CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3747257

Available online at: http://www.iajps.com Research Article

CLINICAL ANALYSIS OF HEPATOCELLULAR CARCINOMA AFTER HEPATIC RESECTION IN YOUNGER VERSUS ELDERLY PATIENTS

Waseem Sami Malik, Wang Hai Jiu, Fan Hai Ning, Wang Zhi Xin, Muhammad Ali, Ren Li

Hepatobiliry Surgery department of Qinghai University Affiliated Hospital

Article Received: February 2020 **Accepted:** March 2020 **Published:** April 2020

Abstract:

Objectives: *Analyze the clinical preoperative laboratory data, intraoperative findings, and surgical outcome of HCC in older v/s younger patients those who underwent surgical resection.*

Methods: *A total of 51 "elderly" (≥65 years old) and 102 "younger" (≤65 years old) who underwent hepatic resection between January 2013 to February 2020 were identified and included in this study. Demographic and operative data, pathological findings, and postoperative outcomes were collected. Prognostic factors were analyzed by univariate and multivariate analysis.*

Results: *In both of groups, younger males (91.17%) and older female (23.6%) with a combined P-value <0.004, have a higher proportion of HCC. More underlying Hepatitis B virus infection and cirrhosis found in younger (84.4% - 94.1%). More underlying diabetes mellitus and Hepatitis C were observed in elderly HCC. There was no significant statistical difference in the Child-Pugh class in both groups. The intraoperative parameters younger patients received right-sided hepatectomy, right hepatectomy (65.7%), and right trisegmentomy (10.8%) while the older patients mostly received left-sided hepatectomy, left hepatectomy (37.3%). Post-operative pneumonia and pleural effusion common in younger group (9.8%,P<0.514 and 34.5%,P<0.312 respectively), while wound infections were most commonly seen in the elderly (19.6%, P<0.530). The overall estimated mortality and hospitalization were not significantly different in both groups.*

Conclusion: *Two groups of operative outcomes indicated that the right lobe of liver HCC more in the younger and left lobe more in older patients and post-operative wound infection in elderly and pleural effusion. Still, it proves that a hepatic resection is a safe option in Hepatocellular carcinoma.*

Keywords: *hepatocellular carcinoma, wound infection, hepatectomy.*

Corresponding author:

Waseem Sami Malik,

Hepatobiliry Surgery Department of Qinghai University Affiliated Hospital

QR code

Please cite this article in press Waseem Sami Malik et al, ***Clinical Analysis Of Hepatocellular Carcinoma After Hepatic Resection In Younger Versus Elderly Patients,*** *Indo Am. J. P. Sci, 2020; 07(04).*

INTRODUCTION:

Hepatocellular carcinoma (HCC) is a primary malignancy of the liver and occurs predominantly in patients with underlying chronic liver diseases like Hepatitis B virus infections and cirrhosis. HCC is now the third most common cause of death worldwide, and the incidence is gradually increasing [1, 2]. The frequency of HCC is highest in Asia and Africa, where the endemic high prevalence of hepatitis B and hepatitis C strongly predisposes to the development of chronic liver disease and subsequent development of HCC, the most deadly cancer in China and the critical cause of HCC is hepatitis B virus. The peak onset of age is 40 to 50 years HCC in China.

Life expectancy has increased because of advancement in surgical techniques. A few years back liver surgeons hesitated to perform hepatic resections because of older patients with large tumors or tumors near to the hilum and vascular invasions, if ruptures there are high risk of massive bleedings or even cause mortality and more postoperative complications in older patients as compared to younger patients, Nowadays surgeons perform hepatic resections frequently and unavoidable. A few reports are comparing the outcomes of younger and elderly HCC patients after hepatic resection in China, and they determined the significance of hepatic resection in the two groups [3, 4].

The progression of a tumor with local expansion distant metastases, some previous data reveals that poor prognosis in the elderly as compared to younger patients and few studies show no noticeable difference in outcomes of both younger and older age groups of patients. The primary purpose of this study is to analyze the clinical preoperative laboratory data, intraoperative findings, and surgical outcome of HCC in older v/s younger patients who underwent surgical resection.

PATIENTS AND METHODS:

From January 2013 to February 2020, the number of 153 patients diagnosed with HCC underwent surgical R0 Hepatic resection at the Qinghai University Affiliated Hospital in a single hepatobiliary surgery department that was included in this study. We divided 153 patients into two groups elderly>65 years of age (n=51) and younger <65 years (n=102). R0 Resection indicates the complete removal of all tumors. We consider age >65 elderly because most developed countries around the world accepted the chronological age 65 years as 'elderly' or older person as WHO health statistic system described. Before surgery, every patient was subjected to physical examination; laboratory examination like complete blood count, liver functions includes serum transaminases, alkaline phosphate, Prothrombin time, and albumin. The etiology represents the chronic course of liver disease like hepatitis B surface antigen (HBsAg) and anti-hepatitis C (Anti-HCV antibody), which was found in hepatic markers studies and cirrhosis. HCC Diagnosis based on pathology results and radiology scanning like computed tomography and magnetic resonance imaging results or specific tumor markers an alpha-fetoprotein concentration>200 ng/ml, Carbohydrate antigen(CA)19-9 and Carcinoembryonic antigen (CEA) increase levels, ultrasonographic and endoscopic signs of portal hypertension. Child-Pugh class A and B and the Model for End-Stage Liver Disease (MELD) scoring system were used for evaluation of performance status and functional status of the liver [5, 6].

Table 1 clinical characteristics

Variable		Older Age (n = 51)	Younger Age (n =102)	P value
Gender	Male	39(76.5%)	93(91.17%)	.004
	Female	12(23.6%)	9(8.83%)	
Age		69.29 ± 4.8	50.29 ±8.8	.519
Diabetes		14(27.5%)	20.6(20.6%)	.411
Hypertension		21(41.2%)	27(26.5%)	.378
Jaundice		9(17.6%)	12(11.8%)	.764
Splenomegaly		13(25.5%)	56(54.9%)	.211
Etiology				.006
Cirrhosis		42(82.4%)	96(94.1%)	.695
HBV		34(66.1%)	86(84.3%)	
HCV		7(13.7%)	6(5.9%)	
NBNC		10(20.2%)	10(9.8)	

Data are expressed as numbers (percentage) or mean ± SD. HBV = hepatitis B virus; HCV = hepatitis C virus; NBNC = Non-B, Non-C.

Table 2 Pre-operative Laboratory Results

Variable	Older Age (n = 51)	Younger Age (n = 102)	P
WBC	5.52 2.64	4.94 1.75	0.32
RBC	4.85 4.95	4.45 0.53	0.94
Platelet	140.96 52.53	134.60 67.86	0.43
Hemoglobin	127.07 18.11	137.45 18.36	0.18
INR	1.07 0.11	1.10 0.15	0.50
HCT	38.10 15.97	84.30 411.86	0.43
APTT	33.33	33.44 6.20	0.13
PA	178.59 68.02	179.99 57.71	0.26
Direct Bilirubin	4.79 2.54	5.26 8.47	0.36
Total Bilirubin	13.11 4.96	14.88 11.94	0.45
BUN	5.94 2.56	5.55 1.58	0.71
CRE	72.24 49.01	69.52 13.61	0.65
ALB	39.45 4.29	40.06 5.55	0.22
ALP	102.02 53.44	100.64 48.31	0.19
ALT	39.18 39.44	55.73 87.37	0.73
AST	49.16 40.64	53.33 75.22	0.85
GGT	91.12 91.85	95.29 115.70	0.00
UA	281.08 76.70	302.15 89.06	0.04
Sodium	138.79 11.19	139.28 5.50	0.16
Pugh-Child			
Class A	48(94.1%)	84(82.4%)	
Class B	3(5.9%)	18(17.6%)	
AFP	347.13 759.10	4089.83 18937.45	0.73
CA19-9	244.60 1400.27	48.71 176.74	0.92
CEA	2.66 2.22	2.70 1.83	0.00

Data are expressed as numbers (percentage) or mean +- SD. WBC = White Blood Cells ; RBC = Red Blood Cells ; INR = International normalized ratio ; HCT = Hematocrit ; APTT = Activated partial thromboplastin time ; PA = pre-albumin; BUN = Blood Urea Nitrogen ; CRE = Creatinine ; ALB = Albumin; ALP = Alkaline phosphate ; ALT = Alanine Aminotransferase ; AST = Aspartate aminotransferase ; GGT = γ –glutamyltransferase ; UA ; Uric acid; AFP ;α –fetoprotein; CA19-9 = carbohydrate antigen 19-9 ; CEA = Carcinoembryonic antigen.

The peri-operative standard techniques were used for hepatectomy. Anatomic resection defines removal of more than two or more segments of the liver, while non-anatomic resection referred to as removal one section with its free margins. The performed hepatic resections types included left, right, or extended medial plus a portion of right or left lobe lobectomy, The Sectionectomy refers to resection of two couinaud subsegments or segmentectomy (resection of one couinaud subsegment) [7]. Trisegmentectomy refers to the removal of three segments of the liver. The gross intra-operative tumor examination includes tumor vascular involvement, tumor size, tumor numbers, and capsular formation was done Tumor size more than 5cm considered as primary tumor resection while less than 5 cm tumors as minor tumor resection. The resected tumor specimen sent for histological results, microscopic examination reveals tumor characteristics as solitary, uninodular, envelop formation tiny vascular invasions. The extent of tumor staging evaluate by the Barcelona Clinic Liver Cancer BCLC staging system was used [8]. All the procedures were safe; there was operative mortality.

Table 3 Intra-operative Findings & Pathological Feature

Variable	Older Age (n = 51)	Younger Age (n = 102)	P
Type of surgery			0.274
Anatomic	30(58.8%)	63(61.8%)	
Non-anatomic	21(41.2%)	39(31.8%)	
Limited Resection	30(58.8%)	60(60.8%)	0.381
Lobectomy			
Left lobectomy	19(37.3%)	27(26.5%)	
Extended lobectomy	8(15.9%)	8(7.8%)	
Right lobectomy	24(46.8%)	67(65.7%)	
Sectionectomy/Segmentectomy			0.105
Single Segmentectomy	22(43.1%)	40(39.2%)	
Multiple Segmentectomy	29(56.9%)	62(61.8%)	
Trisegmentomy	2（3.9%）	11(10.8%)	0.127
Tumor size			
Major > 5cm	26(51.0%)	58(56.9%)	
Minor < 5cm	25(49.0%)	44(43.1%)	
Number of tumors			0.896
Single tumor	40(78.4%)	87(85.3%)	
Multiple tumors	11(21.6%)	15(14.7%)	
Type of tumor			0.191
Solitary	25(49.0%)	16(15.7%)	
Nodular	26(51.0%)	86(84.3%)	
Vascular invasion	5(9.8%)	10(9.6%)	0.557
Portal vein invasion	5(9.8%)	10(9.6%)	0.557
Intra-hepatic metastasis	16(31.4%)	25(24.5%)	0.044
Thrombosis	4(7.8%)	7(6.9%)	0.553
BCLC Stage, n (%)			
0	4(7.84%)	2(1.97%)	
A	11(21.57%)	28(27.45%)	
B	34(66.67%)	63(61.76%)	
C	2(3.92%)	9(8.82%)	
Estimated Blood Loss (in ML)	123.32 368.65	285.24 354.79	0.836
Blood transfusion			
RBC	23.53 89.19	35.29 106.84	0.676
Plasma	44.12 108.93	10.29 54.65	0.385
Operative Mortality	0(0%)	0(0%)	

Data are expressed as numbers (percentage) or mean +- SD.
BCLC = Barcelona Clinic Liver Cancer.

Statistical analysis: To perform data analysis, SPSS 22.0 for Windows (SPSS, Chicago, IL, USA) was used. All data described as percentages of patients, mean, and standard deviation. The continuous variables are expressed as median (range). T-test and Pearson Chi-square used for continuous variables. Kaplan-Meier method used to calculate disease-free survival rate and log-rank test for comparison of groups. Cox regression model helped to get multivariate analysis. Every analysis, P<0.05 consideration, show statistical significance.

RESULTS:

Table 4 Post-operative Outcomes & Characteristics

Variable	Older Age (n = 51)	Younger Age (n = 102)	P
Post-Operative Hospital stay	9.82 4.49	9.05 2.79	0.861
Wound infection	10(19.6%)	10(9.8%)	0.530
Pneumonia	2(3.9%)	10(9.8%)	0.514
Pleural effusion	8(15.8%)	25(24.5%)	0.312
Bile leakage	0(0%)	2(1.9%)	0.000
Ascites	0(0%)	10(9.8%)	0.000
Liver failure	0(0%)	2(1.9%)	0.000
Renal failure	0(0%)	1(0.9%)	0.000
Peak ALT	98.80 80.88	109.82 152.57	0.852
Peak AST	84.22 107.76	70.19 136.29	0.727
MELD Score	8.04 2.17	8.15 2.29	0.369
<8	28(54.90%)	45(44.11%)	
8–11	19(37.25%)	51(50%)	
>11	4(7.85%)	6(5.89%)	
3-Months Estimated Mortality	2.78% 1.70%	2.87%2.34%	0.284
Recurrence	4(7.84%)	0(0%)	0.000

Data are expressed as numbers (percentage) or mean +- SD.
MELD = Model for End-Stage Liver Disease.

Pre-operative Results: All patients divided into two groups older (n=51) and younger age group (n=102) in table 1. In both groups, males are most commonly HCC affected as compared to females with combined P-value (<0.004). Positive Hepatitis C virus infection 7(13.7%), diabetes 14(27.5%) and hypertension 21(41.2%), more commonly found in the elder age group as compared to the younger group. While Hepatitis B virus infection 86(84.3%), cirrhosis 96(94.1%), and Splenomegaly 56(54.9%) more commonly found in the elderly group. More patients, mostly with Child-Pugh Classification class A 48(94.1%) in older and 84(82.4%) in younger patients, were found. Alpha Protein P-value and other laboratory finding there was no statistically significant difference were located in P-values in both groups. In both old age and young age groups, patients were operated with the same surgical approach, and there was no statistical significant difference found in surgery blood loss, during an operation blood transfusion. Left lobectomy was mostly done in elderly 19(37.3%) as compared to younger age group while right lobectomy was mostly in younger age group 67(65.7%). The size of tumors, type of tumors, and the number of tumors, vascular, and portal vein involvement of tumors were not many significantly relevant. For the tumor stage, Barcelona Clinic Liver Cancer (BCLC) B stage was observed in both groups. There was no intra-operative mortality in both groups.

Post-operative complications: The postoperative hospital stay duration was almost similar in both groups, which were shown in Table 4.Post-operative pneumonia (9.8%, P<0.514) and pleural effusion 25(24.5% P<0.0321) commonly seen in the younger age group, while wound infections was most commonly seen in the elderly (19.6%, P<0.530). Bile leakage, ascites, liver, and renal failure are not statistically significant. The post-operative liver transaminases level under control levels. The Model for End-Stage Liver disease (MELD) scores and three months estimated mortality rate was almost the same in both groups. Recurrence of HCC was seen only in 4 patients belongs to the elder age group. Long-term prognosis after hepatic resection for HCC of elderly participants is not different from younger participants [9,10,11].

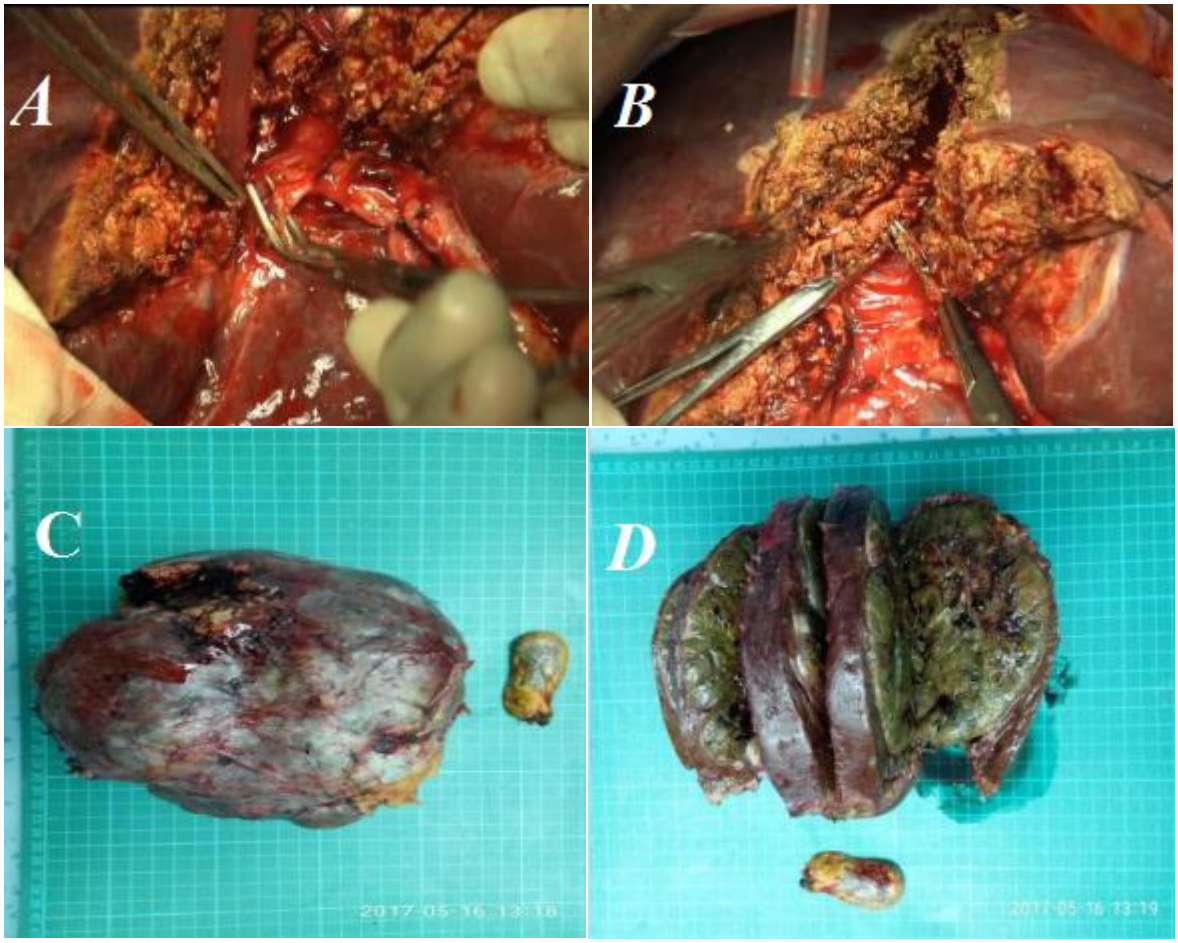

Figure A and B are showing the procedure of treatment & Figure; C and D showing the removal tumor of the liver.

DISCUSSION:

There are different types of treatment pattern methods for HCC. Hepatic resection is the first-line treatment option for Hepatocellular carcinoma in that where hepatic resection is possible [12]. The improvement in preoperative screening with the advancement in surgical procedures, techniques and postoperative management decreases old age contraindications of hepatic resection in China. The newer surgical technologies, improvement in life quality, the average expectancy of life increase, although old age people have a higher risk of developing HCC, the incidence is also increasing in younger age significantly [6,13,14,].

There are only a few studies demonstrate differences in clinical changes of old age HCC patients compared with younger age HCC patients [6,14,15,16,] previously, and there are just one or two studies that were conducted in China which shows clinical changes between these old and young group [17]. In our study, we compared two groups who went for hepatic resection. Which is represents as an elder age group>65 versus young age <65 years of age. There are many controversies about the exact old age definition, which is considered different in Asia, Europe, and the USA. WHO (world health organization) defines the classification of elderly which is >65 years old referred to as old age [18] so we choose period >65 is old age and divide patients into two groups >65 is old age group patients and <65 is young age group patients.

In our study findings, HCC most commonly found in male's patients as compared to female patients in both groups. However, females in the old age group (23.6%) were at a higher rate than younger age females patients (8.83%), which is also similar in some previous studies [13,15,16]. Around all over the world, males have a higher incidence rate of HCC than females [19].

The rate of hepatitis B virus infection was much higher in the younger age group (84.3%) as compared to the older age group, which is (66.1%). However, the rate of hepatitis C virus infection is higher in the mature age group (13.7%) as compared to the younger age group (5.9%). Although Non-Hep B and Non-Hep C etiology also mostly seen in the old age group (20.2%) as compared to the younger age group (9.8%).

Cirrhosis and Hepatitis B virus infection still the most common cause of HCC in both age groups in China. Hepatitis C virus is widespread in adulthood, which causes the HCC many years after a prior infection [20]. HBV infected HCC patients younger than HCC infected patients just because HCV takes decades to induce HCC.

Our study findings show comorbidities such as hypertension and diabetes (41.2%, 27.5%) commonly seen in older age group patients. There was a very high rate of splenomegaly (54.9%) in younger age group patients, as shown in pre-operative findings.

CONCLUSIONS:

There are very similar results outcomes in both age groups. The results of this study suggest that both ages must receive the same pattern of treatment for HCC. Age itself is not a contraindication of surgery for Hepatocellular carcinoma, but age group patients required conservative observations.

ACKNOWLEDGEMENT:

This research was done and supported by the key research and development department of Qinghai University Affiliated Hospital. All data was collected by informed consent of the patients in the end I would like to thank my professor and teachers who helped me with the research ideas and data collection.

Conflict of interest:

The author declares no conflict of interest.

REFERENCES:

1. HB El-Serag. Hepatocellular carcinoma: an epidemiologic view. J Clin Gastroenterol. 2002; 35:S72–S78.
2. Parkin D. Global cancer statistics in the year 2000. Lancet oncology. 2001;2:533–543.
3. Nanashima A, Abo T, Nonaka T, et al. Prognosis of patients with Hepatocellular carcinoma after hepatic resection: are elderly patients Suitable for surgery? Journal of surgical oncology. 2011;104(3):284–291.
4. Takeishi K, Shirabe K, Muto J, Toshima T, Taketomi A, MaeharaY. Clinicopathological features and outcomes of young patients with Hepatocellular carcinoma after Hepatectomy. World journal of Surgery. 2011; 35(5):1063–1071.
5. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982; 5(6):649–655
6. Sheth M, Riggs M, Patel T (2002) Utility of the Mayo End-Stage Liver Disease (MELD) score in assessing prognosis of patients with alcoholic hepatitis. BMC gastroenterology 2:2
7. Couinaud C editors: Le Foie: Etudes Anatomiques et Chirurgicales.Paris: Masson; 1957.
8. Llovet JM, Bru C, Bruix J .Prognosis of hepatocellularcarcinoma: the BCLC staging classification. Semin Liver Dis1999(3):329–338. doi:10.1055/s-2007-1007122.
9. Huang J, Li BK, Chen G, et al. Long-term outcomes and prognostic factors of elderly patients with hepatocellular carcinoma undergoing Hepatectomy. Journal of gastrointestinal surgery. 2009;13(9):1627–1635
10. Kaibori M, Matsui K, Ishizaki M, Saito T, Kitade H, Matsui Y, Kwon AH. Hepatic resection for hepatocellular carcinoma in the elderly. J Surg Oncol 2009(3):154–160.
11. Ozenne V, Bouattour M, Goutte N, Vullierme MP, Ripault MP, Castelnau C, Valla DC, Degos F, Farges O Prospective evaluation of the management of hepatocellular carcinoma in the elderly. Dig Liver Dis 2011;43(12):1001–1005.
12 . Chang PE, Ong WC, Lui HF, Tan CK. Is the prognosis of young patients with hepatocellular carcinoma poorer than the prognosis of older patients? A comparative analysis of clinical characteristics, prognostic features, and survival outcome. J Gastroenterology 2008;
13. Kozyreva ON, Chi D, Clark JW, Wang H, Theall KP, Ryan DP,Zhu AX A multicenter retrospective study on clinical characteristics, treatment patterns, and outcome in elderly Patients with hepatocellular carcinoma.Oncologist 2011;16(3):310–318.
14. Pignata S, Gallo C, Daniele B, Elba S, Giorgio A, Capuano G,Adinolfi LE, De Sio I, Izzo F, Farinati F, Del Naja C, Stanzione M, Castiglione F, Marone G, Cuomo O, Felder M, Gaeta GB, De Maio E, Di Maio M, Signoriello G, Perrone F. Characteristics at presentation and outcome of hepatocellular carcinoma (HCC) in the elderly. A study of the Cancer of the Liver Italian Program (CLIP). Crit Rev Oncol Hematol 2006; 59(3):243–249.
15. Kim YJ, Jang BK, Kim ES, Chung WJ, Park KS, Cho KB,Hwang JS Hepatocellular carcinoma in the elderly: clinical characteristics, treatment, survival analysis in Korean patients older than 70 years. J Korean Med Sci 2012; 27(10): 1147–1154.
16. Mirici-Cappa F, Gramenzi A, Santi V, Zambruni A, Di Micoli A,Frigerio M, Maraldi F, Di Nolfo MA, Del Poggio P, Benvegnu L,Rapaccini G, Farinati F, Zoli M, Borzio F, Giannini EG, Caturelli E, Bernardi M, Trevisani F Treatments for hepatocellular

carcinoma in elderly patients are as effective as in younger patients: a 20-year multicentre experience. Gut 2010; 59(3):387–396.

17.Clinical characteristics, treatment patterns and survival outcome of hepatocellular carcinoma patients aged 70 years or older: a single-center retrospective study from China Chengjuan Fan • Guangxin Jin • Chen Sun •Donglai Ma • Chongyan Chen • Pengfei Qiao •Dequan Wu

18. Hepatectomy is a reasonable option for older patients with hepatocellular carcinoma Jong Man Kim, M.D., Ph.D.a, Bong Ick Cho, M.D.a, Choon Hyuck David Kwon, M.D., Ph.D.a, Jae-Won Joh, M.D., Ph.D.a,*, Jae Berm Park, M.D., Ph.D.a, Joon Hyeok Lee, M.D., Ph.D.b, Sung Joo Kim, M.D., Ph.D.a, Seung Woon Paik, M.D., Ph.D.b, Cheol Keun Park, M.D., Ph.D.c The American Journal of Surgery 2015; 209, 391-397

19. Shariff MI, Cox IJ, Gomaa AI, Khan SA, Gedroyc W, Taylor Robinson SD. Hepatocellular carcinoma: current trends in worldwide epidemiology, risk factors, diagnosis and therapeutics. Expert review of gastroenterology & hepatology. 2009;3(4):353–367.

20. Huang Z, Xu L, Yang T, et al. Hepatic resection: an analysis of the impact of operative and perioperative factors on morbidity and mortality rates in 2008 consecutive hepatectomy cases. Chinese medical journal. 2009;122(19):2268–2277.