

*“LUCIAN BLAGA” UNIVERSITY OF SIBIU  
MEDICINE*

THESIS

- SUMMARY -

# **LAPAROSCOPIC CHOLECYSTECTOMY – GOLDEN STANDARD**

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## Introduction

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### B. SPECIAL PART

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**Keywords:** laparoscopic cholecystectomy, acute cholecystitis, gallstones, open intervention, SARS-CoV-19, conversion, minimally invasive.

The doctoral thesis title is "Laparoscopic cholecystectomy - golden standard" and has 309 pages, divided into 2 large chapters: general part and special part. The general chapter is in turn divided into 2 other subchapters, respectively: the physiological gallbladder and the pathological gallbladder.

Within the subchapter of physiological gallbladder, the gallbladder was discussed from all points of normality, respectively: embryology, histology, anatomy, physiology and semiology.

In the subchapter of pathological gallbladder was discussed the pathology of the gallbladder - Acute cholecystitis with or without gallstones. Within it we reached the following sub-points: definition, epidemiology, risk factors, pathophysiology, histopathology, clinical forms, symptomatology, clinical examination, paraclinical examination, guidelines, positive diagnosis, differential diagnosis, complications, treatment, evolution, prevention and prognosis.

In the chapter, Special part, 4 types of lots were analyzed:

1. The group of patients from the Surgery Section II of the Sibiu County Emergency Clinical Hospital;
2. The group of patients from the Department of Upper Digestive Surgery and Emergency IV of the University Emergency Hospital of Bucharest;
3. The whole group of patients entered into the study following the inclusion criteria in both studies.

4. The group of patients who presented during the state of emergency (March-May 2020) of the SARS-CoV-19 2020 pandemic in the emergency room of the Bucharest University Emergency Hospital.

A complex group with a total number of 819 cases with pathology of the gallbladder and bladder was initially considered, which determined the choice of only 595 cases with acute pathology. The basic diagnosis was acute non- / lithiasic cholecystitis or chronic acute cholecystitis, a histopathologically confirmed pathology.

The duration of the study included data spread over 2 years (2018-2019) of patients admitted to the Surgery Section II of the Sibiu County Emergency Clinical Hospital but also to the Upper Digestive and Emergency Surgery Section IV of the Bucharest University Emergency Hospital. At the end of the study we wanted to specify a separate study period for the state of emergency of 2020 between March and May.

This is a randomized, analytical and retrospective study on a group of 595 patients, of which 262 in Sibiu and 333 in Bucharest.

For the study, documents were consulted regarding the clinical and paraclinical examination (laboratory analyzes, radiological investigations, histopathological results) of patients both preoperatively and postoperatively (operative protocols, postoperative evolution sheet).

The inclusion criteria of the study are:

- ✓ Diagnosis “acute non- / lithiasis cholecystitis” or “Chronic acute non- / lithiasis cholecystitis”;
- ✓ Histopathological certainty diagnosis;
- ✓ Surgical treatment of the pathology.

The exclusion criteria of the study are:

- ✓ Diagnosis “Chronic non- / lithiasic cholecystitis”;
- ✓ Lack of diagnosis of histopathological certainty;
- ✓ Conservative non-surgical treatment of the pathology or refusal of surgical treatment by the patient or relatives in special cases.

In the attached part of the paper, related to acute lithiasic cholecystitis or non lithiasic cholecystitis with the SARS-CoV-19 pandemic, the study shows the laparoscopic cholecystectomy remains the gold standard for acute cholecystitis, because it guarantees the best results for patients. Conservative management is not to be avoided for mild cases that allow the postponement of laparoscopic cholecystectomy and urgent treatment of the pathology, but it presents the risk of symptoms recurrence and the increased incidence of severe complications.

The sample of cholecystectomies in COVID-positive patients is small (11), suggesting an eclectic approach, with the possibility of resorting to delayed urgency, using conservative therapies whenever possible. Cholecystectomy in the case of the COVID positive patient remains an exceptional solution in the viral outbreak.

Panic and the solutions applied initially or later, have demonstrated inefficiency and the surgery lack of adaptability during the pandemic represented by pandemic dynamics and its waves.

Another important conclusion is that this virus probably will not be able to be completely eradicated and it still suffers and will undergo genetic changes with the most likely increase in aggression, demonstrating this predictable viral capacity, which will determine the population and the entire health system. to reorganize both from a managerial and infectious point of view, as well as financial but also others, requiring the introduction of modular hospitals for infectious patients (positive COVID or others), but also new rules for handling data necessary for hospitalization , as well as treatment (specific to COVID and other accidental or non-accidental biological attacks).

The number of deaths due to digestion has been on the rise since 2011, but without the association with the SARS-Cov-19 virus in terms of pathology. One detail that can be taken into account but without being able to prove it, is the fear caused by the media coverage of the pandemic in 2020 can be a statistical error factor.

Since the 90's, globally, laparoscopic cholecystectomy has been called the "Golden Standard" intervention of this type of pathology, and in 1991 began the era of this intervention in Romania. Our study shows that this type of intervention is still the golden standard for 30 years. During all this time this technique has evolved both from a technological point of view and from a surgeon's point of view. At present, the residents of general surgery are performing a pre-specialization internship for this type of technique.

In the randomized study we introduced 595 patients who presented in the two county hospitals during 2018-2019, but who met all the inclusion criteria.

From the study we can see that a much larger number of patients are found in Bucharest, but if we analyze by comparison with the number of inhabitants in those areas we will see that Sibiu actually has a much larger number of patients presented.

The age groups found are associated with the nomenclature of 61-70 years in both cities, however, there is an exception in Bucharest of 41-50 years. The risk factors in the metropolitan area are much higher, so the predisposition to this pathology is much higher.

The specialized books state that the female sex represents a risk factor, and our study confirms this statement, as there are more women with this pathology compared to men. From the environmental point of view, it is observed that within Sibiu there is no significant difference between rural and urban environment, instead in Bucharest the number of urban ones is double compared to rural ones.

The vast majority of patients in outpatients care presented acute forms, while in emergency room the patients present major complications.

Obesity in our study does not prove to be a risk factor.

Due to daily life and financial problems many patients do not put their health first, so most people go to the doctor more than 72 hours after the onset of symptoms. This delay can take up to days, months and even years. And our study proves the same in both cities.

When the laboratory paraclinical data were discussed, we found that the most relevant laboratory investigations are: leukocytes, total bilirubin, direct bilirubin, transaminases, inflammatory markers. If we consider the possibility of complications we will associate: amylase, lipase, platelets, creatinine, INR.

According to the study, we noticed that not many patients with acute cholecystitis also had an associated acute pancreatitis, which is a complication of this pathology.

From the imaging point of view, we demonstrated that all patients performed abdominal ultrasound, this type of investigation being both effective and cheap, but also easy to perform without subjecting the patient to side effects (radiation). It was observed that a very high percentage of patients (70%) had gallstones (in both cities) on abdominal ultrasound.

We can divide the rest of the imaging investigations into those necessary for the surgery, the heart-lung radiography, the EKG that are present in both cities, and the spirometry much more performed in Bucharest. Imaging investigations that may add delays in the diagnosis of acute cholecystitis are: abdominal computed tomography, cholangio-MRI, abdominal radiography, ERCP. By comparison, the study showed that no abdominal radiography was performed for this type of pathology, although the literature records it, instead the CT scan was frequently performed in both cities and only a few patients resorted to cholangio-MRI ( 2 patients in Sibiu out of 262 and 5 patients in Bucharest out of 333).

The most common associated comorbidities are found to be cardiac as common in both cities, and digestive more common in Bucharest.

Modern medicine has introduced guidelines that can guide us towards possible evolutions or ways of patient management in the future, such as: Charlson Score, Tokyo Score 2013/2018 or ASA Score.

In the data collected, we studied patients who, in addition to acute cholecystitis, had associated neurological and cardiac pathology, if the current state of health has decompensated the two types of pathologies mentioned above. From a neurological point of view, the study showed that the pathology of the gallbladder did not decompensate this type of comorbidity (96% of them), but if we talk about the heart we could see that there was a much greater decompensation than the neurological one ( 24% submitted changes).

The most important part of the study is the one related to the surgical treatment method, where we demonstrated how important the laparoscopic intervention is both from the point of view of the patient and the medical system, including both the doctor and the hospital itself.

In the study we revealed that most patients (252 out of 262 in Sibiu and 294 out of 333 in Bucharest) had a laparoscopic intervention and just a few the classic interventions (10 out of 262 in Sibiu and 13 out of 333 in Bucharest), and in particular the complete lack of conversion in Sibiu, and in Bucharest the number double compared to the classic ones, which proves to us that the first intention intervention was also the laparoscopic one.

We were interested to observe why the doctors chose classic intervention instead of laparoscopic, but also the reasons for the conversion decision.

If we refer to the classical intervention, we will notice that it was the best choice considering their comorbidities and ages, which imposed an increased risk of laparoscopic intervention, but also mechanical reasons. , palpable (eg eventration, adhesion syndrome, ascites, etc.) that could have led to the transformation of laparoscopic intervention into a classic one (conversion). The most common reason discovered in the study for performing the classic intervention per primam, was the adhesion syndrome, suspected especially in patients with previous large-scale surgeries.

From the point of view of conversion, and as mentioned above, we refer strictly to the section in Bucharest, because only here there were conversions, we noticed in the study that the most common reason for transformation of this intervention was gangrenous gallbladder, which caused problems in the discovery of the cystic artery and canal, but also in their ligation being friable, but also in the adhesion syndrome formed as a result of this suffering. Other reasons were: intraoperative hemorrhage, adhesion syndrome or biliary fistula.

Also in the study, we were interested in the appearance of the gallbladder observed macroscopically, at the beginning of the intervention. Most frequently I noticed that from a macroscopic anatomo-pathological point of view it was the ganrenos. We mention that an

inclusion criterion was the presence of a stage of acute cholecystitis demonstrated microscopically and not necessarily macroscopically.

We would like to mention that it can be seen in the study that the presence of gangrene is not an absolute criterion for performing the classic intervention, but is very important decision-making management of each surgeon, so it is observed that there are advanced degenerative forms in laparoscopic interventions. , without conversion. We consider that the macroscopic aspect of the gallbladder is not an absolute criterion for classical intervention or conversion.

If we talk about the adhesion syndrome, the scope of the previous intervention is important, because for a laparoscopic intervention the supraumbilical area is important and not the subumbilical one, but without excluding it completely.  $\frac{1}{4}$  of the patients included in the study have previously had other surgeries.

When we discuss the effectiveness of surgery, we are not just talking about the advantages or disadvantages of the patient, as well as those of the health system, and in this category we can introduce both hospitalization and postoperative days. In Bucharest, most patients had only 2 days of postoperative hospitalization, and in the case of Sibiu about 4 days if we talk about laparoscopic intervention. If we talk about the classic one we will notice that the number of hospitalization days doubles or even triples, which causes disadvantages both for the patient because reintroduction into society and resumption of daily activities is difficult will cause significant emotional damage to him and the system, for that every day of hospitalization costs money for accommodation, food, medicine, medical service. That is why we noted how advantageous the laparoscopic intervention is from these points of view as well.

From the point of view of complications due to acute lithiasis cholecystitis, angiolocolitis and lithiasis of the main bile ducts were analyzed. Following the collected data, we noticed that gallstones are more common compared to angiolocolitis in both cities, but this is not very common either.

In the case of gallstones, ERCP can be performed preoperatively, concomitantly with surgery or postoperatively. From the information gathered, we concluded that ERCP is performed frequently postoperatively and no patient was involved during the intervention of this type of treatment.

An important aspect of surgery is the complications due to the operation itself. In Sibiu, the study showed that in the case of classic intervention, the most common, respectively 2 patients had ligature slip, and in the case of laparoscopic the most common is postoperative hemorrhage, respectively 10 patients, and ligature slip, 5 patients. In Bucharest, in the classic intervention there was no postoperative complication due to the intervention, and for the laparoscopic one

the ligature slip was more frequent (8 patients), and the frequency of hemorrhage is lower (6 patients).

Postoperative complications are not only due to the intervention, they can also be due to comorbidities that can be decompensated after general anesthesia. We noticed that the most common patients had nosocomial infections, and in the second place death (90% of patients were patients with extreme age > 80 years).

Because the study period included 2019 and its completion lasted another year, we considered that we could compare the period of normality in 2019 with the period of emergency in 2020 due to the pandemic SARS - Cov - 19. We showed that the laparoscopic intervention was the method of treatment of these patients, even if initially due to the air blown into the abdominal cavity, on exhalation there would have been a risk of contamination. In conclusion, laparoscopic cholecystectomy remained the gold standard in acute cholecystitis.

### ***Bibliography***

1. [ACS . COVID-19 Guidelines for Triage of Emergency General Surgery Patients \[American College of Surgeons: COVID-19 and Surgery web site\], 2020. Accessed May 14, 2020. <https://www.facs.org/covid-19/clinical-guidance/elective-case/emergency-surgery>;](#)
2. Agresta, F.; Campanile, F.C.; Vettoreto, N. et al. Laparoscopic cholecystectomy: consensus conference-based guidelines. *Langenbecks Arch Surg*, 2015; 400, 429–453;
3. Al Salamah SM. Outcome of laparoscopic cholecystectomy in acute cholecystitis. *J Coll Physicians Surg Pak*. 2005 Jul;15(7):400-3. PMID: 16197867;
4. [Alius C, Tudor C, Badiu CD, Dascălu AM, Smarandache CG, Sabău AD, Tănăsescu C, Bălăşescu SA, Şerban D. Indocyanine Green-Enhanced Colorectal Surgery—between Being Superfluous and Being a Game-Changer. \*Diagnostics\*. 2020; 10\(10\):742. <https://doi.org/10.3390/diagnostics10100742>;](#)
5. [Ambe, P.C., Plambeck, J., Fernandez-Jesberg, V. et al. The role of indocyanine green fluoroscopy for intraoperative bile duct visualization during laparoscopic cholecystectomy: an observational cohort study in 70 patients. \*Patient Saf Surg\* 13, 2 \(2019\). <https://doi.org/10.1186/s13037-019-0182-8>;](#)
6. Angelescu N. - "Caiete de tehnici chirurgicale", vol. 3, Ed. Medicală, Bucureşti, pp. 55-58, 90-91 (2008);
7. Ansaloni, L., Pisano, M., Coccolini, F et al. WSES guidelines on acute calculous cholecystitis. *World J Emerg Surg*. 2016;2016(11):25;

8. Aplicația "Listă medicamente" - producător Modra Jagoda d.o.o. - Slovenia;
9. Badea I. R. - "Tratat de ultrasonografie clinică" volumul I, Ed. Medicală, București, pp. 176-231 (2007);
10. Badiu Gh., Exarcu Teodorescu I. - "Fiziologia umană", Ed. Medicală, București, pp. 296-304 (2014);
11. Bănica R., Samoilă M., Anghel L., Negru M. - "Analize de laborator și alte explorări diagnostice", MedicArt (2007);
12. Beers M. H. - "Manualul Merck de diagnostic și tratament", ediția a XVIII-a, Ed. ALL, București, pp. 240-243 (2006);
13. Beuran M. - "Curs de chirurgie pentru studenți", volumul II, Ed. ILEX, București, pp. 134-139, 156-159 (2013);
14. Bickley L. S. - "Bates' - Ghid de examinare clinică și anamneză", ediția a X-a, Ed. Medicală Callisto, București, pp. 434-451 (2012);
15. Block B. - "Ghid de ecografie - atlas color de anatomie ecografică", Ed. FarmaMedia, pp.101-112 (2016);
16. Bone RC. The pathogenesis of sepsis. *Ann Intern Med.* 1991;115(6):457-69;
17. Borda A. - "Histologie. Țesuturile", Ed. University Press, pp. 21 (2010);
18. Braun J., Dormann A. J. - "Ghid Clinic Medicină Internă", ediția a XI-a, Ed. Medicală, București, pp. 380-382 (2013);
19. Brănescu C, Șerban D, Dascălu AM, Oprescu SM, Savlovschi C. Interleukin 6 and lipopolysaccharide binding protein - markers of inflammation in acute appendicitis. *Chirurgia (Bucur).* 2013 Mar-Apr;108(2):206-14. PMID: 23618571;
20. Campanile FC, Podda M, Arezzo A, et al. Acute cholecystitis during COVID-19 pandemic: a multisocietary position statement. *World J Emerg Surg.* 2020;15(1):38. Published 2020 Jun 8. doi:10.1186/s13017-020-00317-0;
21. [Campanile, F.C.; Pisano, M.; Coccolini, F. et al. Acute cholecystitis: WSES position statement. World J Emerg Surg , 2014; 9, 58. https://doi.org/10.1186/1749-7922-9-58;](https://doi.org/10.1186/1749-7922-9-58)
22. Cano-Valderrama O, Morales X, Ferrigni CJ, et al. Reduction in emergency surgery activity during COVID-19 pandemic in three Spanish hospitals. *Br J Surg.* 2020;107(8):e239. doi:10.1002/bjs.11667;
23. Corneci D. „Risc și prognostic în anestezie și terapie intensiva sisteme de scoruri”;
24. [COVIDSurg Collaborative . Global Guidance for surgical care during the COVID-19 pandemic. Br J Surg 2020; 107: 1097–1103. \[Google Scholar\];](https://doi.org/10.1097/BJS.0000000000001103)

25. Dambro M. R. -"Consultul medical în 5 minute". Ed. Medicală Callisto, pp.288-289 (2008);
26. Dascălu, AM, Tudosie, MS ; Smarandache, GC; Șerban, D : Impact of the covid-19 pandemic upon the ophthalmological clinical practice; *Rom J Legal Med*, **2020**, 28(1),pg. 96-100, DOI: 10.4323/rjlm.2020.96;
27. De Simone, B., Chouillard, E., Di Saverio, S et al. Emergency surgery during the COVID-19 pandemic: what you need to know for practice. *Ann R Coll Surg Engl*. 2020;102(5):323-332.doi:10.1308/rcsann.2020.0097;
28. Dumitrascu D., Acalovschi M., Grigorescu M. - "Litiaza biliară", Ed. Academiei Republicii Socialiste Române, București (1989);
29. [F. Narvaez, J. R., Cooper, C., Brewer, J. J., Schwaitzberg, S. D., & Guo, W. A. \(2020\). Do We “Do No Harm” in the Management of Acute Cholecystitis in COVID-19 Patients? The American Surgeon. https://doi.org/10.1177/0003134820939881 ;](https://doi.org/10.1177/0003134820939881)
30. Flemming S., Hankir M., Hering I. Abdominal fluid samples (negative for SARS-CoV-2) from a critically unwell patient with respiratory COVID-19 [published online ahead of print, 2020 May 26] *Br. J. Surg.* 2020 doi: 10.1002/bjs.11713. 10.1002/bjs.11713. [PMC free article] [PubMed] [CrossRef] [Google Scholar];
31. Gherasim F. - "Chirurgie- volum II, Semiologie chirurgicală", Ed. Sitech, Craiova, pp.273-278 (2012);
32. Giulio M., Achilli P., Dario M. An underestimated "false negative COVID cholecystitis" in Northern Italy and the contagion of a surgical ward: it can happen everywhere [published online ahead of print, 2020 May 13] *Surgery*. 2020;1-2 doi: 10.1007/s13304-020-00781-y. [PMC free article] [PubMed] [CrossRef] [Google Scholar];
33. Gupta N, Agrawal H. COVID 19 and laparoscopic surgeons, the Indian scenario - Perspective. *Int J Surg*. 2020;79:165-167. doi:10.1016/j.ijssu.2020.05.076;
34. Gurusamy, K.S.; Davidson, C., Gluud, C. et al. Early versus delayed laparoscopic cholecystectomy for people with acute cholecystitis. *Cochrane Database Syst Rev*. 2013;6:CD005440;
35. Guyton A. C. - "Tratat de fiziologie a omului", ediția a XI-a, Ed. Medicală Callisto, pp.802-804 (2006);
36. Hartnett KP, Kite-Powell A, DeVies J, et al. Impact of the COVID-19 Pandemic on Emergency Department Visits — United States, January 1, 2019–May 30, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:699–704. DOI: <http://dx.doi.org/10.15585/mmwr.mm6923e1>external icon;

37. Hiwatashi K, Okumura H, Setoyama T, et al. Evaluation of laparoscopic cholecystectomy using indocyanine green cholangiography including cholecystitis: A retrospective study. *Medicine (Baltimore)*. 2018;97(30):e11654. doi:10.1097/MD.00000000000011654;
38. [https://en.wikipedia.org/wiki/Accessory\\_bile\\_duct](https://en.wikipedia.org/wiki/Accessory_bile_duct);
39. [https://ro.qaz.wiki/wiki/Mallampati\\_score](https://ro.qaz.wiki/wiki/Mallampati_score);
40. Junqueira L. C. -"Histologie - tratat & atlas", editia a XI-a, Ed. Medicală Callisto, București, pp. 336- 338 (2008);
41. Juvara I. „Probleme medico-chirurgicale de patologie hepato-biliara”, Ed. Medicala, Bucuresti (1969);
42. Kabir T, Kam JH, Chew MH. Cholecystectomy during the COVID-19 pandemic: Current evidence and an understanding of the 'new' critical view of safety: Correspondence. *Int J Surg*. 2020;79:307-308. doi:10.1016/j.ijssu.2020.06.012;
43. Kabir T, Ngaserin SH, Koh FH, Ong BC, Chew MH. The Covid Conundrum: SARS-CoV-2 is not present in bile. Accepted for publication in *Br J Surg*;
44. Kasprzak A, Szmyt M, Malkowski W, Przybyszewska W, Helak-Lapaj C, Seraszek-Jaros A, Surdacka A, Małkowska-Lanzafame A, Kaczmarek E. Analysis of immunohistochemical expression of proinflammatory cytokines (IL-1 $\alpha$ , IL-6, and TNF- $\alpha$ ) in gallbladder mucosa: comparative study in acute and chronic calculous cholecystitis. *Folia Morphol (Warsz)*. 2015;74(1):65-72. doi: 10.5603/FM.2015.0011;
45. Katzel J. A. - "Ghidul medicului de gardă", Ed. FarmaMedia, pp.158 (2011);
46. Klatt E. C. - "Robbins and Cotran - Atlas of Pathology", ediția a II-a, Ed. Saunders Elsevier, pp. 213-240 (2010);
47. Le VH, Smith DE, Johnson BL. Conversion of laparoscopic to open cholecystectomy in the current era of laparoscopic surgery. *Am Surg*. 2012 Dec;78(12):1392-5. PMID: 23265130;
48. Longo D. L., Fauci A. S., - "Harrison Gastroenterologie și hepatologie", editia a II-a, Ed. ALL, pp. 458-475 (2017);
49. [Manzia T M, Angelico R, Parente A, Muiesan P, Tisone G, & MEGAVID \(ManagEment of GAllstone disease during coVID-19 pandemic\) Clinical Investigator Group \(2020\). Global management of a common, underrated surgical task during the COVID-19 pandemic: Gallstone disease - An international survey. \*Annals of medicine and surgery\*,2020\(57\): 95–102. <https://doi.org/10.1016/j.amsu.2020.07.021>;](https://doi.org/10.1016/j.amsu.2020.07.021)

50. Minutolo V, Licciardello A, Arena M, Nicosia A, Di Stefano B, Cali G, Arena G. Laparoscopic cholecystectomy in the treatment of acute cholecystitis: comparison of outcomes and costs between early and delayed cholecystectomy. *Eur Rev Med Pharmacol Sci*. 2014 Dec;18(2 Suppl):40-6. PMID: 25535191;
51. [Miura, F., Okamoto, K., Takada, T., Strasberg, S.M., Asbun, H.J., Pitt, H.A., Gomi, H., Solomkin, J.S., Schlossberg, et al: Tokyo Guidelines 2018: initial management of acute biliary infection and flowchart for acute cholangitis. \*J Hepatobiliary Pancreat Sci\*, 2018;25: 31-40. <https://doi.org/10.1002/jhbp.509>;](#)
52. Moore L. K. -"Anatomia clinica - fundamente și aplicații", editura Medicală Callisto, București, pp. 277-289 (2012);
53. Nahshon C., Bitterman A., Haddad R., Hazzan D., Lavie O. Hazardous postoperative outcomes of unexpected COVID-19 infected patients: a call for global consideration of sampling all asymptomatic patients before surgical treatment [published online ahead of print, 2020 may 16] *World J. Surg.* 2020;1–5. doi: 10.1007/s00268-020-05575-2. [PMC free article] [PubMed] [CrossRef] [Google Scholar];
54. O. Popescu, D. Baz , "Matematici aplicate in economie", Ed. Didactica si pedagogica R.A., Bucuresti, 1997;
55. Oseran, Andrew S., et al. "Changes in Hospital Admissions for Urgent Conditions During COVID-19 Pandemic." *Am J Manag Care* 26 (2020): 8;
56. Palade R. S. - "Manual de chirurgie generală", ediția a II-a, Ed. ALL, pp.127-131 (2008);
57. Papilian V. - "Anatomia omului", volumul II, Ed. Didactica și pedagogică, București, pp. 163-167 (1982);
58. Paulman P.M. - "Taylor - Manual de diagnostic diferențial", ediția a III-a, Ed. ALL, pp. 233-235 (2016);
59. Popescu I. - "Tratat de chirurgie", volumul IX, partea a II-a, Ed. Academiei Române, pp. 825- (2009 );
60. Popescu I., Beuran M. - "Manual de chirurgie", volumul II, Ed. Universitară Carol Davila, Bucuresti, pp. 737-760 (2017);
61. Ranga V. - "Tubul digestiv abdominal și glandele anexe. Splina"; Ed. Cerna, București, pp. 120-155 (1994);
62. Rasezu V. - "Chirurgie generala", Ed. Răzeșu, pp. 493-515;
63. Roffman, C.; Buchanan, J.; Allison, G. Charlson comorbidities index. *Journal of physiotherapy*, 2016;62(3);

64. S.J. Fu, E.L. George, P.M. Maggio, et al., The consequences of delaying elective surgery: surgical perspective, *Ann. Surg.* (2020), <https://doi.org/10.1097/SLA>. T.M. Manzia, et al. *Annals of Medicine and Surgery* 57 (2020) 95–102 101 0000000000003998 [Epub ahead of print]. Accessed on June 20, 2020;
65. Sabatine M. S. - " Date medicale esențiale - ghid de buzunar" ediția a V-a, Ed. ALL, București, pp. 3.35-3.37 (2017);
66. Sabau D. „Curs colecist”, Sibiu;
67. Sailer C. - "Ghid clinic de diagnostic diferențial", Ed. FarmaMedia, pp.79-80 (2014);
68. Sartelli, M.; Abu-Zidan, F.M.; Catena, F.; Griffiths, E.A.; Di Saverio, S.; Coimbra, R.; Ordoñez, C.A.; Leppaniemi, A.; Fraga, G.P.; Coccolini, F. et al. Global validation of the WSES Sepsis Severity Score for patients with complicated intra-abdominal infections: a prospective multicentre study (WISS Study) *World J Emerg Surg.* 2015;10:61;
69. Savlovschi C, Brănescu C, Șerban D, et al. Hernia Amyand--caz clinic [Amyand's hernia--a clinical case]. *Chirurgia (Bucur).* 2010;105(3):409-414;
70. Savlovschi C, Șerban D, Andreescu C, Dascălu A, Pantu H. Economic analysis of medical management applied for left colostomy. *Chirurgia (Bucur).* 2013;108(5):666-669;
71. Săftoiu A, Tomulescu V, Tanțău M, et al. SRED-ARCE Recommendations for Minimally Invasive Interventions During the COVID-19 Pandemic in Romania. *Chirurgia (Bucur).* 2020;115(3):289-306. doi:10.21614/chirurgia.115.3.289;
72. Schimitzer G. - "Radiologie medicală", volumul II, Ed. Didactică și pedagogică, București, pp. 282-302 (1966);
73. Schumann RR, Rietschel ET, Loppnow H. The role of CD14 and lipopolysaccharide-binding protein (LBP) in the activation of different cell types by endotoxin. *Med Microbiol Immunol.* 1994;183(6):279-97;
74. Seidel, Gruene, Borte -"Clasificări medicale", Ed. Farma Media, Târgul Mureș, pp.193 (2010);
75. Shabbir A., Menon R.K., Somani J. ELSA recommendations for minimally invasive surgery during a community spread pandemic: a centered approach in Asia from widespread to recovery phases [published online ahead of print, 2020 May 11] *Surg. Endosc.* 2020:1–6. doi: 10.1007/s00464-020-07618-0;
76. Silbernagl S. - "Fiziopatologie - Atlas color", ediția a II-a, Ed. Callisto, pp. 178-180 (2011);
77. [Society of American Gastrointestinal and Endoscopic Surgeons SAGES and EAES, recommendations regarding surgical response to COVID-19 cases.](#)

2020. <https://www.sages.org/recommendations-surgical-response-covid-19/> Accessed March 30;

78. Su PY, Liu SJ, Chen YH, Wu SS, Chen YL, Ke JR, Peng CY, Sher YP. Increased IL-8 and IL-1 $\beta$  in the bile of acute cholecystitis patients, *BioMedicine*, 2013;3(4): 181-185, <https://doi.org/10.1016/j.biomed.2013.08.001>;

79. Suc B, Fontes Dislaire I, Fournanier G, Escat J. 3606 cholecystectomies under celioscopy. The Register of the French Society of Digestive Surgery. *Ann Chir*. 1992;46:219–26;

80. Şavlovschi C, Comandaşu M, Şerban D. Specifics of diagnosis and treatment in synchronous colorectal cancers (SCC). *Chirurgia (Bucur)*. 2013;108(1):43-45;

81. Şerban D, Soce B, Bălăşescu SA, Badiu CD, Tudor C, Dascălu AM, Vancea G, Spătaru RI, Sabău AD, Sabău D, Tănăsescu C. Safety of Laparoscopic Cholecystectomy for Acute Cholecystitis in the Elderly: A Multivariate Analysis of Risk Factors for Intra and Postoperative Complications. *Medicina*. 2021; 57(3):230. <https://doi.org/10.3390/medicina57030230>;

82. Şerban D, Spătaru RI, Vancea G, Bălăşescu SA, Socea B, Tudor C, Dascălu AM: Informed consent in all surgical specialties: from legal obligation to patient satisfaction *Rom J Leg Med*, 2020; 28(3): 317-321;

83. Şerban D., Smarandache CG, Tudor C, Duţă L Dascălu AM, Alius C: Laparoscopic Surgery in COVID-19 Era – Safety and Ethical issues, *Diagnostics*, [Epub ahead of print]. Accessed on September, 2020;

84. Tarcoveanu E. - "Elemente de chirurgie laparoscopică", volumul II, Ed. Polirom, Iasi, pp. 22-68 (1998);

85. The Royal College of Surgeons of England. Intercollegiate General Surgery Guidance on COVID-19. <https://www.rcseng.ac.uk/coronavirus/joint-guidance-for-surgeons-v2/>;

86. Tucker, J.J.; Yanagawa, F.; Grim, R.; Bell, T.; Ahuja, V. Laparoscopic cholecystectomy is safe but underused in the elderly. *Am. Surg.* **2011**, *77*, 1014–1020;

87. Vasilescu G. - "Dicţionar de medicină", ediţia a VI-a, Ed. ALL, pp. 169 (2010);

88. Wakabayashi G., Iwashita Y., Hibi T. Tokyo Guidelines 2018: surgical management of acute cholecystitis: safe steps in laparoscopic cholecystectomy for acute cholecystitis (with videos) *J Hepatobiliary Pancreat Sci*. 2018;25(1):73–86. doi: 10.1002/jhbp.517. [PubMed] [CrossRef] [Google Scholar];

89. Weber E. C. - "Netter's Concise Radiologic anatomy", ediţia a II-a, Ed. Elsevier, pp. 252-253 (2014);

90. Wiener L. S. - "Diagnosticul diferențial în durere acută", Ed. Științelor Medicale, București, pp. 184-186 (1998);
91. [www.cnsisp.insp.gov.ro](http://www.cnsisp.insp.gov.ro)
92. [www.insse.ro](http://www.insse.ro)
93. [www.websurg.com](http://www.websurg.com);
94. Zollinger R.M.Jr. - "Atlas de tehnici chirurgicale", Ed. Științelor Medicale, București, pp. 182-197 (2007);
95. Zucker KA, Bailey RW, Flowers J. Laparoscopic management of acute and chronic cholecystitis. *Surg Clin North Am.* 1992;72:1045–67;