

Characteristics of Hepatocellular Carcinoma Patients According to Their Cancer Stage at the Time of Diagnosis in Korea

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Abstract

There is a relatively high incidence of hepatocellular carcinoma in South Korea. In general, hepatocellular carcinoma is diagnosed between ages 45 to 65 with differing rates among the age groups; also the causative links to this particular cancer type is thought to be different from country to country. This study aimed to analyze the proportion of the patients who were diagnosed with hepatocellular carcinoma by gender and document the differences in survival rates according to the stages of the cancer. Our study was based on the insurance claims data filed with one company from 2009 to 2011 for liver cancer. This data was used to classify patients according to their cancer stage, age and gender. We also analyzed survival rates in each group and noted their differences. From our study the proportions of deaths in males were higher than in females, but within each group there were no significant differences by age. Our analysis also indicated that the survival rate for stages 1-2 cancer patients were relative high at more than 70%. The proportion of patients surviving stages 3 and 4 cancer diagnosis was considerably lower with 20% surviving in 5 years. Considering the age groups of the patients, the mortality rate for patients aged 50-60 due to cancer was higher than patients aged 20-40. Because of the lower survival rates in stages 3 and 4 diagnosis group and in the 50-60 age population, it is necessary that we rethink our practices for treatment and nursing for these groups to better provide for them. In addition the insurance health coverage may also be tiered to this population set according to age and stage groupings.

Keywords: *carcinoma, hepatocellular, stage factors, age factor, TNM stage*

1. Introduction

Drinking culture in Korea is known as a main cause of the high incidence of liver cancer because Koreans commonly consider drinking as a sufficient way to communicate with others in same society [1]. Survival rate among the patients with hepatocellular carcinoma is likely to be different according to age of the patient and the stage at which the cancer was diagnosed. The incidence of hepatocellular carcinoma may be high in South Korea and one this may be partly due high rates of drinking at social gatherings and business meetings.

From published survival data, liver cancer compares poorly with respect to the other major cancer types. The overall 5-year survival rates for liver and lung cancers are 42.8%

and 46.3%, respectively; this compares with rates for stomach cancer of 92.4%, colorectal 93.0%, breast 97.6%, cervical 91.1%, prostate 99.2%, and thyroid cancers 100.4% [2].

There is a research analyzing clinical features of hepatocellular carcinoma with reference to ages in Korean patients performed by the department of internal medicine in Hanyang University in 2000. And there is a cohort research in terms of 5-year survival rate of hepatocellular carcinoma patients conducted by the national cancer center as well. Liver cancer, occurred in liver, is usually defined as hepatocellular carcinoma which has the highest occurrence frequency among primary liver cancers in adults [3]. Among the liver cancers, primary hepatocellular carcinoma (defined as originating in the liver) has the highest frequency of occurrence among the adults [3]. For Korean patients, there have been a number of recent studies on analyzing the clinical features of hepatocellular carcinoma with respect to age [3] and 5-year survival [4, 5]. In addition, there was a study about linking the prognosis of patients with hepatocellular carcinoma to the stage of their cancer [6].

As serious a disease as liver cancer is, the survival numbers have shown a positive trend; most recently in a cancer registry program run by Severance Hospital in Korea and published in 2013, the 5-year survival rates for liver cancer patients have improved: from 1996 to 2000 was 17.0%, from 2001 until 2005 was 25.9%, and from 2004 to 2008 was 29.9% respectively [7].

As there are various kinds of primary liver cancer, namely hepatocellular carcinoma, cholangiocarcinoma, hepatoblastoma, and angiosarcoma, hepatocellular carcinoma being the most prevalent originates from hepatocyte liver cell and accounts for approximately 85% of the primary liver cancers in South Korea and followed by cholangiocarcinoma, which is a bile duct cancer. The incidences of the remaining liver cancer types are much lower than these two mentioned above [4]. About 16,000 new patients got primary liver cancer in Korea in 2010 (11,818 males and 4,103 females), which accounted for 7.9% of the total cancers. Primary liver cancer was ranked the 5th cancer following thyroid cancer, stomach cancer, colon cancer and lung cancer [8].

Liver cancer is diagnosed through imaging and from a blood test against a panel of cancer antigens. However, a liver biopsy of the suspected mass should also be performed if the two above examinations do not provide a solid confirmation [9]. Following the initial diagnosis, the type and stage of the cancer is confirmed as these determine the course of the treatment for the patient. Primary hepatocellular carcinoma is classified into four stages (stage 1, 2, 3 and 4) according to how widespread the cancer is. In addition, the Child-Pugh grades are sometimes given (grade A, grade B, grade C) which are indicators of liver function and should be considered after a cancer diagnosis [10].

In addition to the initial diagnosis, a screening program has an added benefit in overall survival rates. In one study the 1-year survival for primary hepatocarcinoma was 91.4% vs 70.7% for screened vs. non-screened patients; 2-year numbers were 71.5% vs. 59.9% respectively ($P < 0.05$) [11].

Our study of cancer rates among the affected population and their survival rates would be of interest health care providers and the insurance providers to determine the best allocation of funds for the cancer patients and their families and this analysis of costs and benefits of early diagnosis and screening.

2. Materials & Methods

2.1. Research Subjects

This study collected and analyzed the survival rates of diagnosed of hepatocellular carcinoma patients based by gender and age depending on the stage of their cancers. The sample size was made up of 1,804 patients who had available medical records with details of their diagnosis and treatment outcome.

2.2. Study Design

Our study was carried out based on the insurance claims data from 2008 to 2011 for patients diagnosed with hepatocellular carcinoma. The collection of the data was based on written informed consent as the purpose of the research was explained to the patients and they agreed with the premise of the study. From the collected medical records of the 1,804 patients, four registered nurses analyzed and tabulated the records based on contents of medical certificate and histopathologic examination. This work was reexamined by a physician. By design, data from patients under the age of 20 were excluded.

2.3. Data Analysis

The collected data were analyzed by using SAS 3.0 program [12]. Hospital occupancy and clinic visits analysis was performed to identify the point of diagnosis and the follow-up period. We also collected gender and age data. Follow up survey had been carried out for 5 years from January 2009 until December 2013. Five-year survival rate of liver cancer patients was calculated by using the life table method and log-rank test was performed to demonstrate the statistical significance of the data. Our study also identified the distribution of patients with hepatocellular carcinoma according to the cause of death.

3. Result

3.1 General Characteristics of Study Participants

Total number of participants consisted of 1406 (77.9%) males and 398 (22.1%) females. When dividing the study participants by age, the 50-59 age groups made up the highest proportion: the participants were 4.3% of age 20-39, 22.5% of age 40-49, 44.5% of age 50-59, and 28.7% of age 60-79.

3.2 The Distribution of the Cancer Stages of Study Participants With Hepatocellular Carcinoma

This data covered five years from January 2009 until December 2013, summarizes the distribution of the patient case numbers collected for each year <Table 1>.

Table 1. The Point Of Diagnosis and The Distribution Of Follow-up Period (n=1,804)

The point of diagnosis	Follow-up year (Cases)					Total
	2009	2010	2011	2012	2013	
2009	113	91	55	36	341	636
2010		115	91	43	365	614
2011			102	68	384	554
Total	113	206	248	147	1,090	1,804

3.3 The Distribution of Stages of Study Participants with Hepatocellular Carcinoma

A total of 730 persons, 524 males and 206 females, were diagnosed at Stage 1; a total of 437 persons, 343 males and 94 females, at Stage 2; a total of 315 persons, 258 males and 57 females, at Stage 3; and a total of 322 persons, 281 males and 41 females, at Stage 4. In sum, most persons were diagnosed at lower stages.

There were 77.9% males, 22.1% females in the sample population <Table 2>. For males, the distribution was 71.8%, 78.5%, 81.9%, and 87.3% from stage 1 to stage 4 at the time of diagnosis. This indicated a higher % of male population getting diagnosed for the late stage of the disease. For the early stage of the disease, a higher proportion of females were being diagnosed (51.8%). The 4th stage cancer rate in men was twice the level of the share of women with 20.0%.

Table 2. The Distribution of Stages of Study Participants With Hepatocellular Carcinoma By Gender (n=1,804)

Stages	The number of study participants (Cases)			Proportion (%)		
	Male	Female	Total	Male	Female	Total
Stage1	524	206	730	71.8	28.2	100
Stage 2	343	94	437	78.5	21.5	100
Stage 3	258	57	315	81.9	18.1	100
Stage 4	281	41	322	87.3	12.7	100
Total	1,406	398	1,804	77.9	22.1	100

3.4 The Distribution Of Cancer Stages Of Study Participants By Age

Following our analysis there were no differences in cancer stages according to age.

At Stage 1, the number of patients aged 20-39 were 26 persons (3.6%); that of those aged 40-49, 148 persons (20.3%); that of those aged 50-59, 321 persons (44.0%); and that of those aged 60-79, 235 persons (32.2%). The total number of patients was 730 persons. At Stage 2, the number of patients aged 20-39 were 14 persons (3.2%); that of those aged 40-49, 93 persons (21.3%); that of those aged 50-59, 201 persons (46.0%); and that of those aged 60-79, 129 persons (29.5%). The total number of patients was 437 persons. At Stage 3, the number of patients aged 20-39, 23 persons (7.3%); that of those aged 40-49, 78 persons (24.8%); that of those aged 50-59, 144 persons (45.7%); and that of those aged 60-79, 70 persons (22.2%). The total number of patients was 315 persons. At Stage 4, the number of patients aged 20-39 were 15 persons (4.7%); that of those aged 40-49, 87 persons (27.0%); that of those aged 50-59, 137 persons (42.5%); and that of those aged 60-79, 83 persons (25.8%). The total number of patients was 322 persons.

However, the proportion of patients aged 50-59, 44.5%, was higher than in other age groups. Also, the proportion of patients aged over 50, 73.2%, was higher in stage 4 than other age groups <Table 3>.

Table 3. The Age Distribution of Cancer Stages of Study Participants With Hepatocellular Carcinoma (n=1,804)

Stage	The number of participants (n, %)				
	20-39	40-49	50-59	60-79	Total
Stage 1	26(3.6)	148(20.3)	321(44.0)	235(32.2)	730(100)
Stage 2	14(3.2)	93(21.3)	201(46.0)	129(29.5)	437(100)
Stage 3	23(7.3)	78(24.8)	144(45.7)	70(22.2)	315(100)
Stage 4	15(4.7)	87(27.0)	137(42.5)	83(25.8)	322(100)
Total	78(4.3)	406(22.5)	803(44.5)	517(28.7)	1,804(100)

3.5 The Survival Distribution of Study Participants With Hepatocellular Carcinoma

Survival was defined from the point of diagnosis to death or amputation. Right censoring was performed in case of survival duration of over 5 years (60 months) [11].

As a result of an analysis, of 1,406 females, 669 persons (47.6%) died; of 398 males, 134 persons (33.7%) died and the mortality rate of females was 13.9% higher than that of males. By age group, of 78 patients aged 20-39, 35 persons (44.9%) died; of 406 patients aged 40-49, 197 persons (48.5%) died; of 803 patients aged 50-59, 356 persons (44.5%) died; and of 517 patients aged 60-69, 215 persons (41.6%) died. As a result, the mortality rate of patients aged 40-49 was the highest. At Stage 1, of 730 patients, 140 persons (19.2%) died; at Stage 2, of 437 patients, 131 persons (30.0%) died; at Stage 3, of 315 patients, 252 persons (80.0%) died; and at Stage 4, of 322 patients, 280 persons (87.0%) died. To sum it up, it turned out that the higher the stage at which the patients are in, the higher their mortality rate becomes.

In terms of survival distribution of study patients with hepatocellular carcinoma, at five years post diagnosis, the proportion of death from cancer in males were higher than in females (Table 4). Also, not surprisingly, the proportion of death in stages 1-2 was lower, less than 30%, than the proportion of death in stage 3-4 which had a rate of 80%. There were no statistically significant differences by age <Table 4>.

Table 4. The Survival Distribution of Study Participants with Hepatocellular Carcinoma (n=1,804)

Criteria for classification	The number of study participants (n)	Death		Relative Hazard		
		The number of the dead (n)	Proportion (%)	Hazard Ratio	95% CI	
					Lower limit	Upper limit
Female	1,406	669	47.6	1.00	-	-
Male	398	134	33.7	0.72	0.53	0.96
20-39	78	35	44.9	1.00	-	-
40-49	406	197	48.5	1.64	0.89	3.03
50-59	803	356	44.3	1.57	0.87	2.83

60-69	517	215	41.6	1.76	0.96	3.24
Stage 1	730	140	19.2	1.00	-	-
Stage 2	437	131	30.0	1.77	1.34	2.34
Stage 3	315	252	80.0	17.04	12.18	23.85
Stage 4	322	280	87.0	27.41	18.83	39.90

3.6 Cause of Death of Study Participants With Hepatocellular Carcinoma

In general, hepatocellular carcinoma is the number one cause of death for patients diagnosed with the disease.

At Stage 1, 126 persons (90.0%) had hepatocellular carcinoma, and 14 persons (10.0%) had other cancers and diseases. At Stage 2, 125 persons (95.4%) had hepatocellular carcinoma, and 6 persons (4.6%) had other cancers and diseases. At Stage 3, 243 persons (96.4%) had hepatocellular carcinoma, and 9 persons (3.6%) had other cancers and diseases. At Stage 4, 273 persons (97.5%) had hepatocellular carcinoma, and 7 persons (2.5%) had other cancers and diseases.

This is striking particularly in the case of stage 4 cancer patients where the rate of death from the cancer and without other complications or comorbidities was 97.5% <Table 5>.

Table 5. The Cause of Death of Study Participants With Hepatocellular Carcinoma (n=1,606)

Stage	The number of dead people (n, %)			
	Hepatocellular carcinoma	Other cancers	Other diseases	Total
Stage 1	126(90.0)	7(5.0)	7(5.0)	140(100)
Stage 2	125(95.4)	2(1.5)	4(3.1)	131(100)
Stage 3	243(96.4)	5(2.0)	4(1.6)	252(100)
Stage 4	273(97.5)	6(2.1)	1(0.4)	280(100)
Total	767(95.5)	20(2.5)	16(2.0)	803(100)

3.7 The Duration of Survival among the Study Participants with Hepatocellular Carcinoma

Males survived slightly longer than females whereas there were no differences in each age group. In addition, patients in stage 1 and 2 survived less than 2 years and patients in stage 3 and 4 survived less than a year, on average 10 months and 8 months respectively <Table 6>.

Table 6. The Distribution of Survival Duration Of Study Participants With Hepatocellular Carcinoma

(n=803)

Criteria for classification	The number of participants (n)	Survival duration		Relative Hazard	
		Duration (Months)	Post-hoc comparison result	F	P
Males	669	13.5	A	0.29	0.5901
Females	134	12.9	A		

20-39	35	13.7	A	1.03	0.3766
40-49	197	12.3	A		
50-59	356	14.2	A		
60-69	215	13.0	A		
Stage 1	140	22.4	A	97.33	<.0001***
Stage 2	131	22.0	A		
Stage 3	252	10.1	B		
Stage 4	280	7.8	C		

- Survival duration: The duration that follow up survey had been carried out for 5 years (60 months) from the point that the hepatocellular carcinoma was diagnosed, January 2009, until the end of study on December 2013.
- F-value: Post-hoc comparison result
*: P<.05, **<.005, ***<.001

3.8 The Distribution of 5-year Survival Rate in Patients with Hepatocellular Carcinoma

As a result of an analysis of 1-year through 5-year survival rate, at Stage 1, 1-year survival rate was 94.0%; 2-year survival rate, 89.5%; 3-year survival rate, 83.3%; 4-year survival rate, 78.8%; and 5-year survival rate, 75.0%. At Stage 2, 1-year survival rate was 91.8%; 2-year survival rate, 83.3%; 3-year survival rate, 73.3%; 4-year survival rate, 67.0%; and 5-year survival rate, 61.0%. At Stage 3, 1-year survival rate was 44.4%; 2-year survival rate, 29.2%; 3-year survival rate, 21.3%; 4-year survival rate, 17.5%; and 5-year survival rate, 14.4%. At Stage 4, 1-year survival rate was 29.2.0%; 2-year survival rate, 18.0%; 3-year survival rate, 14.3%; 4-year survival rate, 12.5%; and 5-year survival rate, 11.2%. As a result of an analysis regardless of the stage, 1-year survival rate was 73.6%; 2-year survival rate, 64.7%; 3-year survival rate, 57.7%; 4-year survival rate, 53.4%; and 5-year survival rate, 49.6%. To sum it up, there was a big difference in the 5-year survival rate of the patients at Stage 1 and 2 as compared to that of those at Stages 3 and 4.

There were distinct differences in 5-year survival rate depending on the stages. 75% of patients survived if it was a stage 1 diagnosis whereas only 11% of patients survived in a stage 4 diagnosis <Table 7>. There were no differences observed between the groups according to gender or age.

Table 7. The Distribution of 1 to 5-year Survival Rates in Patients with Hepatocellular Carcinoma (n=1,804)

Stage	Survival rates (%)				
	1 year	2 year	3 year	4 year	5 year
Stage 1	94.9	89.5	83.3	78.8	75.0
Stage 2	91.8	83.3	73.3	67.0	61.0
Stage 3	44.4	29.2	21.3	17.5	14.4
Stage 4	29.2	18.0	14.3	12.5	11.2
Total	73.6	64.7	57.7	53.4	49.6

4. Conclusions

From our study, the distribution of patients with hepatocellular carcinoma was higher in males than in females for all the stages. Further, the proportion of male patients with stage 4 cancer diagnosis was highest for patients in their 40s. In patients who are in stage 3 and 4 of cancer, the proportion of death was relatively high with an 80% succumbing to the disease without other complications or comorbidities. Also from our study, the survival duration of patients with hepatocellular carcinoma was longer in males than in females.

From our data, a varying approach to treatment and nursing for these cancer patients is possible according to the stage of their cancer and differing physical and mental symptoms, although the impact of the mental status was not considered in this study.

There was a clear difference in the 5-year survival of patients with hepatocellular carcinoma depending on the stage and no differences were observed between the groups according to gender or age. We believe that an insurance company should develop a customer oriented product for insurance according to differences in the stages if the diagnosed cancer and not providing claim settlement equally to all the patients.

As our data was collected from claims from only one company, our analysis may be limited. Nevertheless, this study may be significant as its results were comparable with the results of the study performed in Severance hospital based on accumulated data that went back 15 years.

To sum up, after analyzing total 1,804 of medical records for 5 years as a follow up survey from January 2009 until December 2013, it turned out that the 5-year survival curve of liver cancer patients has a significant difference depending on each stage. Regarding the survival duration of liver cancer patients, 1-year survival rate and 5-year survival rate was 94.9% and 75.0% respectively in stage 1. Also, it appeared 91.8%, 61.0% in case of stage 2 and 44.4% and 14.4% in stage 3 respectively. Lastly, 1-year survival rate was 29.2% and 5-year survival rate was 11.2% in stage 4. And this result shows that the survival rate in stage 3, 4 decline rapidly compared to stage 1, 2 [1].

However, you have to bear in mind that this study was performed using the data from only 1 company.

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