktadır. Bu çalışma, 65 yaşın üstünde biliyer pankreatit tanısıyla yatan ve aynı yatışta laparoskopik kolesistektomi (LK) yapılan hastaların tedavi yöntemlerini ve sonuçlarını değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Ocak 2010 - Aralık 2015 tarihleri arasında İstanbul Tıp Fakültesi, Genel Cerrahi Anabilim Dalı'nda, biliyer pankreatit tanısıyla erken laparoskopik kolesistektomi yapılan 65 yaş üstü hastalar retrospektif olarak değerlendirildi. Hastalar Grup A (65-75 yaş) ve Grup B (> 75 yaş) olarak ayrıldı. Hastalar, ek hastalıkları, önceden geçirilmiş karın ameliyatı, ameliyat süresi, ameliyat sonrası mortalite/morbidite oranı, hastanede yatış süresi ve Amerika Anesteziyoloji Derneği'nin (ASA) skoruna göre değerlendirildi.

Bulgular: Toplam 192 akut biliyer pankreatit geçiren yaşlı hasta değerlendirildi. Bu hastaların 79'una hastaneye ilk yatışları sırasında akut biliyer pankreatit tanısıyla erken LK yapıldı. İki grup arasında ameliyat ve hastanede kalış süresi açısından anlamlı fark saptanmadı. Ameliyat sonrası 8 saat içinde oral gıda alınmaya başlandı. Grup A ve Grup B arasında mortalite ve morbidite bakımından fark bulunmadı.

Sonuç: Yaşlılık ve eşlik eden hastalıklar cerrahi sonuçların esas belirleyicileridir. Erken dönemde LK, hafif pankreatit geçiren yaşlı hastalara taburculuktan önce kabul edilebilir düzeyde mortalite ve morbiditeyle önerilebilir. Bu hastalara güvenli ve etkili bir şekilde LK yapılabilir. Kolesistektomi, rekürren pankreatiti önlemede kesin tedavi olabilir.

Anahtar Sözcükler: Geriatri; Yaşlı; Laparoskopik Kolesistektomi; Safra Taşı.



INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas. This disease can be divided into two main categories, interstitial and necrotizing AP (1). The pathogenesis of AP is very complicated. The etiology of pancreatitis is mostly biliary (80%-90%), but sometimes it may be idiopathic. Mortality rates for interstitial edematous pancreatitis increase with the development of pancreatic necrosis (2,3). The modern lifestyle and eating habits have led to an increase in the incidence of cholelithiasis (4). Gallstones are the most common causes of acute abdominal pain in elderly patients and are the reason for a significant percentage of abdominal operations in patients aged >65 years (5,6). The frequency of occurrence of this disease increases with age in all populations, in both sexes, and in industrialized and non-industrialized countries (7,8).

Cholecystectomy, which is performed in the first biliary pancreatitis attack, decreases the risk of recurrent biliary pancreatitis and other gallstone-related complications. Currently, cholecystectomy is delayed for 6 weeks because it is risky to operate while pancreatitis is in the active state in the early days (9). However, the patient is at risk of biliary events throughout this period, which is why cholecystectomy should be performed during the initial hospitalization in patients with non-severe biliary pancreatitis (10). Keeping in mind that elderly patients have similar results to younger patients, age is not a contraindication for cholecystectomy. The increased mortality in elderly patients is due to the presence of concomitant diseases. Age is generally an independent risk factor for elderly patients who undergo surgery (6,7). This study aimed to evaluate outcomes of treatment methods for patients aged >65 years who were hospitalized for biliary pancreatitis and underwent cholecystectomy during the initial hospitalization.

MATERIALS AND METHOD

Elderly patients who were admitted to the Emergency Surgery Clinic at Istanbul Faculty of Medicine, Department of General Surgery, between January 2010 and December 2015 were evaluated. Their written and electronic medical records were retrospectively reviewed, seeking the terms "abdominal pain," "gallstones," "biliary disease," "cholecystitis," and "cholangitis," and patients with pancreatitis as the primary diagnosis. This retrospective study was approved by the Istanbul Faculty of Medicine Institutional Review Board of Istanbul University.

All diagnoses were made with a combination of medical history, physical examination, laboratory tests, and imaging techniques [ultrasonography, magnetic resonance cholangiopancreatography (MRCP), computed tomography (CT)]. Acute biliary pancreatitis was diagnosed with the presence of gallbladder lithiasis, elevated serum amylase level, and biliary pain. Choledocholithiasis was identified with the presence of biliary symptoms, jaundice, abnormal liver function test results, and gallbladder lithiasis. Following the definitive diagnosis, an oral regimen and analgesic treatment were initiated in all patients.

Contrast-enhanced, spiral CT was performed on patients with severe AP to detect edematous or necrotizing pancreatitis. Patients who were confirmed to have common bile duct stones with ultrasonography or MRCP underwent endoscopic retrograde cholangiopancreatography (ERCP).

Cholecystectomy was performed on patients who tolerated the oral regimen and who were clinically recovered during initial hospitalization, in accordance with the latest guidelines (11). Laparoscopic cholecystectomy (LC) and ERCP procedures were performed after the risks, complications, and alternatives had been discussed. All patients signed an informed consent form before the procedure.

LC was performed using a standard 3- or 4-port technique by an experienced surgical team. A Veress needle was inserted, and the abdominal cavity was insufflated with carbon dioxide, with the maximum insufflation pressure being 12 mm Hg. Calot's triangle was identified, and the cystic duct and cystic artery were clipped, taking care not to injure the common bile duct. The gall bladder was removed from the liver bed by laparoscopic surgical heat devices. When laparoscopic exploration was inefficient, cholecystectomy was performed by laparotomy. ERCP with endoscopic sphincterotomy was performed in patients who did not accept to undergo an operation to prevent recurrent pancreatitis (6,12).

Patients aged <65 years; those with necrotizing pancreatitis, primary sclerosing cholangitis, pseudocysts, non-biliary pancreatitis, intrahepatic lithiasis, primary biliary cirrhosis, gall bladder and biliary duct tumors, or drug-induced pancreatitis; and those who did not accept an operation were excluded from the study.

Patients who were aged >65 years, hospitalized for biliary pancreatitis, and underwent cholecystectomy during the initial hospitalization were included in the study. These patients were divided into two groups: group A (aged 65-75 years) and group B (aged >75 years). Patients' demographics, comorbidities, American Society of Anesthesiology (ASA) scores, his-



tory of previous abdominal operations, operation duration, postoperative morbidity and mortality, and length of hospital stay were analyzed.

Statistical Analysis

The findings were compared using IBM Statistical Package for the Social Sciences 21. The distribution of variables was analyzed using the Shapiro-Wilk test. For the comparison between the two groups, the Mann-Whitney U test was used. The results had a 95% confidence interval, and statistical significance was assessed as $p < 0.05$.

RESULTS

In total, 782 patients with ABP were retrospectively analyzed. A total of 590 patients were aged <65 years and were

excluded from the study; 192 patients were aged >65 years, 42 of which refused to undergo an operation.

A multidetector contrast-enhanced CT scan using a pancreatic protocol was performed in 51 patients who were diagnosed as having severe ABP, and necrosis or fluid collection was detected in 32. Elective cholecystectomy was suggested for patients with severe pancreatitis (Figure 1A-B).

Fourteen patients were a high surgical risk according to their ASA score and underwent ERCP to reduce the risk of recurrence. These high-risk patients and six other patients with incomplete data were excluded from the study. The remaining 79 patients underwent early LC for acute biliary pancreatitis during hospitalization. Four patients who were preoperatively diagnosed as having biliary tract stones underwent ERCP; stones were extracted from the common bile duct, after which cholecystectomy was performed (Figure 2A, B).

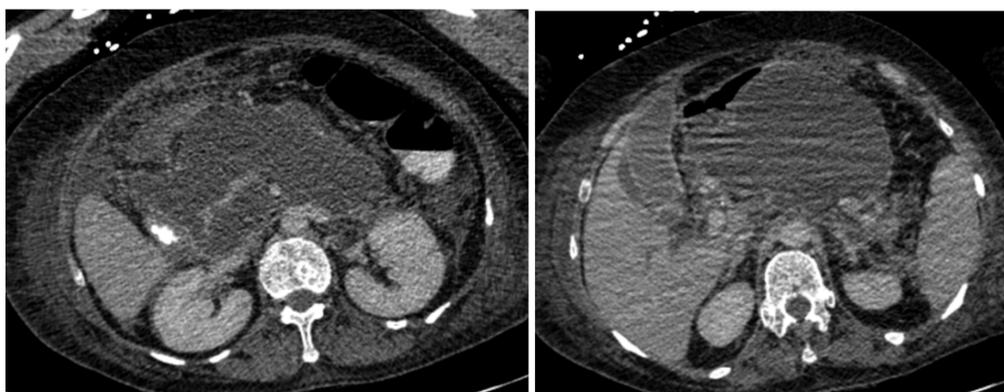


Figure 1— A man aged 72 years with acute pancreatitis. A coronal contrast-enhanced CT scan demonstrates multiple loculi of fluid. Almost the entire pancreas is non-enhancing and necrosed.

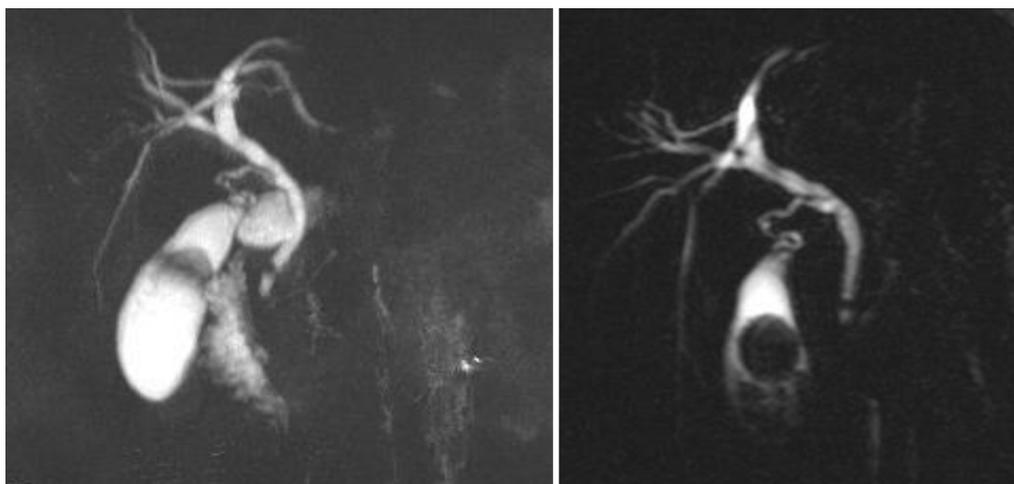


Figure 2— MRCP detected calculi in the gallbladder and bile duct. A woman aged 68 years with acute biliary pancreatitis who underwent cholecystectomy after extraction of stones from the common bile duct with ERCP.



Table 1— Distribution of Patients According to Group, Sex, Length of Hospital Stay, and Length of Stay in the Intensive Care Unit

	Preoperative Hospital Stay		Hospital Stay		Intensive Care Unit Stay		N	%
	Mean±sd	p	Mean±sd	p	Mean±sd	p		
GROUP A	3.01±0.78	0.573	5.83±1.52	0.575	0.86±0.90	0.982	58	73.5
GROUP B	2.90±0.76		6.05±1.56		0.86±0.72		21	26.5
Women	2.98±0.72	-	5.67±1.25	-	0.73±0.75	-	45	56.9
Men	1.03±0.96		6.18±1.83		1.03±0.96		34	44.1
Total	2.99±0.77	-	5.89±1.52	-	0.86±0.85	-	79	100.0

N: Number of cases

Table 2— Distribution of Patients According to Ranson Criteria, Group, and Sex

Group Sex		Ranson					Total
		1	2	3	4	5	
A	M	-	5	10	9	1	25
	F	4	7	11	8	3	33
	Total	4	12	21	17	4	58
B	M	-	1	4	3	1	9
	F	-	3	3	5	1	12
	Total	-	4	7	8	2	21
Total	M	-	6	14	12	2	34
	F	4	10	14	13	4	45
	Total	4	16	28	25	6	79

The mean age was 73.4 years (range, 65-96 years). Forty-five patients (56.9%) were women and 34 (44.1%) were men. The mean operation duration for group A and group B was 46 min (range, 25-115 min) and 47 min (range, 30-110 min), respectively. There were no significant differences in the operation duration and length of hospital stay between the two groups. The distribution of patients according to group, sex, length of hospital stay, and length of stay in the intensive care unit (ICU) is shown in Table 1.

The majority of patients (79%) were classified as 3-4 according to the Ranson criteria. According to Ranson criteria, no significant difference was detected between the groups length of hospital stay, operation duration, and complications. The Ranson criteria values of patients according to sex and group are shown in Table 2.

Patients were assessed with the ASA scoring system, but a statistically significant comparison could not be performed because of the low number of patients who were ASA 1. The

groups were then classified into ASA 1-2 and ASA 3-4. There was no significant difference in the operation duration and length of hospital stay between the two groups. However, the length of stay in the ICU was greater in the ASA 3-4 group ($p = 0.301$). The ASA scores of patients according to sex and groups are shown in Table 3.

Hypertension was the most common comorbidity in both groups. Heart disease was more common in men, and diabetes mellitus was more common in women. The distribution of comorbidities according to group and sex is shown in Table 4.

One patient in group A with an ASA score of 4 died in the ICU of respiratory problems. One patient who underwent laparoscopic cholecystectomy required conversion to laparotomy because of the inefficiency of laparoscopic exploration. There was no significant difference in mortality and morbidity rates between group A and group B. Postoperative oral intake started within 8 h in all cases.



Table 3— Relationship Between ASA Score and Complications Among the Groups

Group/Sex		ASA 1	ASA 2	ASA 3	ASA 4	Total
A	M	2	7	12	4	25
	F	3	10	16	4	33
	Total	5	17	28	8	58
B	M	2	2	1	4	9
	F	2	4	5	1	12
	Total	4	6	6	5	21
Total	M	4	9	13	8	34
	F	5	14	21	5	45
	Total	9	23	34	13	79

ASA scores of patients according to sex and groups

Table 4— Distribution of Comorbidities Among the Groups

Group/Sex		Hypertension		Lung Disease		DM		Renal Disease		Heart Disease	
		N	%	N	%	N	%	N	%	N	%
A	M	7	12	2	3	6	10	-	-	8	13
	F	16	27	1	1.7	8	13	2	3%	5	8
B	M	3	14	1	4	-	-	1	4	5	19
	F	7	33	3	14	3	14	-	-	2	9

DM: Diabetes Mellitus

DISCUSSION

AP, which is the inflammation of the pancreas, can present in a large spectrum, from a self-limiting disease to a serious clinical picture, which can lead to sepsis and death. Acute biliary pancreatitis may present as a mild condition that can resolve in a few days, as well as a severe condition that requires hospitalization, presents with local and systemic complications, and can lead to death (13). The systemic inflammatory response and complications that accompany pancreatitis cause an increase in disease-related mortality rates (9,12).

A detailed history, physical examination, laboratory tests, and imaging are required for the diagnosis of acute biliary pancreatitis. The etiology of AP is gallstone pancreatitis in 35%-40% of cases worldwide, but it comprises the majority of cases in Turkey [13]. Biliary diseases are one of the most common reasons for acute gastrointestinal hospitalization. The number of elderly patients with symptomatic gallstones is increasing as life expectancy rises (14,15). Elderly patients who are referred to a hospital with gallstones are often hospitalized with the suspicion of AP. Advanced age is also associ-

ated with the presence of comorbid diseases and insufficient functional reserve (16).

Gallstone passage through the common bile duct and ampulla of Vater is the main cause of biliary AP. Biliary decompression can be performed with ERCP and endoscopic sphincterotomy (17,18). In our study, 14 patients were at high surgical risk according to the ASA score, and they underwent ERCP to reduce the risk of recurrence. These patients were excluded from our study. Four cases of stones in the biliary tract were confirmed preoperatively with MRCP; these patients underwent ERCP and stone removal from the common bile duct with ERCP, followed by cholecystectomy.

After biliary pancreatitis, patients may experience recurrence of biliary pancreatitis or other biliary events such as biliary colic, cholangitis, choledochal obstruction, and acute cholecystitis (13,20). Cholecystectomy or endoscopic sphincterotomy following biliary pancreatitis is advised according to the guidelines to prevent these recurrent biliary events (20). Taking this advice into consideration, early LC is performed after recovering from the first episode of mild biliary pancreatitis. Laparoscopic procedures provide the advantages of dec-



reased pain, shorter convalescence, reduced operative stress, and limited inflammatory process.

The safety and efficacy of LC in biliary AP have been accepted as a standard approach and become the standard of care for gallbladder removal, but the timing of LC remains controversial (21). Delayed cholecystectomy is associated with new biliary attacks and may even increase overall morbidity and length of hospital stay.

If there are local complications such as pancreatic necrosis and organ failure, cholecystectomy should be delayed until the complications resolve, typically after approximately 6 weeks (22). In our study, 51 patients were diagnosed as having severe ABP, and elective cholecystectomy was suggested for patients with severe pancreatitis who were discharged after clinical recovery.

There is an undeniable necessity for an evidence-based treatment protocol based on factors such as patient age, comorbidities, presence of complicated gall bladder disease, and previous operations. The current data are insufficient to support the routine use of LC in elderly patients, although the best evidence to date shows a stable tendency in favor of laparoscopic procedures in terms of mortality, morbidity, and cardiac and respiratory complications in selected cases (23).

In the literature, it has been reported that LC is safe in elderly patients, with low morbidity and mortality rates, and the perioperative outcomes in elderly patients depend on the severity of gall bladder disease rather than chronologic age (24). Early LC in patients who have acute cholecystitis is associated with lesser surgical stress and shorter hospital stays.

In conclusion, cholecystectomy is a definitive treatment for elderly patients with gallstone disease in the prevention of recurrent pancreatitis without increasing the surgical complication rate. Early LC can be indicated for elderly patients with mild acute biliary pancreatitis and acceptable morbidity and mortality risks. LC reduces the risk of complications caused by recurrent pancreatitis in elderly patients. Therefore, surgery should be performed at the first admission.

REFERENCES

- Edward LB III. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. *Arch Surg* 1993 May;128 (5):586-90. (PMID:8489394).
- Singh VK, Bollen TL, Wu BU, et al. An assessment of the severity of interstitial pancreatitis. *Clin Gastroenterol Hepatol* 2011 Dec;9(12):1098-103. doi: 10.1016/j.cgh.2011.08.026. Epub 2011 Sep 3. (PMID:21893128).
- Van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology* 2011 Oct;141(4):1254-63. (PMID:21741922).
- Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. *Gut Liver* 2012 Apr;6(2):172-87. (PMID:22570746).
- Lyon C, Clark C. Diagnosis of acute abdominal pain in older patients. *Am Fam Physician* 2006 Nov 1;74(9):1537-44. (PMID:17111893).
- Agrusa A, Romano G, Frazzetta G, et al. Role and outcomes of laparoscopic cholecystectomy in the elderly. *Int J Surg* 2014;12 Suppl 2:S37-9. (PMID:25159549).
- Kuy S, Sosa JA, Roman SA, Desai R, Rosenthal RA. Rosenthal Age matters: a study of clinical and economic outcomes following cholecystectomy in elderly Americans *Am J Surg* 2011 Jun;201(6):789-96. (PMID:21741511).
- Festi D, Dormi A, Capodicasa S, et al. Incidence of gallstone disease in Italy: results from a multicenter population-based Italian study (the MICOL project) *World J Gastroenterol* 2008 Sep 14;14(34):5282-9. (PMID:18785280).
- Bouwense SA, Besselink MG, van Brunshot S, et al. Pancreatitis of biliary origin, optimal timing of cholecystectomy (PONCHO trial): study protocol for a randomized controlled trial. *Trials* 2012 Nov 26;13:225. (PMID:23181667).
- Nealon WH, Bawduniak J, Walser EM. Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone associated acute pancreatitis with peripancreatic fluid collections. *Ann Surg* 2004 Jun;239(6):741-9. (PMID:15166953).
- Overby DW, Apelgren KN, Richardson W, Fanelli R; Society of American Gastrointestinal and Endoscopic Surgeons. SAGES guidelines for the clinical application of laparoscopic biliary tract surgery *Surg Endosc* 2010 Oct;24(10):2368-86. (PMID:20706739).
- Agresta F, Ansaloni L, Baiocchi GL, et al. Laparoscopic approach to acute abdomen from the Consensus Development Conference of the Società Italiana di Chirurgia Endoscopica e nuove tecnologie (SICE), Associazione Chirurghi Ospedalieri Italiani (ACOI), Società Italiana di Chirurgia (SIC), Società Italiana di Chirurgia d'Urgenza e del Trauma (SICUT), Società Italiana di Chirurgia nell'Ospedalità Privata (SICOP), and the European Association for Endoscopic Surgery (EAES). *Surg Endosc* 2012 Aug;26(8):2134-64. (PMID:22736283).
- Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology* 2007 May;132(5):2022-44. (PMID:17484894).
- Lupinacci RM, Nadal LR, Rego RE, Vege SS. Surgical management of gallbladder disease in the very elderly: are we operating them at the right time? *Eur J Gastroenterol Hepatol* 2013 Mar;25(3):380-4. (PMID:23169310).



15. Tenner S, Baillie J, DeWitt J, et al. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013 Sep;108(9):1400-15;1416. (PMID:2389695).
16. Marcari RS, Lupinacci RM, Nadal LR, Rego RE, Coelho AM, Farah JFM. Outcomes of laparoscopic cholecystectomy in octogenarians. *JLS* 2012 Apr-Jun;16(2):271-5. (PMID:23477177).
17. Visnjevac O, Lee J, Pourafkari L, Dosluoglu HH, Nader ND. Functional capacity as a significant independent predictor of postoperative mortality for octogenarian ASA III patients. *J Gerontol A Biol Sci Med Sci* 2014 Oct;69(10):1229-35. (PMID:24789693).
18. Petrov MS, van Santvoort HC, Besselink MG, et al. Early endoscopic retrograde cholangiopancreatography versus conservative management in acute biliary pancreatitis without cholangitis: a meta-analysis of randomized trials. *Ann Surg* 2008 Feb;247(2):250-7. (PMID:18216529).
19. Working Party of the British Society of Gastroenterology; Association of Surgeons of Great Britain and Ireland; Pancreatic Society of Great Britain and Ireland; Association of Upper GI Surgeons of Great Britain and Ireland. UK guidelines for the management of acute pancreatitis. *Gut* 2005 May;54 Suppl 3:iii1-9. (PMID:15831893).
20. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. *Am J Gastroenterol* 2006 Oct;101(10):2379-400. (PMID:17032204).
21. Shikata S, Noguchi Y, Fukui T. Early versus delayed cholecystectomy for acute cholecystitis: a meta-analysis of randomized controlled trials. *Surg Today* 2005;35(7):553-60. (PMID:15976952).
22. Greenberg JA, Hsu J, Bawazeer M, et al. Clinical practice guideline: management of acute pancreatitis. *Can J Surg* 2016 Apr;59(2):128-40. (PMID:27007094).
23. Antoniou SA, Antoniou GA, Koch OO, Pointner R, Grandrath FA. Meta-analysis of laparoscopic *vs* open cholecystectomy in elderly patients. *World J Gastroenterol* 2014 Dec 14;20(46):17626-34. (PMID:25516678).
24. Rao A, Polanco A, Qiu S, et al. Safety of outpatient laparoscopic cholecystectomy in the elderly: analysis of 15248 patients using the NSQIP database *J Am Coll Surg* 2013 Dec;217(6):1038-43. Epub 2013 Sep 14. (PMID:24045141).