

Review article:

THE SURVIVAL RATE OF HEPATOCELLULAR CARCINOMA IN ASIAN COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Hepatocellular carcinoma or Liver cancer (LC) is the sixth most common cancer and the fourth cause of death worldwide in 2018. There has not been a comprehensive study on the survival rate of patients with LC in Asia yet. Therefore, the present study was conducted to evaluate the survival rate of patients with LC in Asian countries. The methodology of the present study is based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement. The researchers searched five international databases including Medline/PubMed, Scopus, Embase, Web of Knowledge and ProQuest until July 1, 2018. We also searched Google Scholar for detecting grey literature. The Newcastle-Ottawa Quality Assessment Form was used to evaluate the quality of selected papers. A total of 1425 titles were retrieved. 63 studies met the inclusion criteria. Based on the random-effect model one-year, three-year and five-year survival rate of LC were 34.8 % (95 % CI; 30.3-39.3), 19 % (95 % CI; 18.2-21.8) and 18.1 % (95 % CI; 16.1-20.1) respectively. According to the results of our study, the LC survival rate in Asian countries is relatively lower than in Europe and North America.

Keywords: Survival rate, hepatocellular carcinoma, systematic review, meta-analysis, Asia

INTRODUCTION

Cancer is one of the major health problems today and is currently one of the leading causes of death in many countries (Bray et al., 2018). Among malignancies, liver cancer (LC) is one of the most common one, of which more than 85 % of cases of LC has been observed in developing countries (Global Burden of Disease Cancer Collaboration et al., 2017). The highest incidence of this cancer is in Asian and sub-Saharan Africa (Ladep et al., 2014). Evidence suggests that the incidence of this cancer is soaring (McGlynn et al., 2015), which has been observed in Europe, the Pacific, as well as Asian countries (La Vecchia et al., 2000; Mirzaei et al., 2016; Mohammadian et al., 2016; Hassanipour et al., 2019). In terms of mortality, the standardized mortality rate of LC is 5.9 per 100,000. Due to the very poor prognosis of LC, the mortality rate is 95 % (Torre et al., 2016; Nikbakht et al., 2019). Global variation in LC rates can be explained by the distribution of viral hepatitis B and C infection, that should be mentioned here, the two viruses alone account for 78 % of the total mortality rate of LC in the world (Zamor et al., 2017; Jakupi et al., 2018). There is also evidence that the incidence of LC in Asia is declining in many Asian countries as a result of hepatitis B vaccination (Mansour-Ghanaei et al., 2007; Yeo et al., 2013; Joukar et al., 2018; Aniaku et al., 2019). Liver cirrhosis is another major risk factor, of which 80-90 % of these patients have hepatocellular carcinoma (Gao et al., 2012). LC is one of the malignancies that have been studied by genetics, and in this case the relative risk for a person with family history is 6.2 (Fernandez et al., 1994; Turati et al., 2012) and also it is significantly higher in males than in women (Naugler et al., 2007).

The main affecting factors for long-term survival in these patients are, early diagnosis of tumors, and treatment of patients with effec-

tive therapies (Wang et al., 2008). Patients diagnosed at an early stage will be more likely to respond to treatment and have long-term survival (Yuen et al., 2000) Also, in order to diagnose these patients at an early-stage, monitoring high risk people is a key and important factor (Zhang et al., 2004).

Survival rate is one of the most important health indicators that is essential in evaluating diagnostic and therapeutic programs. The first step to control the burden of disease related to cancers in any population, is to understand its status in the population, as well as to collect information about the incidence, survival, type and location of cancers. It is necessary to record effective indicators on the process and survival of cancers in a monitoring area and patients' information in order to perform the correct and appropriate treatment and to apply effective therapeutic methods and prevention strategies. In spite of increasing cancer treatment costs in developing countries, a few researches that were hospital-centered and population-based information have been conducted. Studies on the survival of LC in Asian countries have achieved various results, and the studied population in these surveys has also been different. Familiarity with the various years of survival rate of this cancer in different countries as well as different population groups can provide valuable information on the control, prevention, and treatment outcomes of patients with LC. There has not been a comprehensive study on the survival rate of patients with LC in Asia yet. Therefore, according to the mentioned points, the present study was conducted to evaluate the survival rate of patients with LC in Asian countries.

METHODS

The present study is a systematic review and meta-analysis study of LC survival rate in Asian countries. This study was designed and conducted in 2018. The methodology of the present study is based on the PRISMA (Pre-

ferred Reporting Items for Systematic Reviews and Meta-Analysis) statement (Moher et al., 2015).

Search strategy

The researchers searched five international databases including Medline/PubMed, Scopus, Embase, web of knowledge and ProQuest until July 1, 2018. We also searched the Google Scholar for detecting grey literature. Selected keywords for international databases included: (“neoplasm”, “cancer”, “carcinoma”, “malignancy”, “liver cancer”, “hepatocellular neoplasms”, “hepatocellular carcinoma”, “liver tumor”, “cancer of liver”, “neoplasms of liver”, “survival”, “survival analysis”, “survival rate”, “Afghanistan”, “Armenia”, “Azerbaijan”, “Bahrain”, “Bangladesh”, “Bhutan”, “Brunei”, “Myanmar”, “Cambodia”, “China”, “Georgia”, “Hong Kong”, “India”, “Indonesia”, “Iran”, “Iraq”, “Israel”, “Japan”, “Jordan”, “Kazakhstan”, “North Korea”, “South Korea”, “Kuwait”, “Kyrgyzstan”, “Laos”, “Lebanon”, “Macau”, “Malaysia”, “Maldives”, “Mongolia”, “Nepal”, “Oman”, “Pakistan”, “Philippines”, “Qatar”, “Saudi Arabia”, “Singapore”, “Sri Lanka”, “Syria”, “Taiwan”, “Tajikistan”, “Thailand”, “Timor-Leste”, “Turkmenistan”, “United Arab Emirates”, “Uzbekistan”, “Vietnam”, and “Yemen”).

The initial search was conducted by two researchers (S.H and M.V). The searched record entered the EndNote X7 software, and duplicate articles were deleted. The search strategy of this study is presented in Supplementary Appendix 1.

Inclusion and exclusion criteria

All observational studies (cross-sectional, case-control, and cohort) stated the survival rate of Localize LC in Asian countries were included in the study. Articles of other cancers reported survival in people who reported regional, metastatic, as well as review and meta-analysis studies were excluded. It should be noted that studies that did not report

the sample size or confidence interval of survival rate were not included into the meta-analysis.

Quality assessment

The Newcastle-Ottawa Quality Assessment Form was used to evaluate the quality of selected papers. This tool has 3 different parts including Selection (4 questions), Comparability (1 question) and Outcome (3 questions) and is based on the final scores divided into 3 categories Good (3 or 4 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain), Fair (2 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain) and Poor (0 or 1 star in selection domain or 0 stars in comparability domain or 0 or 1 stars in outcome/exposure domain) (Penson et al., 2012). Result of quality assessment is presented in Supplementary Appendix 2.

Screening of studies

Screening of studies, extraction of results, and evaluation of quality control of articles were performed separately undependably by two authors (M.V and E.A). If there was no agreement between the two, the supervisor (F.M) would announce the final comment on that article.

Data extraction form

All final articles entered into the study process were provided by a checklist that was previously prepared, and were arranged to extract the data. This checklist includes the name of the author, the year of publication, the period of the study, the country of origin, the survival rate by year for each survival period.

Statistical analysis

The heterogeneity of the studies was assessed by Cochran test (with significance less than 0.1) and its composition using I^2 statistics. In the case of heterogeneity, the random effects model was utilized with the inverse-

variance method, and in the absence of heterogeneity, the fixed effects model was applied. In the case of a heterogeneity in the studies, methods such as subgroup analysis were used and factors like the geographical area and the HDI considered in the analysis of subgroups. All analyzes were performed by the STATA (version 13) software.

Additional analysis

Due to the heterogeneity of the studies, the subgroups analysis was used. The indicator applied for this purpose is Human Development Indices and Indicators (HDI). The HDI is a relative measure of life expectancy, education, quality and education level, and in general, it is the living standards in human societies. This Index is estimated using the measure of welfare, especially among children and people of low age. These statistics can be used to measure the development of countries, the impact of economic policies on living standards, and the survival of LC in each of the countries was reported to provide a clear indication of the LC survival status in each country (Human Development Indices and Indicators, 2018).

RESULTS

Study selection

After searching the named international databases 1425 articles were selected and after removing duplicate articles 1132 remained. After reviewing the titles and abstract articles, the number of 178 articles entered the next stage, at which point the full text was examined and the 63 articles entered the final analysis. It should be noted that the referenced articles were also reviewed to add related studies. In the screening stages of studies, some articles were excluded for a variety of reasons, which included the unrelated topic (N=921), the unrelated population (N=133), inadequate information such as sample size, confidence interval and not reported overall survival in both sexes (N=12) and the repeated results (N=3). The study selection process is outlined in Figure 1.

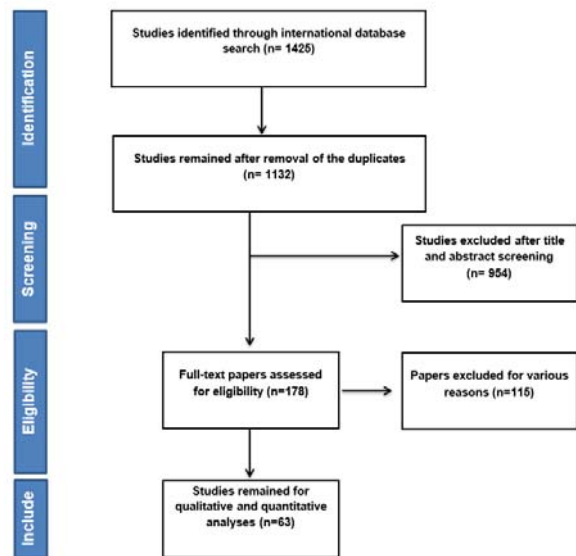


Figure 1: Flowchart of the included studies in systematic review

Results of quality assessment

Based on our result, 30 studies had good quality and 33 studies had fair quality. The result of Quality Assessment is presented in Supplementary Appendix 1.

Description of studies

Based on the geographical location of 63 included studies (Sriamporn et al., 1995; Chen et al., 1998; Esteban et al., 1998; Jin et al., 1998; Martin et al., 1998; Lee et al., 2000; Chia et al., 2001; Sato et al., 2002; Toyoda et al., 2004; Chen et al., 2006; Tsukuma et al., 2006; Yaghi et al., 2006; Chen et al., 2007; Jung et al., 2007; Changchien et al., 2008; Lim et al., 2009; Redaniel et al., 2009; Tanaka et al., 2009; Laudico et al., 2010; Chen et al., 2011; Chia, 2011; Jayalekshmi et al., 2011; Jayant et al., 2011; Jung et al., 2011; Kudo et al., 2011; Law and Mang, 2011; Martin et al., 2011; Matsuda et al., 2011; Redaniel et al., 2011; Sankaranarayanan, 2011; Sriplung and Prechavittayakul, 2011; Sumitsawan et al., 2011; Xiang et al., 2011; Xishan et al., 2011; Azmawati and Krisnan, 2012; Jung et al., 2012; Chen et al., 2013; Ito et al., 2013; Jung et al., 2013; Norsa'adah and Nurhazalini-Zayani, 2013; Fan et al., 2014; Ito et al., 2014; Jung et al., 2014; Pinheiro et al., 2014; Somboon et al., 2014; Jung et al., 2015; Liu et

al., 2015; Maringe et al., 2015; Xiao et al., 2015; Zeng et al., 2015; Zhang et al., 2015; Zheng et al., 2015; Zhu et al., 2015; Chiang et al., 2016; Kudo et al., 2016; Oh et al., 2016; Jung et al., 2017; Li et al., 2017; Nakagawa-Senda et al., 2017; Chen et al., 2018; Chien et al., 2018; Jung et al., 2018; Li-Hsin et al., 2018), twenty-one studies were conducted in China, fourteen in Korea, nine in Japan, nine in Thailand, nine in Taiwan, four in Philippines, four in Singapore, four in India, two in Malaysia, one in Hong-Kong and one study in south Asian countries. The summary characteristics of the included studies were shown in Table 1.

Heterogeneity

The result of chi-squared test and the I^2 index indicated that there was a considerable between-study heterogeneity. For one ($I^2=99.8\%$, $P<0.001$), three ($I^2=99.8\%$,

$P<0.001$), five ($I^2=99.9\%$, $P<0.001$) and ten-year survival rate ($I^2=99.6\%$, $P<0.001$).

Synthesis of results

The articles were sorted according to the year of publication, and then analyzed by survival analysis of 1, 3, 5 and 10 years survival rate based on random effect model.

One-year survival rate

Of the most recent papers, 27 studies reported a one-year survival rate. The results of the study showed that one-year survival rate in Asian countries was 34.8% (95% CI; 30.3-39.3). One-year survival rate of LC based on HDI has been shown in Figure 2. Regarding the results, the highest one-year survival rate in countries with a very high HDI level (46%, 95% CI; 38-54) and the lowest was observed among countries with medium HDI level (25.6%, 95% CI; 8.2-43.6).

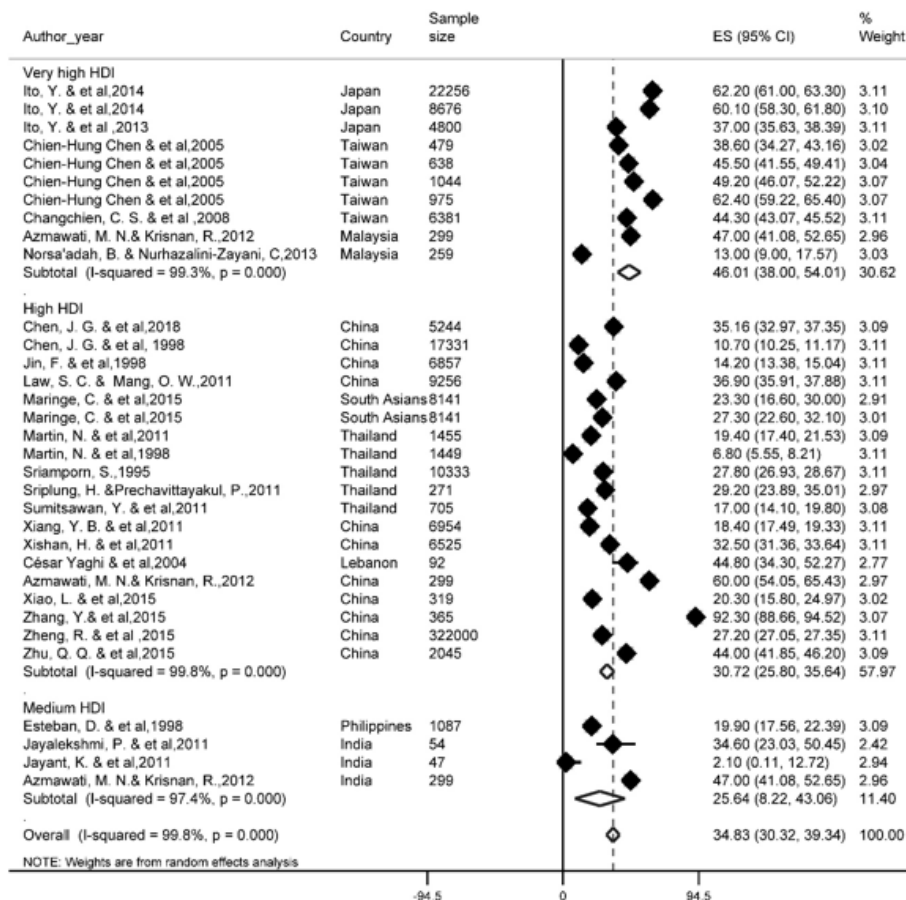


Figure 2: Forest plot of one-year survival rate of liver cancer in Asian countries

Table 1: Basic information of included studies

Order	Author (year)	Location	Time period	Sample size	Survival Rate						
					1		3	5		10	
					male	female		male	female	male	fe- male
1	Sriamporn (1995)	Thailand	1985-1992	10333	27.80		12.00	8.00			
2	Chen (1998)	China	1982-1991	17331	10.70		3.10	2.00			
3	Esteban (1998)	Philippines	1983-1987	1087	19.90		14.10	12.50			
4	Jin (1998)	China	1988-1992	6857	14.20		5.20	3.90			
5	Martin (1998)	Thailand	1988-1992	1449	6.80		1.50	.40			
6	Lee (2000)	Taiwan	1987-1992	2002				15.00			
7	Chia (2001)	Singapore	1983-1987	2282125				3.00			
8	Chia (2001)	Singapore	1988-1992	2705115				3.00			
9	Sato (2002)	Japan	1962-1966	48745				5.20	12.90		
			1967-1971					5.30	9.20		
			1972-1976					7.40	22.70		
			1977-1981					9.30	16.90		
			1982-1986					21.50	22.60		
			1987-1991					36.30	32.40		
			1992-1994					42.70	40.90		
10	Toyoda (2004)	Japan	1976-2000	1365				37.30			
	Tsukuma (2006)	Japan	1993-1996	279000				12.30			
11	Chen (2006)	Taiwan	1986-1989	479	38.60		17.30	11.10			
			1990-1993	638	45.50		27.70	18.70			
			1994-1997	1044	49.20		29.10	21.00			
			1998-2001	975	62.40		42.90				
12	Yaghi (2006)	Lebanon	1998-2003	92	44.80		17.60				
13	Chen (2007)	Taiwan	1985-1994	28939				13.70	17.20		
14	Jung (2007)	Korea	1993-1997	126833				10.40	13.10		
			1998-2002					14.50	15.30		
15	Changchien (2008)	Taiwan	1986-2002	6381	44.30		24.90	17.10			
16	Lim (2009)	Singapore	1978-1982	142252						.30	.60
			1983-1987							.40	.40
			1988-1992							.80	2.20
			1993-1997							1.80	1.30
			1998-2002							6.30	1.80

Order	Author (year)	Location	Time period	Sample size	Survival Rate						
					1		3	5		10	
					male	female		male	female	male	fe- male
17	Redaniel (2009)	Philippines	1998-2002	772				8.50			
18	Tanaka (2009)	Korea	1997-1999	45205				13.00			
		Miyagi						24.00			
		Yamagata						22.30			
		Niigata						22.70			
		Fukui						32.50			
		Osaka						23.40			
		Nagasaki						22.10			
		Taiwan						17.60			
		Korea						14.70			
		Miyagi						22.80			
		Yamagata						19.50			
		Niigata						21.70			
		Fukui						20.40			
		Osaka						21.30			
Nagasaki				25.80							
Taiwan				20.30							
19	Laudico (2010)	Philippines	1993-2002					8.50			
20	Law (2011)	China	1996-2001	9256	36.90	23.00		18.90			
21	Kudo (2011)	Japan	1978-1980	148161				5.10			
			1981-1985					13.90			
			1986-1990					24.90			
			1991-1995					32.00			
			1996-2000					38.80			
			2001-2005					42.70			
22	Sumitsawan (2011)	Thailand	1993-1997	705	17.00	4.50		3.00			
23	Matsuda (2011)	Japan	1993-1999	491772				21.20			
24	Redaniel (2011)	Philippines	1995-1999					5.30			
25	Chen (2011)	China	1992-2000		13.50	6.80		5.60			
26	Chia (2011)	Singapore	1968-1997		19.00	7.50		5.10			
27	Jayalekshmi (2011)	India	1991-1997	54	34.60	9.20		2.30			
28	Jayant (2011)	India	1993-2000	47	2.10	.0		.0			
29	Martin (2011)	Thailand	1990-2000	1455	19.40	13.20		12.20			

Order	Author (year)	Location	Time period	Sample size	Survival Rate						
					1		3	5		10	
					male	female		male	female	male	fe- male
30	Sankaranarayanan (2011)	Hong Kong SAR (China)	1991-2000					24.60			
		Qidong (China)						5.40			
		Shanghai (China)						9.80			
		Tianjin (China)						25.80			
		India						4.50			
		Singapore						6.50			
		Busan (Republic of Korea)						10.00			
		Incheon (Republic of Korea)						16.80			
		Seoul (Republic of Korea)						20.30			
		Chiang mai (Thailand)						3.30			
		Lampang (Thailand)						11.90			
Songkhla (Thailand)	2.50										
31	Jung (2011)	Korea	1993-1995	178816				10.70			
			1996-2000					13.20			
			2001-2005					19.70			
			2004-2008					23.30			
32	Sriplung (2011)	Thailand	1990-1999	271				29.20	8.10	2.20	
33	Xiang (2011)	China	1992-1995	6954				18.40	8.90	7.50	
34	Xishan (2011)	China	1991-1999	6525				32.50	22.60	21.30	
35	Jung (2012)	Korea	1993-1995	192561				10.70			
			1996-2000					13.20			
			2001-2005					20.10			
			2005-2009					25.10			

Order	Author (year)	Location	Time period	Sample size	Survival Rate						
					1		3	5		10	
					male	female		male	female	male	fe- male
36	Azmawati (2012)	China	2003-2006	299	60.00		39.00	21.00			
		Malaysia			47.00			13.00			
		India			47.00			15.00			
37	Chen (2013)	China	2004-2005	633802				4.00			
38	Jung (2013)	Korea	1993-1995	202053				10.70			
			1996-2000					13.20			
			2001-2005					20.10			
			2006-2010					26.70			
39	Ito (2013)	Japan	1990-2004	4800	31.00		33.00	37.00			
40	Norsa'adah (2013)	Malaysia	1987-2008	259	13.00						
41	Pinheiro (2014)	Hispanics and Asians	2000-2008	1471789				7.10			
42	Ito (2014)	Japan	1993-2009	21175				38.00	38.40	9.60	9.10
			1993-2004	30932	62.20	60.10		22.80	21.10		
43	Jung (2014)	Korea	1993-1995	218017				10.70			
			1996-2000					13.20			
			2001-2005					20.20			
			2007-2011					28.60			
44	Fan (2014)	China	2004-2012	164				26.20			
				531				28.30			
45	Somboon (2014)	Thailand	2007-2012	308				5.00			
46	Jung (2015)	Korea	1993-1995	224177				10.70			
			1996-2000					13.20			
			2001-2005					20.20			
			2008-2012					30.10			
47	Maringe (2015)	South Asians	1986-1995	8141	23.30			15.00			
			1996-2004		27.30			15.00			
48	Zeng (2015)	China	2003-2005	16816				10.10			
49	Liu (2015)	China	1990-2009	35				14.30			
50	Xiao (2015)	China	2000-2012	319	20.30		12.60	4.50			
51	Zhang (2015)	China	2002-2013	365	92.30		65.30	44.70			
52	Zheng (2015)	China	2000-2011	322000	27.20		12.70	8.90			
53	Zhu (2015)	China	2002-2011	2045	44.00		25.00	22.00			

Order	Author (year)	Location	Time period	Sample size	Survival Rate						
					1		3	5		10	
					male	female		male	female	male	fe- male
54	Chiang (2016)	Taiwan	2002-2012					28.90			
55	Kudo (2016)	Japan	1967-1978	173378				37.90		16.50	
56	Oh (2016)	Korea	1993-1995	225343				10.70			
			1996-2000					13.20			
			2001-2005					20.20			
			2008-2013					31.40			
57	Nakagawa-Senda (2017)	Japan	2006-2008	120503				19.30			
58	Jung (2017)	Korea	1993-1995					10.70			
			1996-2000					13.20			
			2001-2005					20.20			
			2010-2014					32.80			
59	Li (2017)	Northeast China	2000-2007					10.70			
60	Chen (2018)	China	2002-2014	5244	35.16	17.52		11.69		6.34	
61	Chien (2018)	Taiwan	2000-2010					4.22			
62	Jung (2018)	Korea	1993-1995					10.70			
			1996-2000					13.20			
			2001-2005					20.40			
			2006-2010					28.10			
			2011-2015					33.60			
63	Li-Hsin (2018)	Taiwan	2000-2010	724992				4.22			

Three-year survival rate

There were 22 studies that reported 3-year survival rate. Based on the results of our study, the 3-year survival rate in Asian countries was 19 %, (95 % CI; 16.2-21.8). The three-year survival rate of LC based on HDI is presented in Figure 3. According to the results, the highest three-year survival rate for countries with a high HDI level (26.9 %, 95 % CI; 23.3-30.5) and the lowest for countries with the medium HDI levels was 14 % (95 % CI; 12.2-15.9).

Five-year survival rate

A total of 56 studies reported this survival rate. The 5 years rate of LC was 18.1 % (95 %

CI, 16.2-20.1). The results of the 5-year survival by the HDI is depicted in Figure 4. Based on the findings of our study, the highest five-year survival rate for countries with very high HDI levels (20.7 %, 95 % CI; 18.2-23.2) and the lowest was for the countries with the medium HDI level 8 %, 95 % CI; 5.3-10.7).

Ten-year survival rate

Four studies reported this survival rate and based on the results, the ten-year survival rate was 4.1 % (95 % CI; 1.5-6.7). Ten-year survival of LC by HDI has been shown in Figure 5. Given the limited number of studies conducted for 10-year survival rate, data on countries with medium HDI levels was not available.

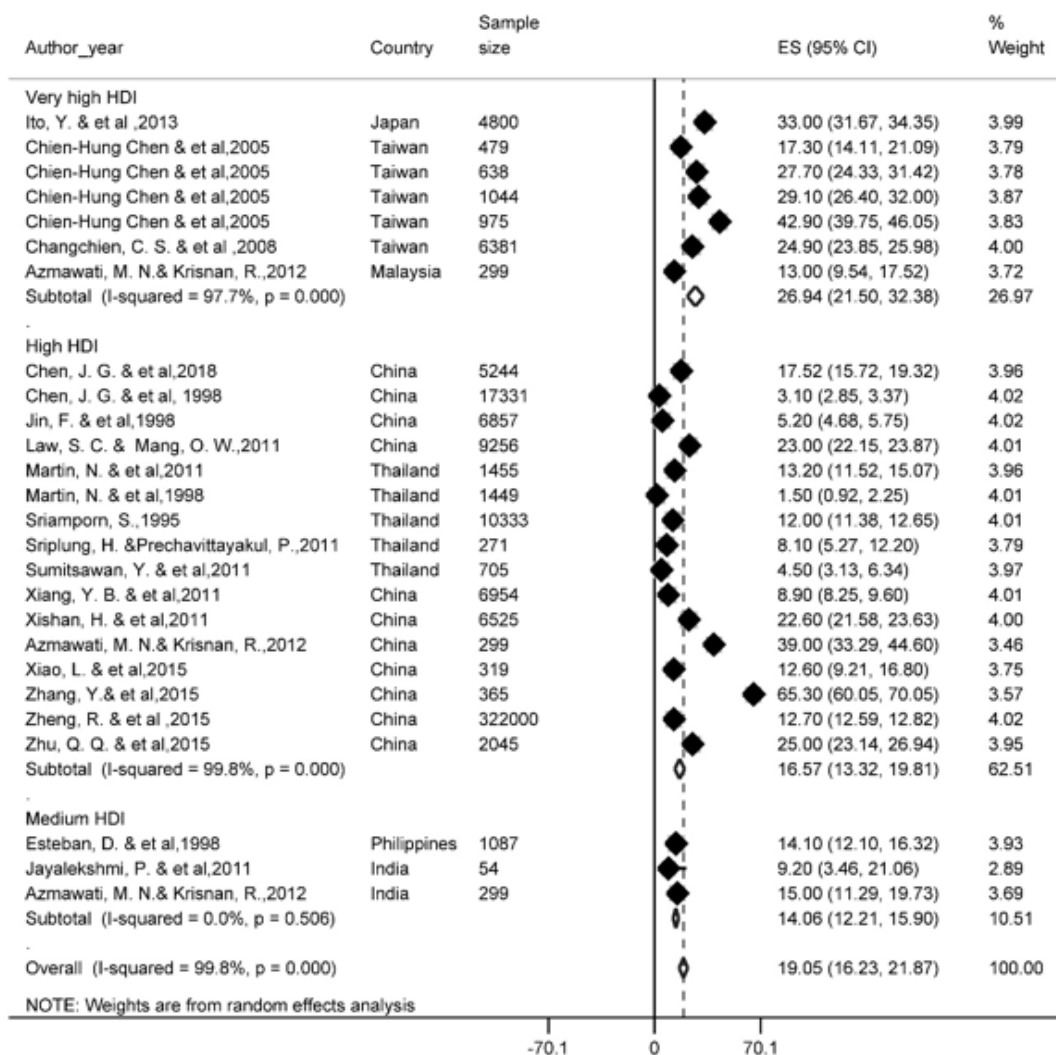


Figure 3: Forest plot of three-year survival rate of liver cancer in Asian countries

Author_year	Country	Sample size	ES (95% CI)	% Weight
Very high HDI				
Chia, K. & et al., 2001	Singapore	2282125	3.00 (2.90, 3.10)	0.97
Chia, K. & et al., 2001	Singapore	2705115	3.00 (2.90, 3.10)	0.97
Kudo, M. & et al., 2011	Japan	148161	5.10 (4.99, 5.21)	0.97
Oh, C.C. & et al., 2016	Korea	225343	10.70 (10.57, 10.83)	0.97
Oh, C.C. & et al., 2016	Korea	225343	20.20 (20.03, 20.37)	0.97
Kudo, M. & et al., 2016	Japan	148161	13.90 (13.72, 14.08)	0.97
Kudo, M. & et al., 2016	Korea	225343	13.20 (12.90, 13.38)	0.97
Kudo, M. & et al., 2016	Japan	148161	24.90 (24.68, 25.12)	0.97
Kudo, M. & et al., 2011	Japan	148161	32.00 (31.76, 32.24)	0.97
Kudo, M. & et al., 2011	Japan	148161	38.80 (38.55, 39.05)	0.97
Kudo, M. & et al., 2011	Japan	148161	42.70 (42.45, 42.95)	0.97
Lanaka, H. & et al., 2009	Japan	45205	22.70 (22.24, 23.01)	0.97
Lanaka, H. & et al., 2009	Korea	45205	13.00 (12.69, 13.31)	0.97
Lanaka, H. & et al., 2009	Korea	45205	14.70 (14.38, 15.03)	0.97
Lanaka, H. & et al., 2009	Taiwan	45205	17.90 (17.28, 17.95)	0.97
Lanaka, H. & et al., 2009	Japan	45205	19.50 (19.14, 19.87)	0.97
Lanaka, H. & et al., 2009	Taiwan	45205	20.30 (19.93, 20.67)	0.97
Lanaka, H. & et al., 2009	Japan	45205	21.70 (21.32, 22.08)	0.97
Lanaka, H. & et al., 2009	Japan	45205	21.30 (20.92, 21.68)	0.97
Lanaka, H. & et al., 2009	Japan	45205	20.40 (20.03, 20.78)	0.97
Lanaka, H. & et al., 2009	Japan	45205	22.10 (21.72, 22.49)	0.97
Lanaka, H. & et al., 2009	Japan	45205	22.30 (21.92, 22.69)	0.97
Lanaka, H. & et al., 2009	Japan	45205	23.40 (23.01, 23.79)	0.97
Lanaka, H. & et al., 2009	Japan	45205	24.00 (23.61, 24.40)	0.97
Matsuda, T. & et al., 2011	Japan	491772	21.00 (20.60, 21.40)	0.97
Jung, K.W. & et al., 2007	Korea	126833	10.40 (10.10, 10.80)	0.97
Jung, K.W. & et al., 2007	Korea	126833	14.50 (14.20, 14.90)	0.97
Chen, P.H. & et al., 2007	Taiwan	28939	13.70 (13.31, 14.10)	0.97
Jung, K. & et al., 2014	Korea	218017	10.70 (10.30, 11.10)	0.97
Matsuda, T. & et al., 2011	Japan	491772	21.20 (20.80, 21.60)	0.97
Chiang, C. & et al., 2016	Taiwan	45205	28.80 (28.40, 29.30)	0.97
Lanaka, H. & et al., 2009	Japan	45205	25.80 (25.40, 26.21)	0.97
Lanaka, H. & et al., 2009	Japan	45205	32.50 (32.07, 32.93)	0.97
Chen, P.H. & et al., 2007	Taiwan	28939	17.20 (16.77, 17.64)	0.97
Jung, K. & et al., 2014	Korea	218017	13.20 (12.70, 13.70)	0.97
Io, Y. & et al., 2014	Japan	22256	22.80 (22.25, 23.36)	0.97
Nakagawa-Senda, Hiroko & et al., 2017	Japan	120503	19.30 (18.90, 19.90)	0.97
Jung, K. & et al., 2014	Korea	218017	20.20 (19.60, 20.80)	0.97
Jung, K.W. & et al., 2007	Korea	126833	15.30 (14.70, 16.00)	0.97
Jung, K.W. & et al., 2011	Korea	178916	23.30 (22.60, 24.00)	0.97
Matsuda, T. & et al., 2011	Japan	491772	21.80 (21.10, 22.50)	0.97
Jung, K.W. & et al., 2012	Korea	215017	28.60 (27.90, 29.30)	0.97
Jung, K.W. & et al., 2012	Korea	192561	25.10 (24.40, 25.80)	0.97
Jung, K.W. & et al., 2007	Korea	126833	13.10 (12.40, 13.90)	0.97
Io, Y. & et al., 2014	Japan	8676	21.10 (20.24, 21.97)	0.97
Kudo, M. & et al., 2016	Japan	173378	37.90 (37.00, 38.80)	0.97
Changchien, C.S. & et al., 2008	Taiwan	6381	17.10 (16.19, 18.05)	0.97
Jung, K.W. & et al., 2015	Korea	224177	30.10 (29.40, 31.08)	0.97
Io, Y. & et al., 2013	Japan	4800	31.00 (29.70, 32.23)	0.96
Lanaka, H. & et al., 2009	Japan	45205	22.80 (21.50, 24.20)	0.96
Lee, C.L. & et al., 2000	Taiwan	2002	15.00 (13.47, 16.65)	0.96
Li-Hsin, Chien & et al., 2018	Taiwan	724992	4.22 (1.64, 6.21)	0.96
Jung, K.W. & et al., 2013	Korea	202053	26.70 (26.51, 28.89)	0.97
Io, Y. & et al., 2014	Japan	14230	38.00 (35.80, 40.20)	0.96
Chien-Hung, Chen & et al., 2005	Taiwan	1044	21.00 (18.57, 23.60)	0.95
Chien-Hung, Chen & et al., 2005	Taiwan	479	11.10 (8.46, 14.30)	0.95
Io, Y. & et al., 2014	Japan	6945	39.40 (35.10, 41.70)	0.94
Chien-Hung, Chen & et al., 2005	Taiwan	638	18.70 (15.70, 22.01)	0.95
Wato, Y. & et al., 2002	Japan	48745	9.30 (5.60, 13.00)	0.94
Wato, Y. & et al., 2002	Japan	48745	21.50 (17.20, 25.70)	0.93
Wato, Y. & et al., 2002	Japan	48745	36.30 (32.10, 40.50)	0.93
Oh, C.M. & et al., 2016	Korea	225343	31.40 (25.10, 35.60)	0.91
Chien, L.H. & et al., 2018	Taiwan	724992	4.22 (0.10, 8.60)	0.93
Wato, Y. & et al., 2002	Japan	48745	42.70 (37.00, 48.50)	0.89
Wato, Y. & et al., 2002	Japan	48745	5.30 (1.20, 11.70)	0.91
Wato, Y. & et al., 2002	Japan	48745	7.40 (0.80, 14.10)	0.87
Wato, Y. & et al., 2002	Japan	48745	5.20 (1.60, 11.90)	0.91
Wato, Y. & et al., 2002	Japan	48745	32.40 (24.60, 40.30)	0.84
Wato, Y. & et al., 2002	Japan	48745	22.60 (13.90, 31.30)	0.81
Toyoda, H. & et al., 2004	Japan	1365	37.30 (29.90, 46.30)	0.83
Wato, Y. & et al., 2002	Japan	48745	16.90 (5.80, 28.00)	0.74
Wato, Y. & et al., 2002	Japan	48745	40.80 (29.30, 52.60)	0.72
Wato, Y. & et al., 2002	Japan	48745	12.90 (3.40, 29.20)	0.68
Wato, Y. & et al., 2002	Japan	48745	9.20 (7.80, 26.20)	0.80
Isukuma, H. & et al., 2006	Japan	279000	12.30 (10.50, 29.40)	0.79
Sato, Y. & et al., 2002	Japan	48745	22.70 (4.40, 49.90)	0.42
Subtotal (I-squared = 100.0%, p = 0.000)			20.66 (18.17, 23.15)	70.87

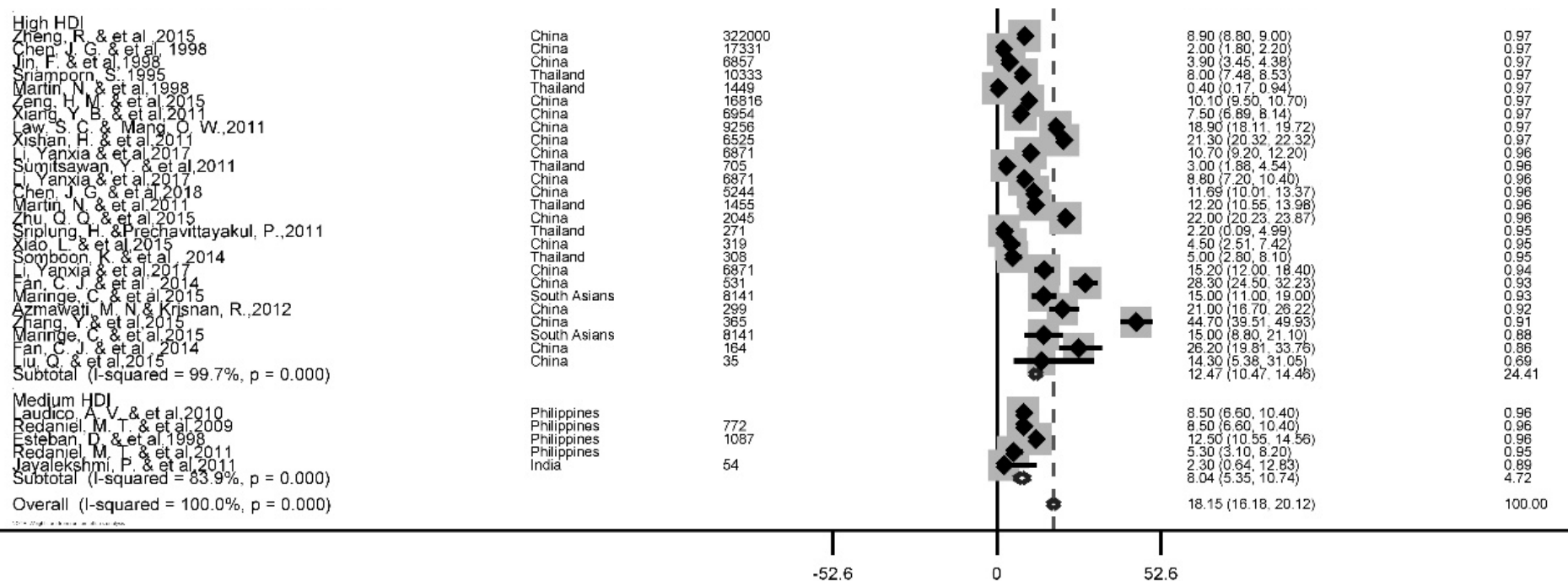


Figure 4: Forest plot of five-year survival rate of liver cancer in Asian countries

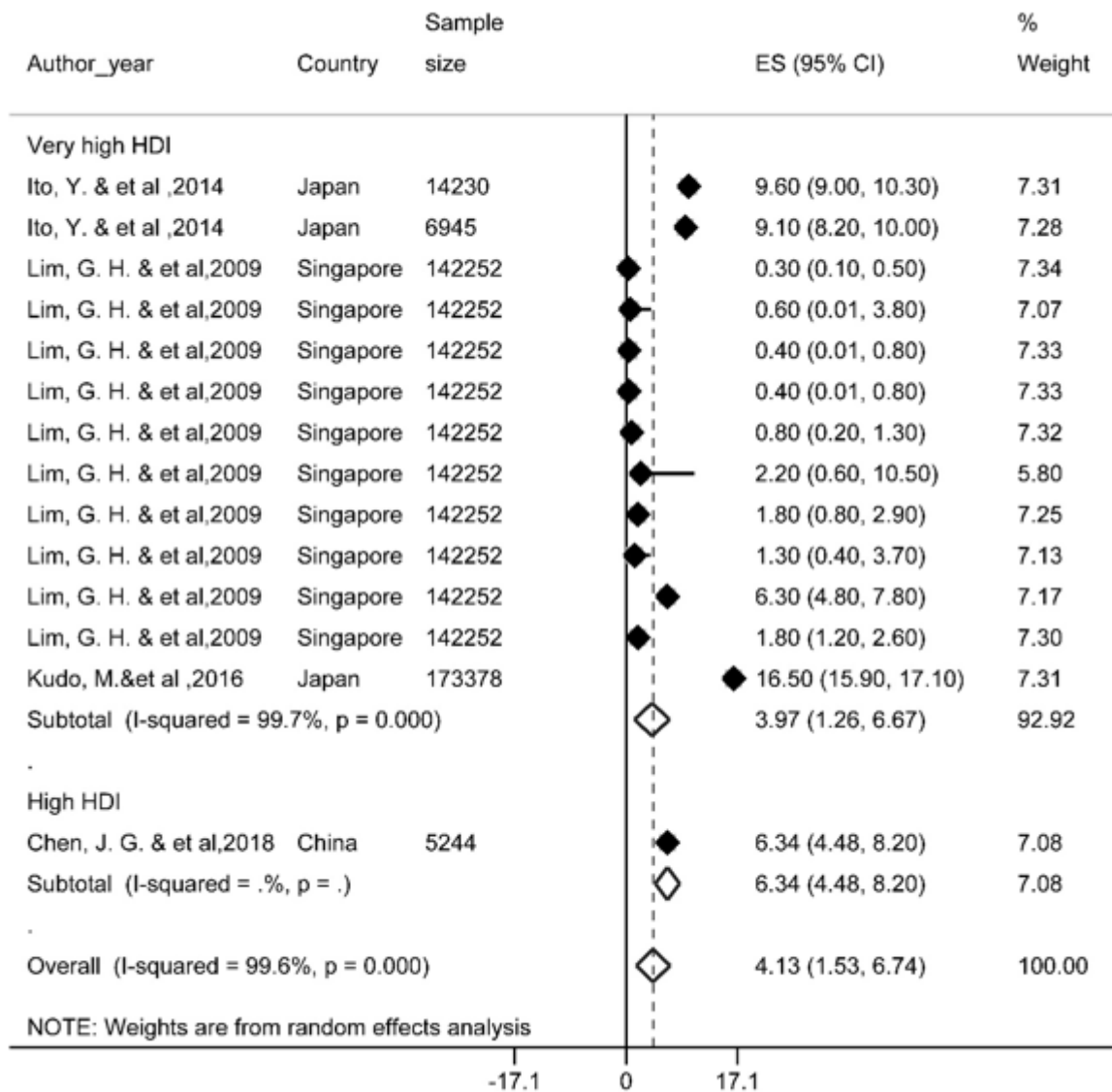


Figure 5: Forest plot of ten-year survival rate of liver cancer in Asian countries

ANALYSIS OF SUBGROUPS

Survival rate of liver cancer in each country

Overall, the results of the survival of the LC in ten countries and another region has been reported in Table 2. The highest survival rates of one, three, five, and ten years were reported in Japan and the lowest survival rates for these years were observed in countries such as the Philippines, Thailand, India and Singapore.

Meta-regression

Results of meta-regression showed a significant association between publication year and survival rate. Thus, year of study is a cause of variability in results of one (Reg Coef= 0.041, $p=0.002$), three (Reg Coef= 0.049, $p=0.017$) and five year survival rate (Reg Coef= 0.036, $p<0.001$). According to results, an increasing survival rate across the study period was observed. Results of meta-regression has been shown in Supplementary Appendix 3.

Table 2: Result of meta-analysis of survival rate of liver cancer in Asia based on each country and year of survival

Country	Year of Survival							
	# of study	1	# of study	3	# of study	5	# of study	10
China	11	35.4 (28.6-42.1)	11	20.6 (16.5-24.7)	18	14.8 (12.4-17.3)	1	6.3 (4.4-8.2)
India	3	27.8 (4.43-60)	2	13.4 (8.3-18.4)	1	2.3 (0.6-12.8)	-	NR
Japan	3	53 (36.6-69.5)	1	33 (31.6-34.3)	44	23.9 (20.1-27.7)	3	11.7 (6.7-16.7)
Korea	-	NR	-	NR	18	18.4 (16-20.7)	-	NR
Lebanon	1	44.8 (34.3-52.2)	-	NR	-	NR	-	NR
Malaysia	2	29.9 (3.3-63.2)	1	13 (9-17)	-	NR	-	NR
Philippines	1	19.9 (17.4-22.3)	1	14.1 (12.1-16.3)	4	8.7 (6-11.4)	-	NR
Singapore	-	NR	-	NR	2	3(2.9-3.1)	10	1.3 (0.7-1.9)
South Asian	2	25.9 (22-29.8)	-	NR	2	15 (11.6-18.3)	-	NR
Taiwan	5	48 (40.9-55.2)	5	28.3 (21.6-35.1)	12	15.9 (12.9-19)	-	NR
Thailand	5	20 (9.7-30.1)	5	7.8 (2.1-13.5)	6	5.1 (1-9.2)	-	NR
Overall	33	34.8 (30.3-39.3)	25	19 (16.2-21.8)	107	18.1 (16.2-20.1)	14	4.1 (1.5-6.7)

NR: not reported

DISCUSSION

LC is the sixth most common cancer and the fourth cause of death worldwide in 2018, with 841,000 new cases and 782,000 deaths annually (Bray et al., 2018). The incidence and mortality of men are two to three times higher than women in most parts of the world (Altekruse et al., 2014).

The results of our study showed that one, three, five and ten-year survival rate of LC in Asian countries was 34.8 %, 19 %, 18.1 %, and 4.1 % respectively. Significant heterogeneity was seen in the between studies. The present study was conducted in identifying high-risk individuals, diagnosis and early treatment of LC. The most important treatment for hepatocellular carcinoma is hepatic resection, trans-arterial embolization, percutaneous ethanol injection therapy, regional chemotherapy, and liver transplantation (Takano et al., 2000; Fakhar et al., 2016; Zhao et al., 2019). For instance, 84.5 % of patients in Pakistan (Yusuf et al., 2007) did not receive any treatment interventions, which was 30.5 % in China (Zhou et al., 2000). Mortality rate for all cancers are 50 % more common in men than in women. Mortality rate in men were 171 per 100,000 in East Africa to 67.4 in Central America, ranging from 7.1 in Melanesia to 2.6 in Central and East Asia (except China) (Ghoncheh and Salehiniya, 2016). The

cumulative mortality risk from cancer among women in East Africa (11.4 %) in 2018 was higher than the estimated risk in North Africa (8.6 %), Northern Europe (9.1 %), and Australia / New Zealand (1.8 %) (Allemani et al., 2018; Bray et al., 2018). In one study which is conducted on localized staged patients treated with invasive methods, blacks have a 12 percent higher mortality rate, while Asian or Pacific islanders have a 16 percent lower mortality rate compared to whites (Wong and Corley, 2009).

The statistics show that about half of the cases of death from primary LC occurred in China (Zheng et al., 2018). The variety of survival rates in Asian countries includes the range of medical and pharmaceutical care and coverage of insurance services, socioeconomic status, ethnicity and lifestyle (Williams et al., 2010). Medical advances have been made in detecting small tumors with a variety of scanning techniques (Takayasu et al., 1995).

In our analysis, the one-year survival rate in Asian countries was 34.8 %. The one-year survival rate is related to factors such as age older than 50 years, CLIP score <3, ALP <120 U/l, LDH <450 IU/l, CRP <0.8 mg/dl, tumor size less than 6 cm, disease stage, and Child-Pugh less than 7 that is associated with increased mortality (Toyoda et al., 2004;

Georgiades et al., 2006; Jun et al., 2013; Agarwal et al., 2015). A meta-analysis study concluded that Transarterial chemoembolization (TACE) in patients with portal vein thrombosis significantly increased the 6 months survival rate (Xue et al., 2013). However, haptoglobin (Hp) serum could be a potential and alternative contributor to alpha-fetoprotein. Contradiction in predicting one year rate in various geographic regions can be due to the selecting patients with demographic and clinical characteristics, diagnostic criteria, severity of the cirrhosis, number and size of the tumor (Shu et al., 2010; Moayedi et al., 2019). Despite the limited number of HCTs available for HCC, one-year survival rates for HCC have almost doubled over the period of 1992-1993 to 2003-2004 in the United States (Altekruse et al., 2009). Of course, this increase in survival is limited to short-term follow-up. In addition, with aggressive treatments including liver transplantation and resection for localized-stage tumors, they are effective in boosting survival rates (Schwarz and Smith, 2008). It is also associated with the expansion of public health and oncology care (Bai et al., 2018).

Based on the results, the five-year survival rate was 18.1 %. The 5-year survival rate of all cancers in Korea in each sex, reached to 7.70 % (2011-2015) from 2.41 % (1995-1993) (Jung et al., 2018). Besides, the five-year survival rate of LC in Shanghai in 1990 was 0.9 percent, reaching 0.1 percent in the last decade (Xiang et al., 2011; Han et al., 2012). Uninodular tumors and non-vascular invasion were associated with a 5-year survival (Jeong et al., 2017). Liver transplant increases 5-year survival to 75 %, which is the best treatment option (Zamora-Valdes et al., 2017). A meta-analysis study of 19 researches illustrated that the median survival rate for 436 patients with liver resection for hepatocyte metastasis to gastric was 17 months and a 5-year survival of 26.5 % (Kerkar et al., 2010). An overall improvement in community health and the use of anti-viral therapies is effective in extending patient survival. Liver transplantation is an appropriate option

(Omata et al., 2010; Zhu et al., 2015). However, the high cost of transplantation and the low number of donors of liver transplantation in most cases make it impractical (Llovet et al., 2005). Resection surgery is recommended as a treatment for BCLC (Barcelona Clinic Liver Cancer) in very early and primary phases without portal hypertension and abnormal bilirubin. However, resection surgery is now the first line of therapy and leads to better patient survival (Dimitroulis et al., 2017).

The gender variable is an independent predictor in the prognostic primary liver cancer (PLC), regardless of the death of the PLC and all causes of death (Chen et al., 2007). However, in other studies, the gender variable was not a predictor of survival due to PLC (Tangkijvanich et al., 2004; Jarnagin et al., 2009). Previous studies have shown that women have a higher rate of survival after surgery. Differences in aspects of medical interventions are attributed to gender disparity in survival rates (Wu et al., 2018). The high alcohol intake in men increases cirrhosis of the liver towards the PLC (Nordenstedt et al., 2010; Kröner et al., 2015).

Analysis of subgroups based on the geographic region show that, the highest survival rates of one, three, five, and ten years are reported in Japan and the lowest survival rates for these years were observed in the Philippines, Thailand, India and Singapore, respectively. The only areas with a high prevalence rate in the past include Japan, Korea and China, which have witnessed a sharp decline in outbreaks in recent years (Bertuccio et al., 2017).

According to the latest global release, the highest incidence has taken place in lower HDI settings, and LC in 13 countries was one of the most common malignancies, including several countries in North and West Africa (Egypt, Gambia, Guinea) and the East and South East Asia (Mongolia, Cambodia and Vietnam) (Hashim et al., 2016). Also, over the most recent years, the mortality rate of HCC is 2 to 5 times higher in Japan, Hong

Kong and Korea than in European and American countries (McGlynn and London, 2011; Zhu et al., 2016). In the case of China, the proportion of Child A was less prevalent, while this proportion was more prevalent in the case of the Italian Child B type (Pons et al., 2005; Azmawati and Krisnan, 2012; Kew, 2014). In addition, Asians have lower survival rates than non-Asians (Chang et al., 2007). Advances have been made in HCC management and treatment, through local ablation, hepatic resection and liver transplantation. The impact of such improvements on HCC mortality was limited, as its 5-year survival rate was about 10 % (Lepage et al., 2015). The five-year survival rate of the cancer in the US rose from 3 % over the 1975-1977 period to 11 % in the period of 2001-2007. While this survival rate ranged from 10.7 % in 1975-1977 to 18.9 % in the period 2001-2005. Approximately 62 % of HCC patients in Japan have undergone resection or ablation as primary care (Korean Liver Cancer Study Group and National Cancer Center Korea, 2015). By comparing these proportions, only 30 % of these patients in the Western countries by the initial diagnosis were under these treatment interventions. Perhaps the care of high-risk patients will cause early detection and early diagnosis in countries such as Japan and Korea (El-Serag and Davila, 2011).

Study limitations

There are certain limitations in systematic review studies, most notably in the absence of access to some of the information that attempts were made to contact the authors of the study to resolve the problem, which in several cases did not receive an adequate response. One of the main limitation in our study was the failure to report sample size and the inability to calculate the confidence interval for survival, which did not allow the study to include the meta-analysis stage. Other limitations included a survival report of less than one year (6 and 9 months), which, given the low level of these, had no significant effect on our results. Ultimately, due to the lack of stud-

ies reporting 10-year survival, the correct estimate of survival requires more robust studies.

Recommendations for future research

According to the results of this study, estimating the survival rate of LC requires more extensive studies at the level of other Asian countries, especially in the West and Central Asia, as most studies in this study were conducted in South and Southeast of Asia, and estimates are somewhat incorrect. Another suggestion could be a study of the survival of LC in patients who metastasized, which was not our study goal, and is an important issue in clinical decision-making and the continuation of treatment.

CONCLUSION

According to the results of our study, the LC survival rate in Asian countries is relatively lower than in Europe and North America, which may be due to less access to diagnostic facilities and higher age at recognition of disease than to advanced countries. Another result of our study was the higher survival rate of LC in countries with very high HDI (such as South Korea and Japan), with similar survival rates within advanced countries such as Europe and North America.

Author contributions

Conceived and designed the experiments: S.H and F.M
 Collected the data: M.V, H.N and E.A
 Analyzed the data: S.H, F.J, M.A and H.S.
 Wrote the paper: S.G, H.N, A.P and A.S.
 Revised the paper: S.H, F.M and F.J.

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Conflict of interests

The authors have no conflict of interest to disclose.

REFERENCES

- Agarwal A, Yadav AK, Kumar A, Gupta S, Panwala HK, Redhu N, et al. Transarterial chemoembolization in unresectable hepatocellular carcinoma--assessing the factors affecting the survival: An audit from a tertiary care center in northern india. *Indian J Gastroenterol.* 2015;34:117-26.
- Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000-14 (concord-3): Analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet.* 2018;391:1023-75.
- Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the united states from 1975 to 2005. *J Clin Oncol.* 2009;27:1485-91.
- Altekruse SF, Henley SJ, Cucinelli JE, McGlynn KA. Changing hepatocellular carcinoma incidence and liver cancer mortality rates in the united states. *Am J Gastroenterol.* 2014;109:542-53.
- Aniaku JK, Amedonu EK, Fusheini A. Assessment of knowledge, attitude and vaccination status of hepatitis b among nursing training students in ho, ghana. *Ann Global Health.* 2019;85(1).
- Azmawati M, Krisnan R. Roles of ethnicity in survival of hepatocellular carcinoma patients in malaysia. *Asian Pac J Cancer Prev.* 2012;13:6023-6.
- Bai L, Liu Z, Fang Q, Yan Q, Shi O, Bao P, et al. The trends and projections in the incidence and mortality of liver cancer in urban shanghai: A population-based study from 1973 to 2020. *Clin Epidemiol.* 2018;10:277-88.
- Bertuccio P, Turati F, Carioli G, Rodriguez T, La Vecchia C, Malvezzi M, et al. Global trends and predictions in hepatocellular carcinoma mortality. *J Hepatol.* 2017;67:302-9.
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68:394-424.
- Chang ET, Keegan THM, Gomez SL, Le GM, Clarke CA, So SKS, et al. The burden of liver cancer in asians and pacific islanders in the greater san francisco bay area, 1990 through 2004. *Cancer.* 2007;109:2100-8.
- Changchien CS, Chen CL, Yen YH, Wang JH, Hu TH, Lee CM, et al. Analysis of 6381 hepatocellular carcinoma patients in southern taiwan: Prognostic features, treatment outcome, and survival. *J Gastroenterol.* 2008;43:159-70.
- Chen CH, Su WW, Yang SS, Chang TT, Cheng KS, Lin HHH, et al. Long-term trends and geographic variations in the survival of patients with hepatocellular carcinoma: Analysis of 11 312 patients in taiwan. *J Gastroenterol Hepatol.* 2006;21:1561-6.
- Chen JG, Li WG, Shen ZC, Yao HY, Zhang BC, Zhu YR. Population-based cancer survival in qidong, people's republic of china. *IARC Sci Publ.* 1998;145:27-35.
- Chen JG, Zhu J, Zhang YH, Lu JH. Cancer survival in qidong, china, 1992-2000. *IARC Sci Publ.* 2011;162:43-53.
- Chen JG, Chen HZ, Zhu J, Yang YL, Zhang YH, Huang PX, et al. Cancer survival in patients from a hospital-based cancer registry, china. *J Cancer.* 2018;9:851-60.
- Chen PH, Lin YC, Tu HP, Chiang SL, Ko AM, Hsu CL, et al. Important prognostic factors for the long-term survival of subjects with primary liver cancer in taiwan: A hyperendemic area. *Eur J Cancer.* 2007;43:1076-84.
- Chen W, Armstrong BK, Rahman B, Zheng R, Zhang S, Clements M. Relationship between cancer survival and ambient ultraviolet b irradiance in china. *Cancer Causes Control.* 2013;24:1323-30.
- Chia KS. Cancer survival in Singapore, 1993-1997. *IARC Sci Publ.* 2011;162:183-98.
- Chia KS, Du WB, Sankaranarayanan R, Sankila R, Seow A, Lee HP. Population-based cancer survival in singapore, 1968 to 1992: An overview. *Int J Cancer.* 2001;93:142-7.
- Chiang CJ, Lo WC, Yang YW, You SL, Chen CJ, Lai MS. Incidence and survival of adult cancer patients in taiwan, 2002-2012. *J Formosan Med Assoc.* 2016;115:1076-88.
- Chien LH, Tseng TJ, Tsai FY, Wang JH, Hsiung CA, Liu TW, et al. Patterns of age-specific socioeconomic inequalities in net survival for common cancers in taiwan, a country with universal health coverage. *Cancer Epidemiol.* 2018;53:42-8.
- Dimitroulis D, Damaskos C, Valsami S, Davakis S, Garmpis N, Spartalis E, et al. From diagnosis to treatment of hepatocellular carcinoma: An epidemic problem for both developed and developing world. *World J Gastroenterol.* 2017;23:5282-94.
-

- El-Serag HB, Davila JA. Surveillance for hepatocellular carcinoma: In whom and how? *Therap Adv Gastroenterol.* 2011;4:5-10.
- Esteban D, Ngelangel C, Lacaya L, Robles E, Monson M. Cancer survival in rizal, philippines. *IARC Sci Publ.* 1998;145:101-8.
- Fakhar N, Nikeghbalian S, Kazemi K, Shamsayefar AR, Gholami S, Kasraianfard A, et al. Transplantation of deceased donor livers with elevated levels of serum transaminases at shiraz transplant center. *Hepat Mon.* 2016;16(10):e40140.
- Fan CJ, Jin GX, Sun C, Ma DL, Chen CY, Qiao PF, et al. Clinical characteristics, treatment patterns and survival outcome of hepatocellular carcinoma patients aged 70 years or older: A single-center retrospective study from china. *Aging Clin Exp Res.* 2014;26:123-30.
- Fernandez E, La Vecchia C, D'Avanzo B, Negri E, Franceschi S. Family history and the risk of liver, gallbladder, and pancreatic cancer. *Cancer Epidemiol Biomarkers Prev.* 1994;3:209-12.
- Gao J, Xie L, Yang WS, Zhang W, Gao S, Wang J, et al. Risk factors of hepatocellular carcinoma--current status and perspectives. *Asian Pac J Cancer Prev.* 2012;13:743-52.
- Georgiades CS, Liapi E, Frangakis C, Park JU, Kim HW, Hong K, et al. Prognostic accuracy of 12 liver staging systems in patients with unresectable hepatocellular carcinoma treated with transarterial chemoembolization. *J Vasc Interv Radiol.* 2006;17:1619-24.
- Ghoncheh M, Salehiniya H. Inequality in the incidence and mortality of all cancers in the world. *Iran J Public Health.* 2016;45:1675-7.
- Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: A systematic analysis for the global burden of disease study. *JAMA Oncol.* 2017;3:524-8.
- Han X, Huang CX, Zhang HW, Qiao P, Xie M, Zhang R, et al. [The occurrence and survival condition of primary liver cancer among residents in yangpu district of shanghai between year 2002 and 2010]. *Zhonghua Yu Fang Yi Xue Za Zhi.* 2012;46:119-24.
- Hashim D, Boffetta P, La Vecchia C, Rota M, Bertuccio P, Malvezzi M, et al. The global decrease in cancer mortality: Trends and disparities. *Ann Oncol.* 2016;27:926-33.
- Hassanipour S, Mohammadzadeh M, Mansour-Ghanaei F, Fathalipour M, Joukar F, Salehiniya H, et al. The incidence of hepatocellular carcinoma in iran from 1996 to 2016: A systematic review and meta-analysis. *J Gastrointest Cancer.* 2019;50:193-200.
- Human Development Indices and Indicators, 2018. http://hdr.undp.org/sites/default/files/2018_human_development_statistical_update.pdf
- Ito Y, Nakayama T, Miyashiro I, Ioka A, Tsukuma H. Conditional survival for longer-term survivors from 2000-2004 using population-based cancer registry data in osaka, Japan. *BMC Cancer.* 2013;13:304.
- Ito Y, Nakaya T, Nakayama T, Miyashiro I, Ioka A, Tsukuma H, et al. Socioeconomic inequalities in cancer survival: A population-based study of adult patients diagnosed in Osaka, Japan, during the period 1993-2004. *Acta Oncol.* 2014;53:1423-33.
- Jakupi X, Lunar MM, Mlakar J, Matković I, Tavakoli NP, Ivanovska BZ, et al. Hcv infection among injecting drug users in Prishtina, Kosovo. *Hepat Mon.* 2018;18.
- Jarnagin WR, Schwartz LH, Gultekin DH, Gönen M, Haviland D, Shia J, et al. Regional chemotherapy for unresectable primary liver cancer: Results of a phase ii clinical trial and assessment of dce-mri as a biomarker of survival. *Ann Oncol.* 2009;20:1589-95.
- Jayalekshmi P, Gangadharan P, Sebastian P. Cancer survival in Karunagappally, India, 1991-1997. *IARC Sci Publ.* 2011;162:125-32.
- Jayant K, Nene BM, Dinshaw KA, Badwe RA, Panse NS, Thorat RV. Cancer survival in Barshi, India, 1993-2000. *IARC Sci Publ.* 2011;162:101-6.
- Jeong SO, Kim EB, Jeong SW, Jang JY, Lee SH, Kim SG, et al. Predictive factors for complete response and recurrence after transarterial chemoembolization in hepatocellular carcinoma. *Gut Liver* 2017;11:409-16.
- Jin F, Xiang YB, Gao YT. Cancer survival in Shanghai, People's Republic of China. *IARC Sci Publ.* 1998;145:37-50.
- Joukar F, Mansour-Ghanaei F, Naghipour MR, Hassanipour S. Knowledge, distribution and risk factors of hepatitis b and c infection in high-risk groups in Guilan province, Iran. *Hepat Mon.* 2018;18.
- Jun CH, Sim DW, Kim SH, Hong HJ, Chung MW, Myoung E, et al. Predictive factors for recurrence and survival in hepatocellular carcinoma in South Korea. *Anticancer Res.* 2013;33:4129-34.

- Jung K-W, Yim S-H, Kong H-J, Hwang S-Y, Won Y-J, Lee J-K, et al. Cancer survival in Korea 1993-2002: A population-based study. *J Korean Med Sci.* 2007;22:S5-S10.
- Jung KW, Park S, Kong HJ, Won YJ, Lee JY, Park EC, et al. Cancer statistics in Korea: Incidence, mortality, survival, and prevalence in 2008. *Cancer Res Treat.* 2011;43:1-11.
- Jung KW, Park S, Kong HJ, Won YJ, Lee JY, Seo HG, et al. Cancer statistics in Korea: Incidence, mortality, survival, and prevalence in 2009. *Cancer Res Treat.* 2012;44:11-24.
- Jung KW, Won YJ, Kong HJ, Oh CM, Seo HG, Lee JS. Cancer statistics in Korea: Incidence, mortality, survival and prevalence in 2010. *Cancer Res Treat.* 2013;45:1-14.
- Jung K, Won Y, Kong H, Oh C, Lee DH, Lee JS. Cancer statistics in Korea: Incidence, mortality, survival and prevalence in 2011. *Cancer Res Treat.* 2014;46:109-23.
- Jung KW, Won YJ, Kong HJ, Oh CM, Cho H, Lee DH, et al. Cancer statistics in Korea: Incidence, mortality, survival, and prevalence in 2012. *Cancer Res Treat.* 2015;47:127-41.
- Jung KW, Won YJ, Oh CM, Kong HJ, Lee DH, Lee KH, et al. Cancer statistics in Korea: Incidence, mortality, survival, and prevalence in 2014. *Cancer Res Treat.* 2017;49:292-305.
- Jung KW, Won YJ, Kong HJ, Lee ES, Kim CH, Yoo CI, et al. Cancer statistics in Korea: Incidence, mortality, survival, and prevalence in 2015. *Cancer Res Treat.* 2018;50:303-16.
- Kerkar SP, Kemp CD, Avital I. Liver resections in metastatic gastric cancer. *HPB (Oxford)* 2010;12:589-96.
- Kew MC. Hepatocellular carcinoma: Epidemiology and risk factors. *J Hepatocell Carcinoma.* 2014;1:115-25.
- Korean Liver Cancer Study Group (KLCSG), National Cancer Center Korea (NCC). 2014 Korean Liver Cancer Study Group, National Cancer Center Korea practice guideline for the management of hepatocellular carcinoma. *Korean J Radiol.* 2015;16:465-522.
- Kröner PT, Mankal PK, Dalpathi V, Shroff K, Abed J, Kotler DP. Alcohol-attributable fraction in liver disease: Does gdp per capita matter? *Ann Global Health.* 2015;81:711-7.
- Kudo M, Izumi N, Kokudo N, Sakamoto M, Matsuyama Y, Ichida T, et al. Improved survival in patients with hepatocellular carcinoma over 30 years in Japan: Analysis of nationwide prospective registry of 148,161 patients. *J Clin Oncol.* 2011;29.
- Kudo M, Izumi N, Sakamoto M, Matsuyama Y, Ichida T, Nakashima O, et al. Survival analysis over 28 years of 173,378 patients with hepatocellular carcinoma in Japan. *Liver Cancer.* 2016;5:190-7.
- La Vecchia C, Lucchini F, Franceschi S, Negri E, Levi F. Trends in mortality from primary liver cancer in Europe. *Eur J Cancer.* 2000;36:909-15.
- Ladep NG, Lesi OA, Mark P, Lemoine M, Onyekwere C, Afihene M, et al. Problem of hepatocellular carcinoma in West Africa. *World J Hepatol.* 2014;6:783-92.
- Laudico AV, Mirasol-Lumague MR, Mapua CA, Uy GB, Toral JAB, Medina VM, et al. Cancer incidence and survival in Metro Manila and Rizal province, Philippines. *Jpn J Clin Oncol.* 2010;40:603-12.
- Law SC, Mang OW. Cancer survival in Hong Kong SAR, China, 1996-2001. *IARC Sci Publ.* 2011;162:33-41.
- Lee CL, Ko YC, Choong CS. Survival rate for liver cancer in Taiwan. *Chin Med J (Taipei).* 2000;63:16-20.
- Lepage C, Capocaccia R, Hackl M, Lemmens V, Molina E, Pierannunzio D, et al. Survival in patients with primary liver cancer, gallbladder and extrahepatic biliary tract cancer and pancreatic cancer in Europe 1999-2007: Results of Eurocare-5. *Eur J Cancer* 2015;51:2169-78.
- Li Y, Yu L, Na J, Li S, Liu L, Mu H, et al. Survival of cancer patients in Northeast China: Analysis of sampled cancers from population-based cancer registries. *Cancer Res Treat.* 2017;49:1106-13.
- Li-Hsin C, Tseng T-J, Fang-Yu T, Wang J-H, Hsiung CA, Tsang-Wu L, et al. Patterns of age-specific socioeconomic inequalities in net survival for common cancers in Taiwan, a country with universal health coverage. *Cancer Epidemiol.* 2018;53:42-8.
- Lim GH, Wong CS, Chow KY, Bhalla V, Chia KS. Trends in long-term cancer survival in Singapore: 1968-2002. *Ann Acad Med Singapore.* 2009;38:99-105.
- Liu Q, Bi JJ, Tian YT, Feng Q, Zheng ZX, Wang Z. Outcome after simultaneous resection of gastric primary tumour and synchronous liver metastases: Survival analysis of a single-center experience in China. *Asian Pac J Cancer Prev.* 2015;16:1665-9.

- Llovet JM, Schwartz M, Mazzaferro V. Resection and liver transplantation for hepatocellular carcinoma. *Semin Liver Dis.* 2005;25:181-200.
- Mansour-Ghanaei F, Fallah M-S, Jafarshad R, Joukar F, Salari A, Tavafzadeh R. Prevalence of hepatitis b surface antigen and hepatitis c virus antibody and their risk factors among Gilan's volunteer blood donors (1998-2003). *Hepat Mon* 2007;7:239-41.
- Maringe C, Li R, Mangtani P, Coleman MP, Rachet B. Cancer survival differences between South Asians and non-South Asians of England in 1986-2004, accounting for age at diagnosis and deprivation. *Brit J Cancer.* 2015;113:173-81.
- Martin N, Srisukho S, Kunpradist O, Suttajit M. Cancer survival in Chiang Mai, Thailand. *IARC Sci Publ.* 1998;145:109-121.
- Martin N, Pongnikorn S, Patel N, Daoprasert K. Cancer survival in Lampang, Thailand, 1990-2000. *IARC Sci Publ.* 2011;162:217-26.
- Matsuda T, Ajiki W, Marugame T, Ioka A, Tsukuma H, Sobue T, et al. Population-based survival of cancer patients diagnosed between 1993 and 1999 in Japan: A chronological and international comparative study. *Jpn J Clin Oncol.* 2011;41:40-51.
- McGlynn KA, London WT. The global epidemiology of hepatocellular carcinoma: Present and future. *Clin Liver Dis.* 2011;15:223-43, vii-x.
- McGlynn KA, Petrick JL, London WT. Global epidemiology of hepatocellular carcinoma: An emphasis on demographic and regional variability. *Clin Liver Dis.* 2015;19:223-38.
- Mirzaei M, Ghoncheh M, Pournamdar Z, Soheilipour F, Salehiniya H. Incidence and trend of liver cancer in Iran. *J Coll Physicians Surg Pak.* 2016;26:306-9.
- Moayedi J, Moini M, Geramizadeh B, Malekhosseini SA, Yaghobi R. Seropositive form of occult hepatitis b virus infection in Iranian patients with cryptogenic liver cirrhosis. *Hepat Mon.* 2019;19.
- Mohammadian M, Soroush A, Mohammadian-Hafshejani A, Towhidi F, Hadadian F, Salehiniya H. Incidence and mortality of liver cancer and their relationship with development in Asia. *Asian Pac J Cancer Prev.* 2016;17:2041-7.
- Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4:1.
- Nakagawa-Senda H, Yamaguchi M, Matsuda T, Koide K, Kondo Y, Tanaka H, et al. Cancer prevalence in Aichi, Japan for 2012: Estimates based on incidence and survival data from population-based cancer registry. *Asian Pac J Cancer Prev.* 2017;18:2151-6.
- Naugler WE, Sakurai T, Kim S, Maeda S, Kim K, Elsharkawy AM, et al. Gender disparity in liver cancer due to sex differences in myd88-dependent il-6 production. *Science.* 2007;317:121-4.
- Nikbakht HA, Sahraian S, Ghaem H, Javadi A, Janfada M, Hassanipour S, et al. Trends in mortality rates for gastrointestinal cancers in Fars Province, Iran (2005–2015). *J Gastrointest Cancer.* 2019; epub ahead of print.
- Nordenstedt H, White DL, El-Serag HB. The changing pattern of epidemiology in hepatocellular carcinoma. *Dig Liver Dis.* 2010;42(Suppl 3):S206-14.
- Norsa'adah B, Nurhazalini-Zayani CGC. Epidemiology and survival of hepatocellular carcinoma in North-East Peninsular Malaysia. *Asian Pac J Cancer Prev.* 2013;14:6955-9.
- Oh CM, Won YJ, Jung KW, Kong HJ, Cho H, Lee JK, et al. Cancer statistics in Korea: Incidence, mortality, survival, and prevalence in 2013. *Cancer Res Treat.* 2016;48:436-50.
- Omata M, Lesmana LA, Tateishi R, Chen PJ, Lin SM, Yoshida H, et al. Asian pacific association for the study of the liver consensus recommendations on hepatocellular carcinoma. *Hepatol Int.* 2010;4:439-74.
- Penson DF, Krishnaswami S, Jules A, Seroogy JC, McPheeters ML. Evaluation and treatment of cryptorchidism. Rockville, MD: Agency for Healthcare Research and Quality (US), 2012. (Report No.: 13-EHC001-EF.2012).
- Pinheiro PS, Morris CR, Liu L, Bungum TJ, Altekruse SF. The impact of follow-up type and missed deaths on population-based cancer survival studies for hispanics and asians. *J Natl Cancer Inst Monogr.* 2014;49:210-7.
- Pons F, Varela M, Llovet JM. Staging systems in hepatocellular carcinoma. *HPB (Oxford).* 2005;7:35-41.
- Redaniel MT, Laudico A, Mirasol-Lumague MR, Gondos A, Pulte D, Mapua C, et al. Cancer survival discrepancies in developed and developing countries: Comparisons between the Philippines and the United States. *Brit J Cancer* 2009;100:858-62.
- Redaniel MT, Laudico A, Mirasol-Lumague MR, Gondos A, Brenner H. Cancer survival differences between European countries and an urban population from the Philippines. *Eur J Public Health.* 2011;21:221-8.

- Sankaranarayanan R. Cancer survival in Africa, Asia, the Caribbean and Central America. Introduction. IARC Sci Publ. 2011;162:1-5.
- Sato Y, Arimoto H, Ishikawa KB, Yoshimura K, Kaneko S, Koshiji M, et al. Survival trends of patients treated at the national cancer center hospital, Japan, from 1962 to 1994. Jpn J Clin Oncol. 2002;32:181-6.
- Schwarz RE, Smith DD. Trends in local therapy for hepatocellular carcinoma and survival outcomes in the US population. Am J Surg. 2008;195:829-36.
- Shu H, Kang X, Guo K, Li S, Li M, Sun L, et al. Diagnostic value of serum haptoglobin protein as hepatocellular carcinoma candidate marker complementary to alpha fetoprotein. Oncol Rep. 2010;24:1271-6.
- Somboon K, Siramolpiwat S, Vilaichone RK. Epidemiology and survival of hepatocellular carcinoma in the central region of Thailand. Asian Pac J Cancer Prev. 2014;15:3567-70.
- Sriamporn S, Black RJ, Sankaranarayanan R, Kamsaad S, Parkin DM, Vatanasapt V. Cancer survival in Khon Kaen Province, Thailand. Int J Cancer. 1995;61:296-300.
- Sriplung H, Prechavittayakul P. Cancer survival in Songkhla, Thailand, 1990-1999. IARC Sci Publ. 2011;162:227-35.
- Sumitsawan Y, Srisukho S, Sastraruji A, Chaisaengkhum U, Maneesai P, Waisri N. Cancer survival in Chiang Mai, Thailand, 1993-1997. IARC Sci Publ. 2011;162:199-209.
- Takano S, Watanabe Y, Ohishi H, Kono S, Nakamura M, Kubota N, et al. Multimodality treatment for patients with hepatocellular carcinoma: A single institution retrospective series. Eur J Surg Oncol. 2000;26:67-72.
- Takayasu K, Furukawa H, Wakao F, Muramatsu Y, Abe H, Terauchi T, et al. CT diagnosis of early hepatocellular carcinoma: Sensitivity, findings, and CT-pathologic correlation. AJR Am J Roentgenol 1995;164:885-90.
- Tanaka H, Tanaka M, Chen WQ, Park S, Jung KW, Chiang CJ, et al. Proposal for a cooperative study on population-based cancer survival in selected registries in East Asia. Asian Pac J Cancer Prev. 2009;10:1191-8.
- Tangkijvanich P, Mahachai V, Suwangool P, Poovorawan Y. Gender difference in clinicopathologic features and survival of patients with hepatocellular carcinoma. World J Gastroenterol. 2004;10:1547-50.
- Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends - an update. Cancer Epidemiol Biomarkers Prev. 2016;25:16-27.
- Toyoda H, Kumada T, Kiriyama S, Sone Y, Tanikawa M, Hisanaga Y, et al. Changes in the characteristics and survival rate of hepatocellular carcinoma from 1976 to 2000 - analysis of 1365 patients in a single institution in Japan. Cancer. 2004;100:2415-2421.
- Tsukuma H, Ajiki W, Ioka A, Oshima A, Research Group of Population-Based Cancer Registries of Japan. Survival of cancer patients diagnosed between 1993 and 1996: A collaborative study of population-based cancer registries in Japan. Jpn J Clin Oncol. 2006;36:602-7.
- Turati F, Edefonti V, Talamini R, Ferraroni M, Malvezzi M, Bravi F, et al. Family history of liver cancer and hepatocellular carcinoma. Hepatology. 2012;55:1416-25.
- Wang JH, Changchien CS, Hu TH, Lee CM, Kee KM, Lin CY, et al. The efficacy of treatment schedules according to Barcelona clinic liver cancer staging for hepatocellular carcinoma - survival analysis of 3892 patients. Eur J Cancer. 2008;44:1000-6.
- Williams DR, Mohammed SA, Leavell J, Collins C. Race, socioeconomic status, and health: Complexities, ongoing challenges, and research opportunities. Ann NY Acad Sci. 2010;1186:69-101.
- Wong RJ, Corley DA. Survival differences by race/ethnicity and treatment for localized hepatocellular carcinoma within the United States. Dig Dis Sci. 2009;54:2031-9.
- Wu EM, Wong LL, Hernandez BY, Ji J-F, Jia W, Kwee SA, et al. Gender differences in hepatocellular cancer: Disparities in nonalcoholic fatty liver disease/steatohepatitis and liver transplantation. Hepatoma Res. 2018;4:66.
- Xiang YB, Jin F, Gao YT. Cancer survival in Shanghai, China, 1992-1995. IARC Sci Publ. 2011;162:55-68.
- Xiao L, Zhang RL, Zhang H, TulaHong A, Zhang YF, Wen H, et al. Comparison of the clinical characteristics and survival between Uyghur patients with hepatitis virus-related and non-b, non-c hepatocellular carcinoma in Xinjiang, China. Chin J Cancer Res. 2015;27:279-87.
- Xishan H, Chen K, Min H, Shufen D, Jifang W. Cancer survival in Tianjin, China, 1991-1999. IARC Sci Publ. 2011;162:69-84.

- Xue TC, Xie XY, Zhang L, Yin X, Zhang BH, Ren ZG. Transarterial chemoembolization for hepatocellular carcinoma with portal vein tumor thrombus: A meta-analysis. *BMC Gastroenterol.* 2013;13:60.
- Yaghi C, Sharara AI, Rassam P, Moucari R, Honein K, BouJaoude J, et al. Hepatocellular carcinoma in Lebanon: Etiology and prognostic factors associated with short-term survival. *World J Gastroenterol.* 2006;12:3575-80.
- Yeo Y, Gwack J, Kang S, Koo B, Jung SJ, Dhamala P, et al. Viral hepatitis and liver cancer in Korea: An epidemiological perspective. *Asian Pac J Cancer Prev.* 2013;14:6227-31.
- Yuen MF, Cheng CC, Lauder IJ, Lam SK, Ooi CG, Lai CL. Early detection of hepatocellular carcinoma increases the chance of treatment: Hong Kong experience. *Hepatology.* 2000;31:330-5.
- Yusuf MA, Badar F, Meerza F, Khokhar RA, Ali FA, Sarwar S, et al. Survival from hepatocellular carcinoma at a cancer hospital in Pakistan. *Asian Pac J Cancer Prev.* 2007;8:272-4.
- Zamor PJ, deLemos AS, Russo MW. Viral hepatitis and hepatocellular carcinoma: Etiology and management. *J Gastrointest Oncol.* 2017;8:229-42.
- Zamora-Valdes D, Taner T, Nagorney DM. Surgical treatment of hepatocellular carcinoma. *Cancer Control.* 2017;24:1073274817729258.
- Zeng HM, Zheng RS, Guo YM, Zhang SW, Zou XN, Wang N, et al. Cancer survival in China, 2003-2005: A population-based study. *Int J Cancer.* 2015;136:1921-30.
- Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol.* 2004;130:417-22.
- Zhang Y, Li Y, Cai J. Surgical management of patients with BCLC b hepatocellular carcinoma and survival analysis - a single center experience in China. *Eur J Cancer.* 2015;51:S425.
- Zhao Y, Zhan X, Zhang Y. Outcomes of non-alcoholic steatohepatitis patients after liver transplantation: A systematic review and meta-analysis. *Hepat Mon.* 2019;19.
- Zheng R, Zuo T, Zeng H, Zhang S, Chen W. Mortality and survival analysis of liver cancer in China. *Zhonghua zhong liu za zhi [Chinese journal of oncology].* 2015;37:697-702.
- Zheng R, Qu C, Zhang S, Zeng H, Sun K, Gu X, et al. Liver cancer incidence and mortality in China: Temporal trends and projections to 2030. *Chin J Cancer Res.* 2018;30:571-9.
- Zhou XD, Tang ZY, Yang BH, Zhang BH. Hepatocellular carcinoma: The role of screening. *Asian Pac J Cancer Prev.* 2000;1:121-6.
- Zhu Q, Li N, Zeng X, Han Q, Li F, Yang C, et al. Hepatocellular carcinoma in a large medical center of China over a 10-year period: Evolving therapeutic option and improving survival. *Oncotarget.* 2015;6:4440-50.
- Zhu RX, Seto W-K, Lai C-L, Yuen M-F. Epidemiology of hepatocellular carcinoma in the Asia-Pacific region. *Gut Liver.* 2016;10:332-9.