

Determining the Survival Rate of Stomach Cancer in Iran: A Systematic Review and Meta-Analysis

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Abstract: Stomach cancer the commonest malignancy and the third major cause of mortality from cancer all over the world. Different studies in Iran indicated different survival rates and there is not general estimation. The present study was carried out in order to determine the 1-5 year survival rate of stomach cancer in Iran through a metaanalytical study. By searching the national and international online databases and taking into account the inclusion and exclusion criteria of the study, articles that possessed inclusion criteria were selected. After the required data were extracted, they were analyzed using Stat 11.0 Software and the survival rate was determined. The present systematic study included 19 articles and survival rate was investigated among 23,589 patients with stomach cancer. The rate of 1-5 year survival of stomach cancer was respectively, 64.7, 40.6, 31.4, 23.5 and 20.3%. According to the results of the present study, the lowest survival rate was related to 5 year survival and the highest to 1 year survival among patients with stomach cancer. The survival rate of patients with stomach cancer in Iran is very low and the most important factors in the survival are the disease stage and the patients age. Therefore, it is necessary to figure out interventional measures in order to diagnose the disease in early stages and provide more efficient treatments.

Key words: Stomach cancer, survival rate, metaanalysis, order, Iran

INTRODUCTION

Despite, significant advances in medical sciences, cancer are discussed as one of the most important diseases, now and are the second cause of death after cardiovascular disease (Farzianpour *et al.*, 2014). Stomach cancer is one of the commonest forms of cancer all over the world (Malekzadeh *et al.*, 2009). Over 70% of new cases of mortality caused by stomach cancer occurs in developing countries (Jemal *et al.*, 2011). Stomach cancer is defined as the uncontrolled growth of malignant cells in the stomach which has no symptoms until the progression stage of the disease (Ali *et al.*, 2014). After correct diagnosis and quick treatment of patients with stomach cancer, one of the most important goals is to enhance survival rate. Unfortunately in Iran, over 80% of the patients with stomach cancer are diagnosed in the progression stage of the disease in which most treatment methods do not lead to a remarkable effect on the patient's survival (Malekzadeh *et al.*, 2009). According to international estimations, >930,000 new cases of stomach cancer are diagnosed every year and approximately 700,000 patients die from this disease per year (Jemal *et al.*, 2008). According to the global statistics,

989,600 new cases of stomach cancer were diagnosed, about 738,000 people died of this type of cancer in 2008 and approximately 10% of all deaths in the world are related to this type of cancer (Jemal *et al.*, 2011). As opposed to Japan, West European countries and North America in Iran stomach cancer has taken an increasing trend since, 30 years ago (Sadjadi *et al.*, 2003; Babaei *et al.*, 2005; Yazdizadeh *et al.*, 2005). The >70% of new cases of mortality from stomach cancer occur in developing countries (Jemal *et al.*, 2011). Development of stomach cancer and survival vary all over the world (Kelley and Duggan, 2003; Biglarian *et al.*, 2009) such that 5 year survival rate in European countries is higher than American countries (23% in Europe and 20% in America) (Coleman *et al.*, 2003). In general, 5 year survival in European countries is between 10 and 30% (Coleman *et al.*, 2003) while it is 15-28% in the United States. Survival range in developing countries varies between 7 and 17%. In their study in Iran, Movahedi *et al.* (2009) reported 1 year survival as 47.6, 2 year survival 27.2, 3 year survival 19.3, 4 year survival 15.7 and 5 year survival 12.8. In their study of patients with stomach cancer in Fars Province Cancer Registry Center, Moghimi Dehbokri *et al* reported 1-5 year survival as 54, 30, 24, 18

and 16, respectively (Moghimi-Dehkordi *et al.*, 2008). In a study conducted in Slovenia. Oblak reported the total survival as 73% (Oblak *et al.*, 2007). The study conducted by Marely indicated that 5 year survival in Korea and Philippine are respectively 37 and 12% (Crew and Neugut, 2006).

Studies conducted in Iran have reported that stomach cancer is more prevalent among men than women and the relative survival is higher among women. Many factors such as inappropriate nutrition, consumption of fruits and vegetables, low socioeconomic status and variables like disease stage, patient's age, presence of metastasis, type of surgery, diagnosis age and gender can affect the disease (Sadjadi *et al.*, 2003; Ding *et al.*, 2004; Schwarz and Zagala-Nevarez, 2002; Biglarian *et al.*, 2009; Zeraati *et al.*, 2005a, 2006). Treatment of stomach cancer is normally carried out through surgery, radiotherapy and chemotherapy. Surgery is the early treatment of stomach cancer followed by radiotherapy as the best treatment and finally chemotherapy is employed as the extended treatment if needed (Ali *et al.*, 2014). In developing medical services, determining the survival rate of the patients is one of the methods that help medical practitioners with the administration of programs related to cancer and evaluation of new medical methods (Gordis, 2000).

Studies on the analysis of survival of stomach cancer should be figured out because up-to-date information on the effective factors in cancer survival is an important factor for doctors, enologists and epidemiologists. There are numerous studies on stomach cancer and the survival of the patients but they have reported different survival rates and there is no uniformity among their results. Metaanalysis is one of the most important approaches to come up with uniform results (Moosazadeh, 2013; Moosazadeh *et al.*, 2013), the present study employed a metaanalytical method in order to estimate the survival rate of stomach cancer.

MATERIALS AND METHODS

Search strategy: To find electronically published articles over March 1993 to July 2015 in the present study, national databases like SID, Magiran and Irandoc and international ones such as PubMed, Google Scholar, Scopus and Science Direct were visited and keywords like Iran, survival rate, gastric cancer and stomach cancer were utilized. The search carried out between June 22 and July 27. The TO make sure about receiving all articles, following studies were also taken into account.

Choosing the articles: After the articles were retrieved, repetitive and irrelevant ones were crossed out based on

their title, abstract and full text format. Moreover, in order to prevent bias caused by republishing (transverse and longitudinal publication bias), the results of the studies published in 2 journals were utilized and one of them was crossed out.

Quality evaluation: In order to evaluate the quality of the selected articles an inventory that was used in previous studies was employed (Moosazadeh *et al.*, 2014). This inventory was developed by examining STROB (Von Elm *et al.*, 2007) statement and composed of 12 questions that cover different aspects of methodology including determination of proper sample size, the type of the study, sampling method, study population, data collection method, definition of the variables, the method of examining the samples, data collection instruments, statistical tests, study objectives, presentation of the findings in an appropriate form and presentation of the results according to the study objectives. Each question was given one score and any study that received a minimum of 12 scores (Moosazadeh *et al.*, 2014) "was included for metaanalysis.

Inclusion criteria: All of the English and Persian articles that had determined 1-5 year survival rates and gained the required score during quality evaluation were chosen.

Exclusion criteria: Studied that had not determined the survival rate, abstracts whose full text format was not provided, articles whose sample size was not specified, articles that did not obtain the minimum evaluation score and those that were case report, experimental-control group type and interventional were crossed out.

Data extraction: The data of each article were extracted based on the study title, the first author, the study year, the study location, sample size, 1-5 year survival rates, the significance level of the relationship between stomach cancer survival rate and the variables of cellular differentiation degree, radiotherapy, tumor size, BMI, chemotherapy, age, gender, disease stage, reoccurrence and metastasis, treatment type and tumor location. Moreover, two of the researchers registered the collected data into excel.

Analysis: Stata Software was utilized to analyze the collected data. The standard error for each study was calculated based on binominal distribution formula. Finally, heterogeneity index among the studies was determined using Cochran (Q) and I^2 . According to the heterogeneity, random or constant effect model was employed to measure survival rate of stomach cancer in Iran.

RESULTS

The initial search in national and international databases led to finding 1211 articles which became 548 ones after the search strategy was changed and the repetitive cases were crossed out due to the overlap of the databases. By screening the titles and the abstracts, 389 irrelevant cases were spotted. The rest of the articles were examined in full text form which resulted in crossing out 125 irrelevant ones. Moreover, two articles were added by examining the references. Afterwards, by evaluating the quality of the articles and based on the inclusion and exclusion criteria, 13 articles were crossed out and 19 were included for metaanalysis (Table 1).

In the present study, the survival of 23,589 cases of stomach cancer was investigated. In studies where the number of the samples had been determined based on gender, there were 1860 women and 4577 men. The mean age of the patients ranged 59 years in the study conducted by Roshanaei *et al.* (2010) with a study sample of 262 patients to 64.7 years in the study carried out by Movahedi *et al.* (2009) with a sample size of 19578. The publication year of the studies range from 2005-2015. In is noteworthy that Movahedi's study with sample size of 19578 individuals, the survival rate of all of the patients over 2001-2005 was determined. In order to avoid transverse bias, 5 articles (Ghori *et al.*, 2014) that completely coincided Movahedi's study in terms of publication time were crossed out.

The 1 year survival rate in the whole population ranged from 25% in the study carried out by Gadimi *et al.* (2010) with a sample size of 110 patients to 8% in the study conducted by Roshanaei *et al.* (2010) with a sample size of 262 patients. The 2 year survival rate

in the whole population varied from 17% in the study administered by Veisani *et al.* (2013) with a sample size of 239 patients to 53.1% in the study done by Biglarian *et al.* (2011) with a sample size of 436 patients. The 3 year survival ranged from 17.9% in the study carried out by Barfei *et al.* (2014) with a sample size of 78 individuals to 53% in the investigation carried out by Larizadeh (2013) with a sample size of 82 patients. The 4 year survival rate varied from 10% in Veisani (2013)'s study with a sample size of 239 patients to 35% in the study administered by Noorkojuri *et al.* (2013) with a sample size of 216 individuals. And, the 5 year survival rate ranged from 5.4% in the study conducted by Veisani *et al.* (2013) with a sample size of 239 patients to 36% in the study carried out by Javadi *et al.* (2015) with a sample size of 67 individuals. The average survival rate ranged from 26.16 months in the study carried out by Baeradeh *et al.* (2015) with a sample size of 136 individuals to 55.9 months with a standard deviation of 5.4 in the study conducted by Roshanaei *et al.* (2010) with a samples size of 262. The median survival rate varied from 8.6 months in the study of Gadimi *et al.* (2010) with a sample size of 110 people to 37 months in the study carried out by Larizadeh (2013) with a sample size of 82 patients (Table 1).

According to random effects model, 1-5 year survival rates of stomach cancer in Iran are respectively 64.7, 40.6, 31.4, 23.5 and 20.3% (Table 2 and Fig. 1-4). Variables of patients mean age and publication year were examined as factors suspected of heterogeneity using meta-regression which had no remarkable effect ($p>0.05$).

Cellular differentiation degree: Asignificant relationship between survival rate in patients with stomach cancer and the cellular differentiation degree was reported in 2 articles (Barfei *et al.*, 2014; Javadi *et al.*, 2015).

Table 1: Distribution of characteristics of primary studies included to meta-analysis

id	First author	Publication year	Sample size			Rate survival (year)							
			Total	Female	Male	One	Two	Three	Four	Five	Average	Median	
1	Barfei <i>et al</i>	2014	78	22	56	59.0	30.8	17.9					14.1
2	Javadi <i>et al</i>	2015	67	19	48	67.0		40.0		36.0	39.90		26.1
3	Larizadeh <i>et al</i>	2013	82	29	53			53.0		22.0			37.1
4	Veisani <i>et al</i>	2013	239	61	178	41.0	17.0	13.0	10.0	5.4			
5	Roshanae <i>et al</i>	2010	262	65	197	85.0		41.0		30.0	55.90		32.1
6	Roshanae <i>et al</i>	2012	400	97	303	74.0		31.0		23.0	41.00		26.1
7	Noorkojur <i>et al</i>	2013	216	60	156	80.0	56.0	40.0	35.0	30.0	46.00		30.1
8	Baeradeh <i>et al</i>	2015	136	45	91	61.3		31.2		24.5	26.16		19.1
9	Baghestani	2010	178			79.0	51.8	34.6					25.3
10	Maroufizadeh <i>et al</i>	2012	213	59	154	79.0		35.0		14.0	31.20		29.6
11	Yazdani <i>et al</i>	2011	190	60	129	60.3							
12	Ghadimi <i>et al</i>	2010	110	27	83	25.0		18.0		17.0			8.6
13	Akhavan <i>et al</i>	2011	47	15	32		50.0	30.0	27.0		29.90		
14	Atoof <i>et al</i>	2011	330	102	228			32.0		24.0			19.9
15	Zeraati <i>et al</i>	2005	330	102	228	66.7				23.6			
16	Khedmat <i>et al</i>	2011	367							14.0			
17	Biglarian <i>et al</i>	2011	436	121	315	77.9	53.1	40.8	32.0	17.4			
18	Ali <i>et al</i>	2014	330			66.0		31.0		21.0			16.33
19	Movahedi <i>et al</i>	2009	19578			47.6	27.2	19.3	15.7	12.8			

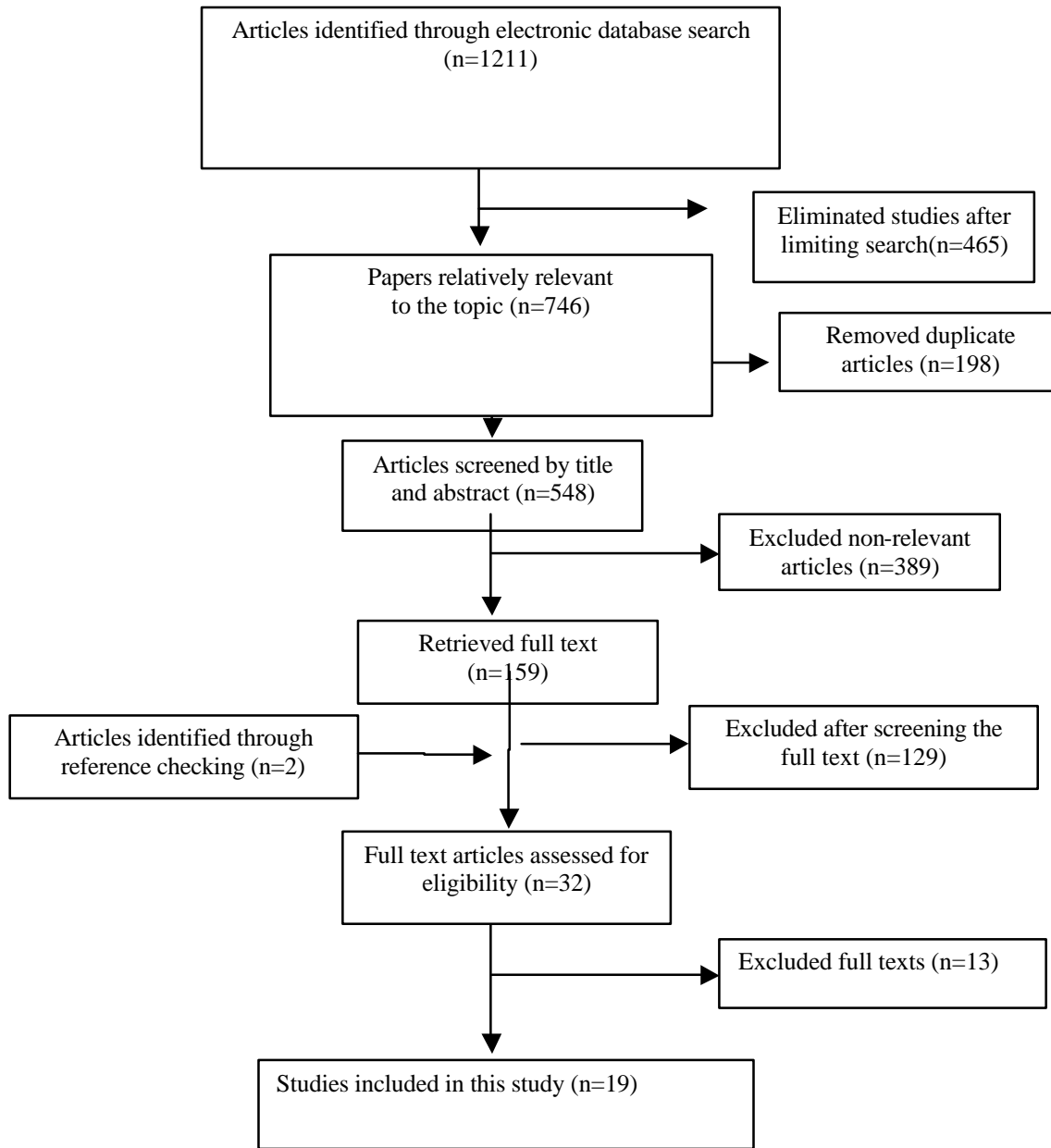


Fig. 1: Literature search and review flowchart for selection of primary studies

Table 2: Pooled estimate of survival rate of stomach cancer in Iran based on random effect model

Variables	Survival percent	Heterogeneity		
		Q	p	I-squared (%)
1 year survival	64.7 (55.2-74.2)	1057.4	<0.001	98.7
2 year survival	40.6 (28.9-52.2)	255.6	<0.001	97.7
3 year survival	31.4 (25.9-36.9)	332.5	<0.001	95.5
4 year survival	23.5 (14.9-31.9)	99.3	<0.001	96.0
5 year survival	20.3 (16.7-23.8)	204.1	<0.001	93.1

Radiotherapy: A significant relationship between survival rate and radio therapy in patients with stomach cancer was reported in 1 article (Barfei *et al.*, 2014).

Tumor size: A significant relationship between survival rate and tumor size was reported in 4 articles (Baghestani *et al.*, 2010; Maroufizadeh *et al.*, 2012; Noorkojuri *et al.*, 2013; Roshanaei *et al.*, 2012).

BMI: A significant relationship between survival rate and BMI was reported in an article (Barfei *et al.*, 2014).

Chemotherapy: A significant relationship between survival rate and chemotherapy was reported in two articles (Barfei *et al.*, 2014; Javadi *et al.*, 2015).

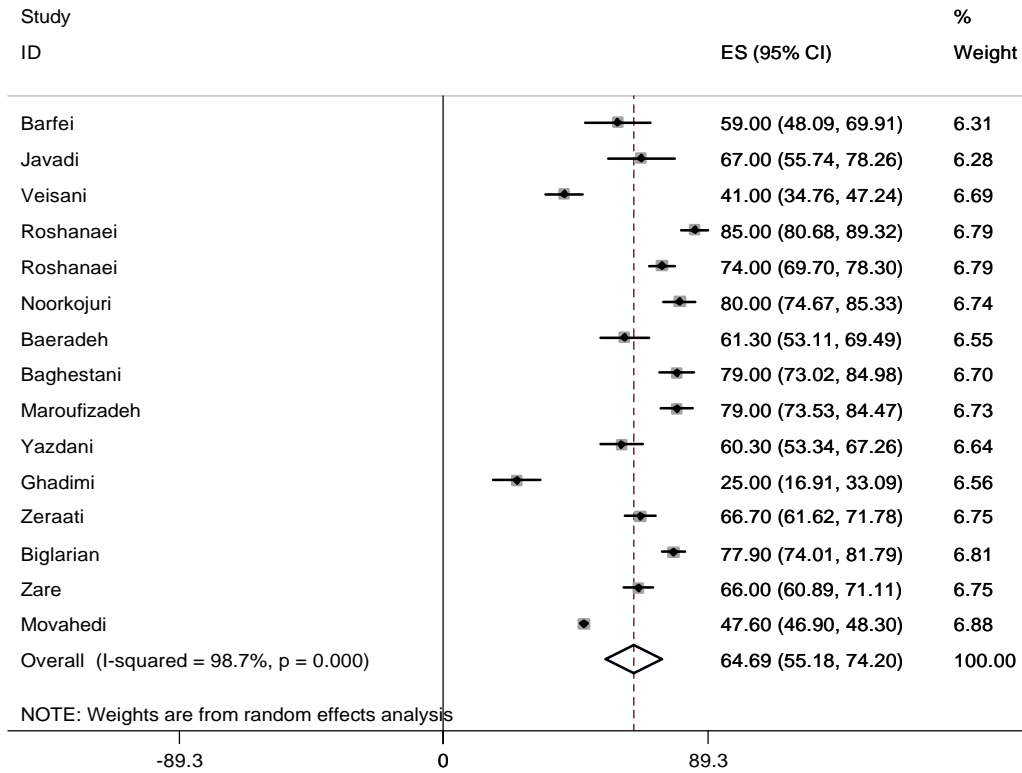


Fig. 2: Percent of 1 year survival of stomach cancer per primary studies and pooled estimate in Iran

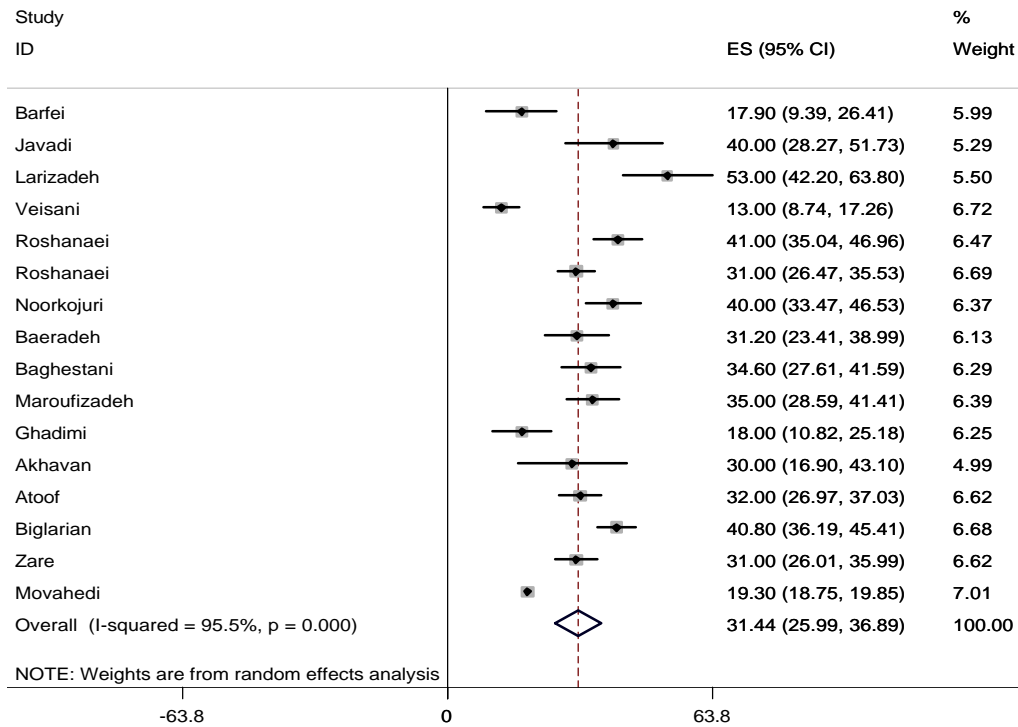


Fig. 3: Percent of 3 year survival of stomach cancer per primary studies and pooled estimate in Iran

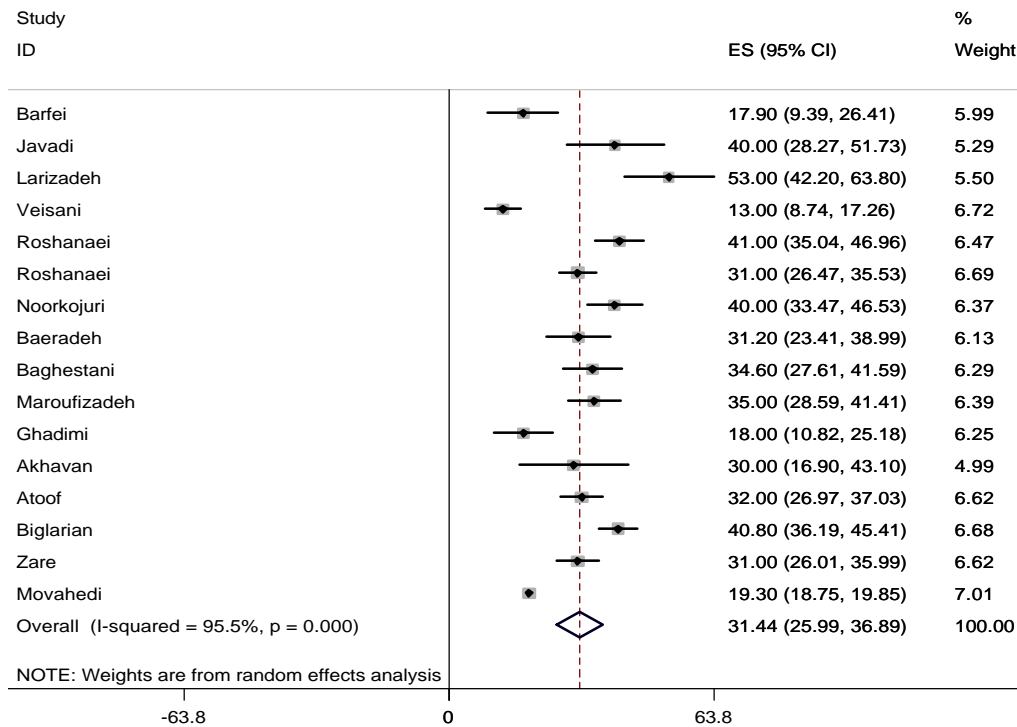


Fig. 4: Percent of 5 year survival of stomach cancer per primary studies and pooled estimate in Iran

Disease stage: A significant relationship between survival rate and disease stage was reported in 9 articles (Javadi *et al.*, 2015; Larizadeh, 2013; Veisani *et al.*, 2013; Roshanaei *et al.*, 2010; Zeraati *et al.*, 2005b; Ali *et al.*, 2014; Akhavan *et al.*, 2011; Roshanaei *et al.*, 2012; Yazdani *et al.*, 2011) such that the higher the stage of the disease, the lower the survival rate will be.

Treatment type: A significant relationship between survival rate and treatment type was reported in two articles (Larizadeh, 2013; Akhavan *et al.*, 2011).

Tumor location: A significant relationship between survival rate and tumor location was reported in an article (Larizadeh, 2013).

Age: A significant relationship between survival rate and age was reported in 12 articles (Javadi *et al.*, 2015; Larizadeh, 2013; Roshanaei *et al.*, 2010, 2012; Noorkojuri *et al.*, 2013; Maroufizadeh *et al.*, 2012; Baghestani *et al.*, 2009; Ali *et al.*, 2014; Yazdani *et al.*, 2011; Roshanaei *et al.*, 2012; Movahedi *et al.*, 2009; Ghadimi *et al.*, 2010) in a way that the patients' lifelong drops with an increase in age.

Gender: A significant relationship between gender and age was reported in 3 articles (Larizadeh, 2013; Roshanaei *et al.*, 2010, 2012).

DISCUSSION

Stomach cancer is the commonest cancer in Iran. The results of the meta-analytical present study reported 1-5 year survival rates as 64.7, 40.6, 31.4, 23.5 and 20.3%, respectively. The 5 year survival rate was reported to be 29.6% in China, 4.4% in Thailand, 22% in Swiss and 30% in France (Ding *et al.*, 2004; Triboulet *et al.*, 2001). The results of a study conducted by Atoof *et al.* (2011) reported that 5 year survival rate was higher in Iran compared to countries like Chile and Brazil (Heise *et al.*, 2009; Bustamante-Teixeira *et al.*, 2006) and lower than countries like America, France, China and Swiss (Ding *et al.*, 2004; Adachi *et al.*, 2003; Schwarz and Zagala-Nevarez, 2002; Wang *et al.*, 2002; Triboulet *et al.*, 2011).

Survival rate of patients with stomach cancer is lower in Iran than other parts of the world (Zeraati *et al.*, 2006). The most important factors affecting survival rate are disease stage and age. Examining the studies indicated

that disease stage variable affects survival of the patients. The higher the stage of the disease, the lower the survival rate will be. Staging of stomach tumors according to TNM system includes the level of tumor extension inward stomach lining (T), the number of lymph nodes involved (N) and presence of absence of distant metastasis (M). Most scholars believe that at least 15 lymph nodes should be removed through surgery and examined by pathologists so that staging can be more precise (Devita *et al.*, 2008). During surgery, if a sufficient number of lymph nodes are not removed or examined by a pathologist, staging will be flawed and survival rate will dropped (Akhavan *et al.*, 2011) as believed by some scholars like Japanese.

The results of the study carried out by Roshanaei (2010) indicated that there is no significant relationship between survival rate and the degree of tumor differentiation which can be attributed to the diagnosis in high stages of the disease. They also showed that diagnosis in stages 3 and 4 increases death risk 3-4 times among these patients. Based on this issue, an important factor that affects the patients survival rate more than other factors (Roshanaei *et al.*, 2010). The results of the study conducted by Veisani *et al.* (2013) also indicated that diagnosis at early stage of tumor is the only variable that has a significant relationship with survival rate. Verdecchia *et al.* (2003) compared survival rate in four different regions including Brazil, North America, Italy and Japan. The results of that study survival rate of stomach cancer can differ according to different social and economic conditions, quality and circumstances of life and food habits. Survival rate was higher in Italy and the United States. In examining the determination variables in disease stage, one factor was reported to be effective on survival rate.

The results of the study conducted by Akhavan *et al.* (2011) indicate that the higher the stage of the disease, the lower the survival rate will be and the highest survival rates are related to patients who have received a combination of surgery, chemotherapy and radiotherapy. Although, surgery is the main treatment of stomach cancer, there is disagreement over the surgery extension and the number of lymph nodes to be removed whether it is better for the patient to receive chemotherapy before surgery or not and chemotherapy continues after surgery or whether the patients should go under surgery followed by chemotherapy and radiotherapy. Unfortunately, treatments like gastrostomy, chemotherapy or radiotherapy cannot be useful in over 80% of the patients with stomach cancer (Samadi *et al.*, 2007; Sadighi *et al.*, 2005). Therefore, after surgery, 5 year survival rate in patients with stomach cancer is low. Macdonald *et al.* (2001) carried out a study in order to investigate the effect of chemo-radiotherapy. In so doing,

the patients were divided into two groups; one group just received surgery and the other one received chemo-radiotherapy after surgery. The 3 year survival rate of those patients who had received chemo-radiotherapy was 50% while it was 41% in the other group. In a study conducted in Singapore, the patients received radiotherapy after surgery and their 3 year survival rate was 60.6% (Leong *et al.*, 2008). Barfei *et al.* (2014) stated that patients who had received chemotherapy after surgery had a higher survival rate compared to other patients. In fact, complementary chemotherapy is considered as an effective treatment after surgery (Noorkojuri *et al.*, 2013). Sun *et al.* (2010) indicated the effect of radiotherapy on stomach cancer patients with metastasis.

CONCLUSION

The results of the study conducted by Atoo *et al.* (2011) indicated that an increase in age led to a reduction in recovery and the recovery of patients of over 70 years was 86% lower than those who were under 60 years. The results of studies carried out in the United States and Italy showed that an increase in age and disease stage led to a reduction in survival rate (Atoo *et al.*, 2011; Buonadonna *et al.*, 2003).

The variable of presence of metastasis can also affect the survival rate of patients with stomach cancer (Atoo *et al.*, 2011; Javadi *et al.*, 2015). The study carried out by Baghestani *et al.* (2010) also indicated that metastasis and tumor size are important factors that affect stomach cancer. Maroufizadeh *et al.* (2012) reported that survival time of disease was significantly related with tumor size in a way that patients with tumor size of 35 mm had significantly shorter lifetime compared to those whose tumor size was under 35 mm.

According to low survival rate among patients with stomach cancer in Iran, the disease needs to be diagnosed in early stages using screening methods in order to enhance recovery and survival rate among the patients. If stomach cancer is diagnosed at an early stage, extensive surgery that is associated with numerous complications will be prevented, especially among old individuals; therefore, their survival rate will rise. Mass screening for stomach cancer is not recommended; however, endoscopic screening can be utilized in order to specify vulnerable and risky groups with high prevalence and survival rate can be enhanced by timely employing interventional measures.

ACKNOWLEDGEMENTS

Researchers would like to acknowledge Mazandaran University of Medical Sciences for financially supporting

this study. Meanwhile, the present study is a systematic review and meta-analysis that was estimated the pooled rate of survival stomach cancer. Therefore, informed consent is not necessary.

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