



Surgical treatment of liver hydatid cyst in elderly patients: A propensity score-matching retrospective cohort study

Isabel Jaén-Torrejimenó^b, Diego López-Guerra^{a,b}, Adela Rojas-Holguín^{a,b}, Noelia De-Armas-Conde^b, Gerardo Blanco-Fernández^{a,b,*}

^a Universidad de Extremadura. Facultad de Medicina y Ciencias de la Salud. Avda. de Elvas sn. 06006. Badajoz. España

^b Hospital Universitario de Badajoz. Servicio de Cirugía Hepatobiliopancreática y Trasplante Hepático. Avda. Elvas sn. 06080 Badajoz. España

ARTICLE INFO

Keywords:

Liver hydatidosis
Elderly
Liver surgery
Morbidity

ABSTRACT

Background: Cystic echinococcosis is a clinically complex chronic parasitic disease and a major socioeconomic problem in endemic areas. The safety of liver resection in elderly patients is often debated among medical professionals. We analyzed the postoperative morbidity and mortality rates of elderly patients who underwent surgery at our unit.

Methods: We retrospectively evaluated patients with liver hydatid cysts which were surgically removed at our unit. Patients were divided into two groups: Group 1 (patients < 70 years), and Group 2 (patients ≥ 70 years). Propensity score matching (PSM) and comparative analyses between groups were performed.

Results: The unmatched cohort consisted of 279 patients (Group 1: 244; Group 2: 35). After PSM, we compared the outcomes for 56 patients from Group 1 to 31 patients from Group 2. A higher rate of severe complications was observed in Group 2 (25.8% vs 5.36%, $p = 0.014$). No difference was found in the rates of infectious, cardiorespiratory, or hemorrhagic complications between both groups, and in the mortality rate either (0.00% vs 6.45%, $p = 0.124$).

Conclusions: Liver surgery in selected elderly patients is safe and practicable. The low postoperative morbidity rate in these patients is acceptable, albeit higher, due to their comorbidities.

1. Introduction

Hepatic hydatidosis is an endemic zoonosis in the Mediterranean region in Europe, South America, Central Asia, and Eastern Europe. Nevertheless, it is also frequently observed in non-endemic areas, due to the rise in global travel and immigration (Mihmanli et al., 2016; Muhtarov et al., 2018). In hydatid disease, infection can be found most often in the liver (50–70% of cases) (Muhtarov et al., 2018).

Although there is a lack of established unanimous action protocols, surgery remains the most common treatment for this condition (Stojkovic et al., 2009). Specifically, radical techniques, including liver resection in certain cases, effectively eliminate the parasite and prevent potential complications and recurrence of the disease (Ramia et al., 2020, 2018). In some cases, medical treatment can be used as adjuvant to surgery treatment (Akbulut and Sahin, 2021; Sozuer et al., 2014).

In recent decades, as life expectancy grows and the population ages, we have seen a larger number of older patients with clinically-relevant

comorbidities who undergo liver surgery (Cho et al., 2011; Dedinska et al., 2017; Reddy et al., 2011). To ensure the best outcomes for these patients, a case-by-case study and an improvement in surgical techniques and postoperative care after a liver procedure is key (Cho et al., 2011). The role of advanced age has been researched in different studies as a possible risk factor for postoperative complications and reduced long-term survival with conflicting findings, given the samples' heterogeneity and their small size in most studies; thus not being able to reach definitive conclusions or a consensus (Andert et al., 2016; Cho et al., 2011).

The influence of age on the outcome of surgery has already been extensively analyzed in some fields, such as cardiovascular surgery, which for epidemiological reasons is more frequently performed on the elderly (Aldrighetti et al., 2003; Aoyama et al., 2018). Most studies concerning hepatic resection in the elderly are within the context of liver tumors, particularly hepatocellular carcinomas and colorectal metastatic cancer (Dedinska et al., 2017).

* Corresponding author.

E-mail address: gerardoblanco@unex.es (G. Blanco-Fernández).

<https://doi.org/10.1016/j.actatropica.2022.106466>

Received 22 February 2022; Received in revised form 16 March 2022; Accepted 11 April 2022

Available online 20 April 2022

0001-706X/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Our goal is to analyze the outcomes of surgical treatment of hepatic hydatidosis in elderly patients by evaluating their postoperative morbidity and mortality, as well as by performing PSM to minimize selection biases.

2. Materials and methods

The work has been report in line with the STROCSS criteria (Agha et al., 2019) and has been registered in ClinicalTrials.gov (NCT 05113550). The study was approved by the Research Ethics Committee of our hospital at September 18th, 2021 (Number Id. 18092021).

2.1. Study design

Retrospective observational study from prospective database focused on liver hydatidosis carried out at our Hepato-Pancreato-Biliary Surgery Unit. The study period spanned from January 2006 to October 2020. An informed consent from the patient was not required since the study was retrospective and observational, and entailed no risk. Seventy years of age was the cutoff age to consider patients as elderly.

Inclusion criteria of patients: liver hydatid cyst (LHC) diagnosed by preoperative computed tomography (CT) or magnetic resonance imaging (MRI) and pathological diagnosis after surgery, and LHC treated by total or partial pericystectomy.

Exclusion criteria of patients: emergency surgery and simple drainage of cyst.

2.2. Preoperative assessment

Preoperative diagnostic workup included abdominal ultrasound and CT scan. The anesthesiology risk was evaluated in all patients by first-level investigations, which included complete blood chemistry tests, standard chest x-ray, basal electrocardiogram, and blood gas analysis. Additional cardiologic evaluations, including an exercise electrocardiogram (ECG) and/or myocardial perfusion scintigraphy, were only performed in patients with a medical history of coronary artery disease, regardless of age. The American Society of Anesthesiologists (ASA) score was used as the morbidity indicator after abdominal surgery in these patients. Comorbidities were tabulated into the Charlson Comorbidity Index (CCI) for each patient (Charlson, 1987).

2.3. Definitions

Patients were divided into two groups: Group 1 (patients < 70 years of age), and Group 2 (patients ≥ 70 years of age). LHCs were grouped into subtypes based on the World Health Organization (WHO) classification (Brunetti et al., 2010).

LHC was considered complicated when it presented with at least one of the following characteristics at the time of diagnosis: abscess formation, rupture, hepatothoracic transit, cystobiliary communication or some other less common type of fistula or communication, or those causing jaundice at diagnosis due to extrinsic compression of the biliary tree (Akbulut, 2018; Koc et al., 2020).

The Couinaud classification was used to define major (≥ 3 segments) and minor (≤ 2 segments) liver resections (Couinaud, 1999). Bile leakage was classified according to the definition and grading system of the International Study Group of Liver Surgery (ISGLS) (Koch et al., 2011).

Radical surgery referred to opened or non-opened cystopericystectomy or to liver resection, while conservative procedures included partial pericystectomy, unroofing of the cyst after content removal and vesicle extraction with external or internal drainage, combined with one of various procedures to manage the residual cavity (El Malki et al., 2014; Jaén-Torrejíméno et al., 2020; Pang et al., 2018).

Relapse was defined as the appearance of new active liver cysts after the patient had undergone surgery to treat the disease. Cysts areas with

no change in size or evidence of daughter cyst sign in imaging tests were not considered a recurrence (Jerraya et al., 2015; Velasco-Tirado et al., 2017).

2.4. Variables

The following variables were gathered from medical records: Epidemiological: age, sex, comorbidities, ASA classification, Charlson Comorbidity Index; clinical: LHC-related symptoms, status (new or previous history of hydatidosis), physical examination; diagnostic: laboratory results, serological tests; radiological and endoscopic diagnostic tests, number, size and location of cysts, type of LHC based on abdominal ultrasonography (US) and computed tomography (CT) scan findings, cysts in other organs, and presence or absence of complications (superinfection, rupture, cystobiliary communication, anaphylactic and compression or invasion of neighboring organs). In certain cases, a magnetic resonance cholangiography was performed. Surgical approach: type of resection; laparoscopic or open approach. Details of the postoperative course were collected: morbidity according to the Clavien-Dindo score (Dindo et al., 2004), “severe complication” (Clavien-Dindo ≥ IIIa) and postoperative mortality; as well as hospital length of stay and postoperative follow-up (months). For the recording of complications, the medical and nursing notes from the patients’ electronic records or histories were referred to.

In patients with complicated or multiple hydatid cysts, albendazole 400 mg twice daily for 28 days before and after surgery is usually prescribed. During albendazole treatment, we perform liver function tests and white blood cell counts. (Nazligul et al., 2015).

2.5. Surgery

Precautions were taken to avoid spillage of the parasite into the abdominal cavity. The peritoneal cavity was liberally protected with scolicidal agents. All patients underwent intraoperative ultrasound in order to locate any cysts which might have been missed by preoperative imaging, as well as to establish the connection between the cyst and large vessels. All patients underwent laparotomy surgery. The type of surgery performed was based on the intraoperative findings and the location and size of the cyst.

Conservative surgical approach: when a conservative surgical approach was employed, all contents were aspirated and the cavity was irrigated with hypertonic saline. The pericyst was cleaned and daughter cysts removed. The LHC was unroofed and partial cystectomy was performed. The residual cavity was examined for biliary fistulas. Obliteration of the remaining cavity was performed by omentoplasty, capitonage, marsupialization, or drainage. Usually, partial cystectomy was performed when the cyst wall abutted and threatened to injure the major vascular and biliary structures (Jaén-Torrejíméno et al., 2021, 2020).

Radical surgical approach: radical LHC procedures consisted of total pericystectomy whether involving the opening before cyst removal (opened cystectomy) or not (non-opened cystectomy), depending on size and location. Location was also the determining factor to decide between anatomical or non-anatomical liver resection. Generally, when the cyst involved an entire lobe and/or the main pedicles, hepatectomy was carried out.

2.6. Follow-up

Patients were followed up with abdominal US or CT scan and hydatid serology. (Jaén-Torrejíméno et al., 2020) The follow-up period for these patients is typically indefinite. Of those included in the study, the minimum follow-up period was six months. Treatment with oral albendazole was indicated for one month post-surgery in the case of complicated cysts.

2.7. Statistical analysis

Categorical variables were shown as number of cases (percentage) and compared by the chi-square with Yates' correction or Fisher's exact test. Normally-distributed continuous data were expressed as mean $\pm$ standard deviation (SD), while non-normally distributed data were presented as median with interquartile range (IQR). Continuous variables were compared by the Student t-test. Pearson's correlation coefficient was used to assess a potential relationship between continuous variables.

Propensity scores (PS) estimated by multiple logistic regression analysis were used to adjust for confounding variables of Charlson Comorbidity Index (CCI), symptomatic cyst, complicated cyst, ruptured cyst, abscessed cyst. ASA classification was not included in the logistic model because of its correlation with the CCI. PS nearest-neighbor matching without replacement was used to match subjects on a 1:2 basis for ≥ 70 years and < 70 years, respectively. The caliper value was set at 0.05. Standardized mean difference was used to test the balance of the matched variables.

The following variables were included in the PSM model: Clavien-Dindo score, "severe complication", postoperative mortality, complications related to infection, wound infection, residual cavity infection, subphrenic abscess, postoperative biliary fistula, postoperative hemorrhage, cardiorespiratory complications, reoperation, and readmission. Variables with too much missing data were not included for PSM. The variables matched were compared between the two age groups both before and after PSM. Comparisons in the matched cohort took into account stratification by matched pairs.

We set statistical significance at 5% ($p \leq 0.05$). All analyses were performed using R software 4.0.3 (<http://www.r-project.org/>), specifically the compareGroups, cobalt, and MatchIt packages.

3. Results

This study looked into a total of 279 patients who had undergone surgery for hepatic hydatidosis at our unit, during the aforementioned study period, with a mean age of 51 years [41.00; 62.00]. The cohort included 149 male patients (53.4%). Before PSM, Group 1 (< 70 years) included 244 patients (87.5%), and Group 2 (≥ 70 years) had 35 patients (12.5%).

3.1. Comparison before PSM

Baseline features of patients in both groups were recorded in Table 1. The percentage of patients who had previously undergone surgery for hydatidosis was 19.4%, with no statistically-significant difference between both groups (19.7% vs. 17.4% $p = 0.900$).

When comparing both groups (Table 1), we can see that Group 1 had a lower rate of patients with ASA ≥ 2 (70.9% vs 100%, $p < 0.001$), as well as a lower rate of obese patients, defined as BMI ≥ 30 , (36.1% vs 68.8%, $p = 0.022$). Among observed comorbidities, Group 2 had a larger number of patients with arterial hypertension, diabetes mellitus, and tumor without metastasis.

The cyst characteristics of each group were recorded in Table 2. Group 1 displayed a lower percentage of complicated cysts at the time of diagnosis than Group 2 (34.4% vs 57.1%, $p = 0.016$). There were no differences found in terms of cyst location, number, and size.

Radical surgery was performed in 58.8% of overall cases (60.2% vs 48.6% for Group 1 and 2, respectively, $p = 0.259$). Minor liver resections were performed in 14.3% of overall cases (13.9% vs 17.1%, respectively in each group, $p = 0.804$), while major liver resections were carried out in 8.24% of overall cases (8.61% vs 5.71%, $p = 0.259$).

Data from postoperative complications before matching were recorded in Table 4. Patients from Group 1 were observed to experience lower rates in the following three categories: postoperative complications (84.3% vs 15.7%, $p = 0.189$), severe complications (defined as

Table 1

Baseline characteristics of patients before PS matching.

	All N=279	Group 1 (< 70 yr) N=244	Group 2 (≥ 70 yr) N=35	P < 0.05
Age (years) Media, SD	51.3 (+/- 14.7)	47.9 (+/- 12.3)	75.0 (+/- 4.38)	< 0.001
Male gender, n (%)	149 (53.4%)	128/149 (52.5%)	21/149 (60.0%)	0.512
Hospital length of stay Median, IQR	7.00 [6.00;10.0]	7.00 [6.00;10.0]	8.00 [6.00;15.5]	0.063
ASA, n (%)				< 0.001
I	60 (21.5%)	60 (29.1%)	0 (0.0%)	
II	142 (50.9%)	127 (61.7%)	15 (71.4%)	
III	25 (9%)	19 (9.2%)	6 (28.6%)	
BMI Median, IQR	28.4 [25.1;31.6]	28.0 [24.9;31.6]	30.5 [27.5;31.6]	0.095
Obesity (BMI ≥ 30), n (%)	72 (38.9%)	61 (36.1%)	11 (68.8%)	0.022
Previous recurrence, n (%)	54 (19.4%)	48 (19.7%)	6 (17.1%)	0.900
Smoker, n (%)	50 (18.1%)	49 (20.2%)	1 (2.86%)	0.023
SAHS, n (%)	10 (3.61%)	8 (3.31%)	2 (5.71%)	0.367
Arterial hypertension, n (%)	77 (27.7%)	55 (22.6%)	22 (62.9%)	< 0.001
Diabetes mellitus, n (%)	25 (8.99%)	15 (6.17%)	10 (28.6%)	< 0.001
Myocardial infarction, n (%)	4 (1.44%)	3 (1.23%)	1 (2.86%)	0.418
Congestive heart failure, n (%)	1 (0.36%)	1 (0.41%)	0 (0.00%)	1.000
Peripheral vascular disease, n (%)	5 (1.80%)	3 (1.23%)	2 (5.71%)	0.121
Cerebrovascular accident, n (%)	4 (1.44%)	3 (1.23%)	1 (2.86%)	0.418
Dementia, n (%)	1 (0.36%)	0 (0.00%)	1 (2.86%)	0.126
COPD, n (%)	8 (2.88%)	6 (2.47%)	2 (5.71%)	0.266
Connective tissue disease, n (%)	3 (1.08%)	3 (1.23%)	0 (0.00%)	1.000
Peptic ulcer disease, n (%)	9 (3.24%)	7 (2.88%)	2 (5.71%)	0.316
Liver disease, n (%)	7 (2.52%)	7 (2.88%)	0 (0.00%)	1.000
Hemiplegia, n (%)	1 (0.36%)	1 (0.41%)	0 (0.00%)	1.000
Moderate to severe CKD, n (%)	4 (1.44%)	3 (1.23%)	1 (2.86%)	0.126
Any tumor, n (%)	8 (2.88%)	4 (1.65%)	4 (11.4%)	0.010
Metastatic solid tumor, n (%)	1 (0.36%)	0 (0.00%)	1 (2.86%)	0.126
CCI Median, IQR	0.00 [0.00;0.00]	0.00 [0.00;0.00]	0.00 [0.00;2.00]	<0.001

PS: propensity score; ASA: American Society of Anesthesiologists; BMI: body mass index; SAHS: sleep apnea-hypopnea syndrome; COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease; CCI: charlson comorbidity index

Clavien-Dindo score $\geq$ IIIa) (9.43% vs 22.9%, $p = 0.038$), and postoperative mortality (0.00% vs 5.71%, $p = 0.015$). No differences were seen with respect to complications derived from infection, or the development of biliary fistulas.

The median length of stay was 7.00 days [6.00; 10.0] for Group 1, and 8.00 days [6.00; 15.5] for Group 2 ($p = 0.063$). No differences were observed in the readmission rate between both groups.

The mean patient follow-up period after surgery was 76.55 months [36.24; 126.03]. During follow-up, no statistically-significant differences were observed in terms of relapse rates (6.56% vs 3.03%, $p = 0.703$).

3.2. Comparison after PSM

After adjusting PSM to the preoperative covariates of comorbidity and cyst characteristics (Table 3), 56 patients were placed in Group 1 (< 70 years), and 31 patients in Group 2 (≥ 70 years) (Table 4).

Table 2
Characteristics of the cysts and surgery performed before PS matching.

	All N=279	Group 1 (< 70 yr) N=244	Group 2 (≥70yr) N=35	P < 0.05
Symptomatic, n (%)	121 (43.4%)	100 (41.0%)	21 (60.0%)	0.052
WHO Classification, n (%)				0.502
- CE 1	23 (8.88%)	18 (7.89%)	5 (16.1%)	
- CE 2	121 (46.7%)	109 (47.8%)	12 (38.7%)	
- CE 3	39 (15.1%)	33 (14.5%)	6 (19.4%)	
- CE 4	53 (20.5%)	47 (20.6%)	6 (19.4%)	
- CE 5	23 (8.88%)	21 (9.21%)	2 (6.45%)	
Jaundice, n (%)	35 (12.5%)	30 (12.3%)	5 (14.3%)	0.784
Hepatothoracic transit, n (%)	25 (8.96%)	21 (8.61%)	4 (11.4%)	0.533
Infected cysts, n (%)	20 (7.17%)	14 (5.74%)	6 (17.1%)	0.026
Rupture cysts, n (%)	11 (3.94%)	6 (2.46%)	5 (14.3%)	0.006
Complicated cysts, n (%)	104 (37.3%)	84 (34.4%)	20 (57.1%)	0.016
Calcified hydatid cyst, n (%)	59 (21.1%)	52 (21.3%)	7 (20.0%)	1.000
Number of cysts	1.00	1.00	1.00	0.859
Median, IQR	[1.00;1.00]	[1.00;1.00]	[1.00;1.00]	
≥ 2 cysts, n (%)	66 (27.3%)	59 (24.2%)	7 (20.0%)	0.740
Diameter cyst	7.00	7.00 [5.00;	9.00 [6.00;	0.176
Median, IQR	[5.00;11.0]	11.0]	11.0]	
Location, n (%)				0.592
Right liver	172 (61.9%)	153 (63.0%)	19 (54.3%)	
Left liver	80 (28.8%)	68 (28.0%)	12 (34.3%)	
Both	26 (9.35%)	22 (9.05%)	4 (11.4%)	
Radical surgery, n (%)	164 (58.8%)	147 (60.2%)	17 (48.6%)	0.259
Opened cystectomy, n (%)	138 (49.5%)	118 (48.4%)	20 (57.1%)	0.429
Partial cystectomy, n (%)	115 (41.2%)	97 (39.8%)	18 (51.4%)	0.259
Minor liver resection, n (%)	40 (14.3%)	34 (13.9%)	6 (17.1%)	0.804
Major liver resection, n (%)	23 (8.24%)	21 (8.61%)	2 (5.71%)	0.750
Postoperative morbidity, n (%)	115 (41.2%)	97 (39.8%)	18 (51.4%)	0.259

PS: propensity score; WHO: World Health Organization; CE: cysts echinococcosis

Statistically-significant differences were found in postoperative complications between the two groups, particularly in severe complications (5.36% vs 25.8%, $p = 0.014$). No statistically-significant differences were seen after matching in cardiorespiratory complications (10.7% vs 22.6%, $p = 0.208$) or infection-related complications (16.1% vs 25.8%, $p = 0.415$). Likewise, no statistically-significant differences were observed in the rate of postoperative hemorrhage or hematoma (1.79% vs 6.45%, $p = 0.288$). Lastly, no statistically-significant differences were recorded in postoperative mortality either (0.00% vs 6.45%, $p = 0.124$).

Comparison in readmission rates did render statistically-significant differences (1.79% vs 16.1%, $p = 0.020$).

Table 3
Covariates chosen to perform PS matching.

	Before PSM		P overall	Std. Mean Diff.	After PSM		P overall	Std. Mean Diff.
	Group 1 (< 70 yr)	Group 2 (≥ 70 yr)			Group 1 (< 70 yr)	Group 2 (≥ 70 yr)		
	N = 244	N = 35			N = 56	N = 31		
CCI	0.26 (0.60)	0.89 (1.18)	0.004	0.531	0.52 (0.91)	0.65 (0.98)	0.556	0.027
Symptomatic	100 (41%)	21 (60.0%)	0.052	0.388	31 (55.4%)	17 (54.8%)	1.000	-0.033
Rupture cyst	6 (2.46%)	5 (14.3%)	0.006	0.338	3 (5.36%)	4 (12.9%)	0.241	0.138
Complicated cyst	84 (34.4%)	20 (57.1%)	0.016	0.459	31 (55.4%)	16 (51.6%)	0.912	-0.163
Infected cyst	14 (5.74%)	6 (17.1%)	0.026	0.303	8 (14.3%)	4 (12.9%)	1.000	-0.128

Std. Mean Diff: standard mean difference; CCI: Charlson's Comorbidity Index

4. Discussion

Hydatid disease currently remains a major health concern in endemic areas (Muhtarov et al., 2018). No consensus has been reached as to what the best treatment approach is, but surgery is considered the standard of care for hepatic hydatidosis (El Malki et al., 2014; Jaén-Torrejímeneo et al., 2020). The management of LHCs mainly depends on the patient's general condition, the size and localization of cysts, pathological involvement, available expertise, and equipment (Pang et al., 2018).

Given the increase in life expectancy and the aging of the population, there has been a rise in the incidence rates of hepatobiliary tumors and benign liver pathologies susceptible to surgical resection in elderly patients (Reddy et al., 2011).

Studies published to date on liver surgery in elderly patients primarily focus on malignancies, with scant literature revolving around benign pathologies, including hepatic hydatidosis. Since this is an endemic and prevalent disease in our region, we wanted to study it further and analyze the outcomes for elderly patients. We performed a propensity score-matched analysis to compare the postoperative morbidity in both groups in an experienced hepatobiliary surgical unit, and to reduce the bias inherent to retrospective studies.

Recent works comparing conservative to radical therapies have rendered conflicting results, due to the limited number of randomized studies available, leaving authors to advocate for their preferred approach based on small retrospective comparative series.

In our series, we performed radical resection in 58.8% of cases, and observed no differences in the approach between elderly patients and younger populations. It is worth noting that, traditionally, liver resection was not indicated in the elderly due to their comorbidities; decrease in renal, liver, and cardiopulmonary functional reserve; and in many cases accompanying malnutrition (Reddy et al., 2011).

In our series, 48.6% of patients in Group 2 were subjected to radical surgery, with 17.1% undergoing minor liver resection, and 5.71% major liver resection. No differences were found between the two groups in terms of the type of surgery performed.

Thanks to the improvements witnessed in recent years in anesthesia management and intensive care units, the understanding of hepatic segmental anatomy, and transection devices, liver resections have produced lower morbidity and mortality rates, which in turn has allowed surgeons to broaden selection criteria in elderly patients (Cho et al., 2011; Reddy et al., 2011) and those with chronic liver disorders (Aldighetti et al., 2003).

However, conflicting outcomes have been observed for elderly patients undergoing hepatic resection or hepatectomies, both in terms of the safety of the surgery and the postoperative long-term survival. A contributing factor in many cases has been the lack of baseline information, such as comorbidities and the American Society of Anesthesiologists (ASA) score (Jin et al., 2020). Recent published research studies have reported no differences in the tolerance of hepatic resection between elderly patients and younger populations, albeit higher associated postoperative morbidity and mortality have been recorded. Usually, these are patients with significant comorbidities, thus having increased risk of perioperative complications (Cieslak et al., 2016; Hung and Guy,

Table 4

Postoperative morbidity and specific complications before and after PS matching.

	Before PS matching					After PS matching				
	All N=279	Group 1 (< 70 yr) N=244	Group 2 (≥70yr) N=35	OR(CI 95%)	P < 0.05	All N=87	Group 1 (< 70 yr) N=56	Group 2 (≥ 70 yr) N =31	OR (CI 95%)	P < 0.05
Clavien Dindo, n (%)					0.008					0.037
None	163 (58.4%)	146(59.8%)	17(48.6%)			47(54%)	31(55.4%)	16(51.6%)		
I	45 (58.4%)	40(59.8%)	5(14.3%)			12 (13.8%)	8(14.3%)	4(12.9%)		
II	40 (16.1%)	35(16.4%)	5(14.3%)			17 (19.5%)	14(25.0%)	3(9.68%)		
IIIa	21 (7.53%)	16(6.56%)	5(14.3%)			7 (8.05%)	2(3.57%)	5(16.1%)		
IIIb	7 (2.51%)	7(2.87%)	0(0.00%)			1 (1.15%)	1(1.79%)	0(0.00%)		
IVa	1 (0.36%)	0(0.00%)	1(2.86%)			1 (1.15%)	0(0.00%)	1(3.23%)		
IVb	0 (0.00%)	0(0.00%)	0(0.00%)			0 (0.00%)	0(0.00%)	0(0.00%)		
V	2 (0.72%)	0(0.00%)	2(5.71%)			2 (2.30%)	0(0.00%)	2(6.45%)		
Severe complication (CD ≥ IIIa), n (%)	31 (11.1%)	23 (9.43%)	8 (22.9%)	2.85 [1.16; 6.99]	0.038	11 (12.6%)	3 (5.36%)	8 (25.8%)	5.84 [1.5 -30.2]	0.014
Postoperative mortality, n (%)	2 (0.72%)	0 (0.00%)	2 (5.71%)	–	0.015	2 (2.30%)	0 (0.00%)	2 (6.45%)	–	0.124
Infectious complications, n (%)	47 (16.8%)	38 (15.6%)	9 (25.7%)	1.88 [0.82; 4.32]	0.209	17 (19.5%)	9 (16.1%)	8 (25.8%)	1.81 [0.59; 5.42]	0.415
Wound infection, n (%)	14 (5.02%)	12 (4.92%)	2 (5.71%)	1.17 [0.25; 5.47]	0.691	6 (6.90%)	5 (8.93%)	1 (3.23%)	0.38 [0.01 - 2.63]	0.415
Residual cavity infection, n (%)	29 (10.4%)	24 (9.84%)	5 (14.3%)	1.53 [0.54; 4.31]	0.383	9 (10.3%)	4 (7.14%)	5 (16.1%)	2.45 [0.58; 11.1]	0.271
Subphrenic abscess, n (%)	(2.87%)	7 (2.87%)	1 (2.86%)	0.99 [0.12; 8.34]	1.000	2 (2.30%)	1 (1.79%)	1 (3.23%)	1.82 [0.05; 72.7]	1.000
Biliary fistula, n (%)	55 (19.7%)	47 (19.3%)	8 (22.9%)	1.24 [0.53; 2.91]	0.785	13 (14.9%)	7 (12.5%)	6 (19.4%)	1.67 [0.48; 5.70]	0.531
Hematoma Hemorrhage, n (%)	6 (2.15%)	4 (1.64%)	2 (5.71%)	3.64 [0.64; 20.63]	0.166	3 (3.45%)	1 (1.79%)	2 (6.45%)	3.52 [0.27; 114]	0.288
Respiratory complications, n (%)	27 (9.68%)	19 (7.79%)	8 (22.9%)	3.51 [1.4; 8.78]	0.011	13 (14.9%)	6 (10.7%)	7 (22.6%)	2.40 [0.71; 8.41]	0.208
Cardiac complications, n (%)	2 (0.72%)	1 (0.41%)	1 (2.86%)	7.15 [0.44; 116.94]	0.236	1 (1.15%)	0 (0.00%)	1 (3.23%)	–	0.356
Reoperation, n (%)	9 (3.23%)	7 (2.87%)	2 (5.71%)	2.05 [0.41; 10.3]	0.314	3 (3.45%)	1 (1.79%)	2 (6.45%)	3.52 [0.27; 114]	0.288
Readmission to hospital, n (%)	24 (8.60%)	19 (7.79%)	5 (14.3%)	1.97 [0.69- 5.67]	0.200	6 (6.90%)	1 (1.79%)	5 (16.1%)	9.32 [1.24; 256]	0.020
Recurrence, n (%)	17 (6.14%)	16 (6.56%)	1 (3.03%)	0.44 [0.06- 3.47]	0.703	9 (10.6%)	8 (14.3%)	1 (3.45%)	0.24 [0.01; 1.46]	0.157

PS: propensity score; CD: Clavien-Dindo; OR: odds ratio; CI: confidence interval

2015).

Existing literature on elderly patients include carefully selected patients, limiting their outcome applicability; in addition, the consequences of aging on liver function remain largely unknown (Cieslak et al., 2016). They are different definitions in medical literature for the cutoff age for an individual to be designated as elderly (Adam et al., 2010; De Blasi et al., 2018). According to the World Health Organization (WHO), the elderly population is defined as people aged 60 and over. However, the most frequently used cutoff age is 70 (Kumari et al., 2020; Van Tuil et al., 2019), which was adopted for our study. We have taken this value because we consider that a lower age is usually associated with less comorbidity in our population and this could generate some biases.

In our series, 12.5% of cases fit this definition. In Group 2 (≥ 70

years) 100% of patients were ASA II-III, whereas in Group 1, 29.1% were ASA I. Before matching and also in Group 2, patients presented with a larger number of complicated cysts (57.1% vs 34.4%, $p = 0.016$); as well as a higher rate, although not statistically-significant, of symptoms at the time of diagnosis (60% vs 41%, $p = 0.052$). This may be explained by the fact that surgical indication for benign pathologies in elderly patients is likely influenced by the cyst characteristics, and the common approach in asymptomatic cases is typically observation instead of surgery.

Surgical treatment of hydatid disease has traditionally been associated with a high postoperative morbidity rate, with most studies reporting a range of 10-26%, but some reaching 60% (Baraket et al., 2014). Furthermore, postoperative morbidity and mortality rates recorded in different works for major liver resections in elderly patients are somewhere in the range of 30-40% and 4-5%, respectively (Cho

et al., 2011). For the elderly patients who do undergo hepatectomy, there have been conflicting results regarding operation safety and long-term survival (Bockhorn et al., 2009; Kumari et al., 2020). Before matching, a larger number of complications was observed among the elderly, as well as a higher rate of severe complications (9.43% vs 22.9%, $p = 0.038$); these rates remained higher for Group 2 after matching as well, but they dropped within the range found in literature. No differences were observed in the rate of complications associated with infection, hemorrhage or reintervention before or after matching. Respiratory complications did show statistically-significant differences before matching among both groups but, after matching, these subsided.

Propensity scoring is a statistical technique for dealing with selection bias in observational studies. Selection bias arises when specific patients are more (or less) likely to receive a treatment owing to confounding by indication. With propensity scoring, patient and provider characteristics are used to calculate the probability that a patient will receive the intervention and to create matched patient cohorts (Adamina et al., 2006; Hemmilla et al., 2010).

Our series has several limitations. Despite trying to homogenize both groups by performing PSM analysis, the study is based on retrospective data. After PSM, we tried to emulate the randomization process and homogenize both study groups to limit confounding factors and selection bias for surgery indication, thus allowing us to establish a better comparison of postoperative morbidity and mortality rates between both groups. The decreased number of cases per group after PSM could influence results.

5. Conclusions

Advanced age should not be considered a contraindication in and of itself for a surgical approach to hepatic hydatidosis. While these patients experience a higher postoperative morbidity rate than the younger population, said rate is low and acceptable when procedures are performed in skilled hepatic surgery units. The key is to consider the physiological characteristics and high rate of comorbidities typically seen in this vulnerable group, in order to establish strict selection criteria for those who could benefit most from a surgical approach.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Date statement

I confirmed that the relevant data is real and you can get them by consulting correspondence author.

CRediT authorship contribution statement

Isabel Jaén-Torrejíméno: Conceptualization, Methodology, Data curation, Writing – original draft. **Diego López-Guerra:** Methodology, Data curation, Writing – review & editing. **Adela Rojas-Holguín:** Methodology, Data curation, Writing – review & editing. **Noelia De-Armas-Conde:** Methodology, Data curation, Writing – review & editing. **Gerardo Blanco-Fernández:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors have no competing interests to declare.

Acknowledgments

None.

References

- Adam, R., Frilling, A., Elias, D., Laurent, C., Ramos, E., Capussotti, L., Poston, G.J., Wicherts, D.A., De Haas, R.J., 2010. Liver resection of colorectal metastases in elderly patients. *Br. J. Surg.* 97, 366–376. <https://doi.org/10.1002/bjs.6889>.
- Adamina, M., Guller, U., Weber, W.P., Oertli, D., 2006. Propensity scores and the surgeon. *Br. J. Surg.* 93, 389–394. <https://doi.org/10.1002/bjs.5265>.
- Agha, R., Abdall-razak, A., Crossley, E., Dowlat, N., Iosifidis, C., Mathew, G., 2019. STROCCS 2019 guideline –Strengthening the reporting of cohort studies in surgery. *Int. J. Surg.* 72, 156–165. <https://doi.org/10.1016/j.ijsu.2019.11.002>.
- Akbulut, S., 2018. Parietal complication of the hydatid disease–Comprehensive literature review. *Medicine (Baltimore)* 97, e10671. doi:10.1097/MD.00000000000010671.
- Akbulut, S., Sahin, T.T., 2021. Comment on treatment of hepatic hydatid disease–role of surgery, ERCP, and percutaneous drainage–A retrospective study. *Surg. Laparosc. Endosc. Percutan. Tech.* 31, 393. <https://doi.org/10.1097/SLE.0000000000000957>.
- Aldrighetti, L., Arru, M., Caterini, R., Finazzi, R., Comotti, L., Torri, G., Ferla, G., 2003. Impact of advanced age on the outcome of liver resection. *World J. Surg.* 27, 1149–1154. <https://doi.org/10.1007/s00268-003-7072-y>.
- Andert, A., Lodewick, T., Ulmer, T.F., Schmeding, M., Schöning, W., Neumann, U., Dejong, K., Heidenhain, C., 2016. Liver resection in the elderly–A retrospective cohort study of 460 patients - Feasible and safe. *Int. J. Surg.* 28, 126–130. <https://doi.org/10.1016/j.ijsu.2016.02.060>.
- Aoyama, T., Kunisawa, S., Fushimi, K., Sawa, T., Imanaka, Y., 2018. Comparison of surgical and conservative treatment outcomes for type a aortic dissection in elderly patients. *J. Cardiothorac. Surg.* 13, 1–8. <https://doi.org/10.1186/s13019-018-0814-6>.
- Baraket, O., Moussa, M., Ayed, K., Kort, B., Bouchoucha, S., 2014. Predictive factors of morbidity after surgical treatment of hydatid cyst of the liver. *Arab J. Gastroenterol.* 15, 119–122. <https://doi.org/10.1016/j.ajg.2014.05.004>.
- Bockhorn, M., Sotiropoulos, G.C., Sgourakis, G., Neuhaus, J.P., Molmenti, E.P., Lang, H., Frilling, A., Broelsch, C.E., 2009. Major liver resections in the elderly - Is an aggressive approach justified? *Int. J. Colorectal Dis.* 24, 83–86. <https://doi.org/10.1007/s00384-008-0571-4>.
- Brunetti, E., Kern, P., Vuitton, D.A., 2010. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. *Acta Trop.* 114, 1–16. <https://doi.org/10.1016/j.actatropica.2009.11.001>.
- Charlson, M., et al., 1987. A new method of classifying prognostic in longitudinal studies –Development. *J. Chronic Dis.* 40, 373–383.
- Cho, S.W., Steel, J., Tsung, A., Marsh, J.W., Geller, D.A., Gamblin, T.C., 2011. Safety of liver resection in the elderly–How important is age? *Ann. Surg. Oncol.* 18, 1088–1095. <https://doi.org/10.1245/s10434-010-1404-6>.
- Cieslak, K.P., Baur, O., Verheij, J., Bennis, R.J., Gulik, T.M., Van, 2016. Liver function declines with increased age. *Int. Hepato-Pancreato-Biliary Assoc.* 18, 691–696. <https://doi.org/10.1016/j.hpb.2016.05.011>.
- Couinaud, C., 1999. Liver anatomy–Portal (and suprahepatic) or biliary segmentation. *Dig. Surg.* 16, 459–467. <https://doi.org/10.1159/000018770>.
- De Blasi, V., Memeo, R., Adam, R., Goéré, D., Cherqui, D., Regimbeau, J.M., Rivoire, M., Perotto, L.O., Navarro, F., Sa Cunha, A., Pessaux, P., Cosse, C., Lignier, D., Marc Regimbeau, J., Barbeux, J., Lermite, E., Hamy, A., Mauvais, F., Laurent, C., Al Naasan, I., Laurent, A., Azoulay, D., Compagnon, P., Lim, C., Sbaildrissi, M., Martin, F., Atger, J., Baulieux, J., Darnis, B., Yves, J., Mabrut Kepenekian, V., Perinel, J., Adham, M., Glehen, O., Hardwigen, J., Palen, A., Grégoire, E., Le Treut, Y.P., Delperro, J.R., Turrini, O., Herrero, A., Panaro, F., Ayav, A., Bresler, L., Rauch, P., Guillemin, F., Marchal, F., Guenheimer, J., Iannelli, A., Benoist, S., Brouquet, A., Pocard, M., Lo Dico, R., Gayet, B., Fuks, D., Scatton, O., Soubrane, O., Vaillant, J.C., Piardi, T., Sommacale, D., Kianmanesh, R., Comy, M., Bachellier, P., Oussoultzoglou, E., Addeo, P., Ntourakis, D., Mutter, D., Marescaux, J., Raoux, L., Suc, B., Muscare, F., Elhomsy, G., Gelli, M., Castaing, D., Pittau, G., Ciacio, O., Vibert, E., Elias, D., Vittalde, F., 2018. Major hepatectomy for colorectal liver metastases in patients aged over 80–A propensity score matching analysis. *Dig. Surg.* 35, 333–341. <https://doi.org/10.1159/000486522>.
- Dedinská, I., Laca, L., Miklušica, J., Palkoci, B., Skálová, P., Lauková, S., Osinová, D., Strmeňová, S., Janík, J., Mokán, M., 2017. Complications of liver resection in geriatric patients. *Ann. Hepatol.* 16, 149–156. <https://doi.org/10.5604/16652681.1226934>.
- Dindo, D., Demartines, N., Clavien, P.-A., 2004. Classification of surgical complications–A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann. Surg.* 240, 205–213. <https://doi.org/10.1097/01.sla.0000133083.54934.ae>.
- El Malki, H.O., Souadka, A., Benkabbou, A., Mohsine, R., Ifrine, L., Abouqal, R., Belkouchi, A., 2014. Radical versus conservative surgical treatment of liver hydatid cysts. *Br. J. Surg.* 101, 669–675. <https://doi.org/10.1002/bjs.9408>.
- Hemmilla, M.R., Birkmeyer, N.J., Arbab, S., Osborne, N.H., Wahl, W.L., Dimick, J.B., 2010. Introduction to propensity scores. *Arch. Surg.* 145 <https://doi.org/10.1111/resp.12312>.
- Hung, A.K., Guy, J., 2015. Hepatocellular carcinoma in the elderly–Meta-analysis and systematic literature review. *World J. Gastroenterol.* 21, 12197–12210. <https://doi.org/10.3748/wjg.v21.i42.12197>.
- Jaén-Torrejíméno, I., Latorre-Fragua, R., López-Guerra, D., Rojas-Holguín, A., Manuel-Vázquez, A., Blanco-Fernández, G., Ramia, J.M., 2021. Jaundice as a clinical presentation in liver hydatidosis increases the risk of postoperative biliary fistula. *Langenbeck's Arch. Surg.* <https://doi.org/10.1007/s00423-020-02070-z>.
- Jaén-Torrejíméno, I., López-Guerra, D., Prada-Villaverde, A., Blanco-Fernández, G., 2020. Pattern of relapse in hepatic hydatidosis–Analysis of 238 cases in a single hospital. *J. Gastrointest. Surg.* 24, 361–367. <https://doi.org/10.1007/s11605-019-04163-7>.

- Jerraya, H., Khalfallah, M., Osman, S., Ben, N., Dziri, C., 2015. Predictive factors of recurrence after surgical treatment for liver hydatid cyst. *Surg. Endosc.* 29, 86–93. <https://doi.org/10.1007/s00464-014-3637-0>.
- Jin, K.M., Wang, K., Bao, Q., Wang, H.W., Xing, B.C., 2020. Liver resection for colorectal liver-limited metastases in elderly patients—A propensity score matching analysis. *World J. Surg. Oncol.* 18, 1–13. <https://doi.org/10.1186/s12957-020-02055-8>.
- Koc, C., Akbulut, S., Sahin, T.T., Tuncer, A., Yilmaz, S., 2020. Intraoperative rupture of the hydatid cyst disease—Single-center experience and literature review. *Ulus. travma ve acil cerrahi Derg. = Turkish. J. trauma Emerg. Surg. TJES* 26, 789–797. <https://doi.org/10.14744/tjes.2020.32223>.
- Koch, M., Garden, O.J., Padbury, R., Rahbari, N.N., Adam, R., Capussotti, L., Fan, S.T., Yokoyama, Y., Crawford, M., Makuuchi, M., Christophi, C., Banting, S., Brooke-Smith, M., Usatoff, V., Nagino, M., Maddern, G., Hugh, T.J., Vauthey, J.N., Greig, P., Rees, M., Nimura, Y., Figueras, J., Dematteo, R.P., Büchler, M.W., Weitz, J., 2011. Bile leakage after hepatobiliary and pancreatic surgery—A definition and grading of severity by the International Study Group of Liver Surgery. *Surgery* 149, 680–688. <https://doi.org/10.1016/j.surg.2010.12.002>.
- Kumari, S., Semira, C., Lee, M., Lee, B., Wong, R., Nott, L., Shapiro, J., Gibbs, P., 2020. Resection of colorectal cancer liver metastases in older patients. *ANZ J. Surg.* 90, 796–801. <https://doi.org/10.1111/ans.15750>.
- Mihmanli, M., Idiz, U.O., Kaya, C., Demir, U., Bostanci, O., Omeroglu, S., Bozkurt, E., 2016. Current status of diagnosis and treatment of hepatic echinococcosis. *World J. Hepatol.* 8, 1169–1181. <https://doi.org/10.4254/wjh.v8.i28.1169>.
- Muhtarov, M., Rainova, I., Tamarozzi, F., 2018. Treatment of hepatic cystic echinococcosis in patients from the southeastern Rhodope Region of Bulgaria in 2004–2013—Comparison of current practices with expert recommendations. *Am. J. Trop. Med. Hyg.* 60, 721–728. <https://doi.org/10.1016/j.amsu.2018.10.032>.
- Nazligul, Y., Kucukazman, M., Akbulut, S., 2015. Role of chemotherapeutic agents in the management of cystic echinococcosis. *Int. Surg.* 100, 112–114. <https://doi.org/10.9738/INTSURG-D-14-00068.1>.
- Pang, Q., Jin, H., Man, Z., Wang, Y., Yang, S., Li, Z., Lu, Y., Liu, H., Zhou, L., 2018. Radical versus conservative surgical treatment of liver hydatid cysts—A meta-analysis. *Front. Med.* 12, 350–359. <https://doi.org/10.1007/s11684-017-0559-y>.
- Ramía, J.M., Manuel-Vázquez, A., Román, C.G., Latorre-Fragua, R., de la Plaza-Llamas, R., 2020. Radical surgery in hepatic hydatidosis—Analysis of results in an endemic area. *Rev. Esp. Enferm. Dig.* 112, 708–711. <https://doi.org/10.17235/REED.2020.6722/2019>.
- Ramía, J.M., Serrablo, A., Serradilla, M., Lopez-Marciano, A., de la Plaza, R., Palomares, A., 2018. Major hepatectomies in liver cystic echinococcosis—A bi-centric experience. Retrospective cohort study. *Int. J. Surg.* 54, 182–186.
- Reddy, S.K., Barbas, A.S., Turley, R.S., Gamblin, T.C., Geller, D.A., Marsh, J.W., Tsung, A., Clary, B.M., Lagoo-Deenadayalan, S., 2011. Major liver resection in elderly patients—A multi-institutional analysis. *J. Am. Coll. Surg.* 212, 787–795. <https://doi.org/10.1016/j.jamcollsurg.2010.12.048>.
- Sozuer, E., Akyuz, M., Akbulut, S., 2014. Open surgery for hepatic hydatid disease. *Int. Surg.* 99, 764–769. <https://doi.org/10.9738/INTSURG-D-14-00069.1>.
- Stojkovic, M., Zwahlen, M., Teggi, A., Vutova, K., Cretu, C.M., Virdone, R., Nicolaidou, P., Cobanoglu, N., Junghanss, T., 2009. Treatment response of cystic echinococcosis to benzimidazoles—A systematic review. *PLoS Negl. Trop. Dis.* 3 <https://doi.org/10.1371/journal.pntd.0000524>.
- Van Tuil, T., Dhaif, A.A., Te Riele, W.W., Van Ramshorst, B., Van Santvoort, H.C., 2019. Systematic review and meta-analysis of liver resection for colorectal metastases in elderly patients. *Dig. Surg.* 36, 111–123. <https://doi.org/10.1159/000487274>.
- Velasco-Tirado, V., Romero-Alegría, Á., Belhassen-García, M., Alonso-Sardón, M., Esteban-Velasco, C., López-Bernús, A., Carpio-Perez, A., López, M.F.J., Bellido, J.L. M., Muro, A., Cordero-Sánchez, M., Pardo-Lledias, J., Muñoz-Bellvis, L., 2017. Recurrence of cystic echinococcosis in an endemic area—A retrospective study. *BMC Infect. Dis.* 17, 455. <https://doi.org/10.1186/s12879-017-2556-9>.