

RESEARCH ARTICLE

Cancer Incidence in Southwest of Iran: First Report from Khuzestan Population-Based Cancer Registry, 2002-2009

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Abstract

Background: Cancer incidence rates are increasing particularly in developing countries. It is crucial for policy makers to know basic cancer epidemiology in each region to design comprehensive prevention plans. There have hitherto been no population-based data available for cancer in Khuzestan province. The present report is a first from the regional population-based cancer registry for the period of 2002-2009. **Materials and Methods:** Data were collected retrospectively reviewing all new cancer patients whom were registered in Khuzestan province cancer registry during an 8-year period (2002-2009). All cases were coded based on the ICD-O-3 coding system and collected data were computerized using SPSS (Chicago, IL) software, version 11.5. The age standardized incidence rates (ASRs) per 100,000 person-year for all cancers were computed using the indirect method of standardization to the world population. **Results:** During the 8-year study period, 16,801 new cancer cases were registered. Based on the computed ASRs, the five most frequent malignancies in females were breast (26.4 per 100,000), skin (13.6), colorectal (5.72), stomach (4.31) and bladder (4.07) and in males, the five most frequent were skin (16.0 per 100,000), bladder (10.7), prostate (7.64), stomach (7.17), and colorectal (6.32). The ASR for all malignancies in women was 92.5 per 100,000, and that for men was 87.4. **Conclusions:** The observed patterns from the analysis of Khuzestan cancer registry data will lead to better understanding of the epidemiology of various malignancies in this part of the country and consequently provide a useful guide for authorities to make efficacious decisions and policies about a cancer control program for south-west Iran.

Keywords: Cancer - incidence - population-based registration - Khuzestan - Iran

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Introduction

The geographic differences in the incidence of certain cancers have been previously reported. The mostly asked question is whether these differences are associated with any clear-cut ethnic, environmental or genetic factors. Hence it is of great importance to illuminate the epidemiology of neoplastic disease in different regions (Boffetta and Parkin, 1994; Masoompour et al., 2011).

There may be substantial discrepancies between developed and developing countries, considering the epidemiology of neoplastic disease. On the other hand the current rapid modernization and industrialization in developing countries, by altering the environment and people life style, may change the epidemiologic patterns of various cancers in these regions (Sobin, 1969).

It seems necessary for each region to illuminate the epidemiological status of neoplastic disease in its own population. Therefore, the present study aimed at

providing the incidence rates (crude and age-standardized) of different types of cancers in Khuzestan province, located in south-west Iran, and to compare these rates with that of other cancer registries throughout the country and the world. To the best of our knowledge, this is the first population-based research assessing the incidence of different cancers in Khuzestan province.

Materials and Methods

Geography

Khuzestan province, located in south-west Iran, has an area of about 64,057 Km² (3.88% of the total land area of Iran, which is about 1,648,195 Km²) and is at 29 deg 58 min to 32 deg 58 min latitude north and 47 deg 42 min to 50 deg 39 min longitude east. Its average elevation from sea level is about 73.82 feet. The climate is hot and humid, generally mild and pleasant winter, and a lot of sunshine throughout the year.

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Population

According to the 2006 census, the total population of Khuzestan province was about 4,531,720 (65% urban vs 35% rural). The male/female ratio was 2,286,209: 2,245,511 and means age 29.86 yrs. The capital city, Ahvaz, has a population of 1,395,184 with a male/female ratio of 701,943: 693,241. The racial structure of the Khuzestan population is heterogeneous, but consists of mainly Caucasians (66.4%) and Arabs (33.6%).

Data collection and analysis

Data were collected retrospectively reviewing all new cancer patients whom were registered in Khuzestan province cancer registry during an 8-year period (2002-2009). The registry has used the ICD-O coding system. All cases have been coded based on the ICD-O-3 coding system (Fritz et al., 2000). All cases were checked for duplications Considering reported last name, first name, age, father's name, topography of tumor, place of residence and date of diagnosis. Data for nonresident patients, residing in neighboring provinces, who sought medical care in Khuzestan province, were excluded from our analysis. The collected data were computerized using SPSS (Chicago, IL) software, version 11.5.

The age standardized incidence rate (ASRs) per 100,000 persons- years for all cancers were computed, using the indirect method of standardization to the world population.

Results

During the 8 year period (2002-2009), 16801 new cancer cases were registered in Khuzestan province. Men accounted for 51.4% of the cases, and women for 48.6%. Mean age (\pm SD) at the time of first diagnosis was 52.91 \pm 20.95 years (55.55 \pm 20.46 for men and 50.12 \pm 21.10 for women). Table 1 illustrates the principle cancer sites, total number of cancer cases, relative frequencies, crude rates and ASRs for both men and women. Based on calculated ASRs, the 6 most frequent cancers in women were breast (26.36 per 100,000), skin (13.63 per 100,000), colon and rectum (5.72 per 100,000), stomach (4.31 per 100,000), bladder (4.07 per 100,000), and lung (2.86 per 100,000); and the 6 most frequent cancer types in men were skin (15.99 per 100,000), bladder (10.69 per 100,000), prostate gland (7.64 per 100,000), stomach (7.17 per 100,000), colon and rectum (6.32 per 100,000), and lung (5.85 per 100,000). The ASR for all cancers in women was 92.50 per 100,000 and that for the men were 87.38 per 100,000 (Table 2).

Discussion

Despite being difficult and fraught with substantial error, epidemiologic studies of cancer in developing countries illuminates certain important geographic differences that couldn't be ignored as Clemensen stated

Table 1. Total Frequency, Percent and Age-Standardized Rates per 100,000 Person-Years(ASR)

Site	Men				Women			
	Total	%	Crude rate	ASR	Total	%	Crude rate	ASR
Bladder	983	11	6.78	10.69	272	3	1.98	4.07
Bone	93	1	0.64	0.63	64	0.8	0.46	0.51
Breast	100	1	0.69	1.02	2529	31	18.36	26.36
Cervix	-	-	-	-	230	3	1.67	2.56
Colon & Rectum	627	7	4.32	6.32	475	6	3.45	5.72
Esophagus	231	3	1.59	2.53	201	2	1.46	2.82
Gallbladder	57	0.7	0.39	0.63	72	0.9	0.52	1.06
Kidney	219	3	1.51	2.26	135	2	0.98	1.41
Larynx	190	2	1.31	2.13	34	0.4	0.24	0.44
Leukemia- Lymphoid	367	4	2.53	2.88	197	2	1.43	1.68
Leukemia- Myeloid	208	2	1.43	1.62	158	2	1.15	1.34
Liver	7	0.08	0.05	0.07	5	0.06	0.04	0.05
Lung	533	6	3.67	5.85	210	3	1.52	2.86
Lymphoma- Hodgkin	123	1	0.85	0.89	88	1	0.64	0.7
Lymphoma- Non-Hodgkin	128	1	0.88	1.08	77	1	0.56	0.74
Multiple Myeloma	140	2	0.97	1.49	84	1	0.61	1.11
Nervous system	251	3	1.73	2.07	175	2	1.27	1.49
Oral cavity	3	0.03	0.02	0.02	3	0.04	0.02	0.02
Ovary	-	-	-	-	241	3	1.75	2.5
Pancreas	41	0.5	0.28	0.44	34	0.4	0.25	0.44
Pharynx	101	1	0.31	0.92	45	0.6	0.33	0.53
Prostate gland	674	8	4.65	7.64	-	-	-	-
Skin	1501	17	10.35	15.99	1007	12	7.31	13.63
Small bowel	28	0.3	0.19	0.26	27	0.3	0.2	0.29
Stomach	667	8	4.6	7.17	322	4	2.34	4.31
Testis	149	2	1.03	1.11	-	-	-	-
Thyroid gland	98	1	0.68	0.9	307	4	2.23	2.84
Uterus	-	-	-	-	234	3	1.7	2.75
Other	1127	13	7.77	10.76	929	11	6.75	10.25
All Sites	8646		59.61	87.38	8155		59.22	92.5

Table 2. Age-Standardized Rates for the 10 Most Frequent Cancers in Khuzestan Province, Iran Compared to Previous Data for Fars Province, Golestan Study, and Globocan 2002 and 2008 Data

Site	Men					Site	Women				
	Khuzestan (present study)	Fars	Golestan	GLOBOCAN 2002	GLOBOCAN 2008		Khuzestan (present study)	Fars	Golestan	GLOBOCAN 2002	GLOBOCAN 2008
Bladder	10.7	6.8	8.7	8	11.2	Bladder	4.1	1.9	-	-	-
Colorectal	6.3	3.4	12.4	8.3	8.7	Colorectal	5.7	2.6	9.5	6.5	6.4
Esophagus	2.5	2	24.3	-	-	Esophagus	2.8	1.4	19.1	-	-
Lung	5.9	6.3	15.4	7.2	9.1	Lung	2.9	2.9	5.9	2.2	3.5
Leukemia	4.5	5.5	10.5	4.8	7.7	Leukemia	3.0	4.4	7.4	3.3	4
Skin	16.0	4.1	12.6	-	-	Skin	13.6	2.7	8.2	-	-
Stomach	7.2	9.2	30.7	26.1	21.9	Stomach	4.3	4.4	12.4	11.1	9
Kidney	2.3	1.3	-	-	-	Breast	26.4	13.0	26.9	17.1	18.4
Larynx	2.1	1	-	-	-	Thyroid	2.8	2.2	-	2.4	2.3
Prostate	7.6	3.5	10.1	5.4	11.6	Uterus	2.8	2.7	-	0.9	1.7
All Sites	87.4	64.5	175.3	116.8	126.1	All Sites	92.5	55.5	141.1	93.1	87.5

that "It is easily appreciated that causal factors in cancer will be regarded as geographical insofar as they are of unknown nature" (Clemmensen, 1967). The cancer registry in Khuzestan province has originated since 2000. The registry has recorded cancer cases that were confirmed histopathologically by pathology department or referred to radiotherapy department for treatment. The Khuzestan cancer registry has published cancer-associated data principally considering overall frequencies and has not provided age-standardized incidence rate. Age-standardized rates (ASRs) for cancer were computed based on cancer frequency data from the Khuzestan cancer registry (2002-2009). Unfortunately due to lack of previous similar studies with calculated ASRs for cancer in our province, it is impossible to compare our data with previous figures and describe the trends of cancer incidence rate in the south-west of the country.

Considering the 10 most frequent cancers in Khuzestan province, there are substantial differences between the results of our study, the Fars study, the Golestan study and the cancer incidence for Iran estimated by GLOBOCAN study (2002 and 2008) (Parkin et al., 2005; Masoompour et al., 2011; Roshandel et al., 2012). The GLOBOCAN study made use of a large amount of data derived from cancer registries from different national populations or subsamples from selected zones (Masoompour et al., 2011). Hence, the difference between our incidence rates and those from the GLOBOCAN studies are maybe due to the fact that the mentioned studies made its estimates according to a hypothetical incidence for all cancer types calculated from other registries in Iran, and the relative frequencies of malignancies reported from other high-incidence regions of Iran. Reports from Golestan province indicate that the overall cancer incidence and especially the incidence of upper gastrointestinal malignant neoplasms were higher than we found for Khuzestan province (Roshandel et al., 2012). These discrepancies could be explained by considering geographic and ethnic factors, as Golestan province are located in the north of Iran, which makes part of the well-known Asian cancer belt (Masoompour et al., 2011; Roshandel et al., 2012). Incidence rates for cancers in different anatomical regions from present study with the rates from Golestan, Fars and the other part of the worlds are compared and discussed

in the following paragraphs.

It seems there is no gender predominance in esophageal malignancies incidence rate (ASR 2.53 per 100,000 in male and ASR 2.82 per 100,000 in female). The Golestan study reported higher rates of esophageal cancer both in women and men (Roshandel et al., 2012). Differences in dietary habits may have contributed to differences between provinces ASRs (Islami et al., 2009; Mosavi-Jarrahi and Mohagheghi, 2006) as in Golestan province, it is popular to drink very hot beverages and eat spicy foods, that it is different from dietary habits in Khuzestan province.

Gastric cancer was the fourth common cancer in both men and women but it occurred more frequently in men (ASR 7.17 per 100,000 vs ASR 4.31 per 100,000), this malignancy was the most common cancer in male and the second one in female in Fars study however the reported incidence in the study is similar to some extent to ours (Table 2) the reported ASR for gastric cancer in Golestan study is dramatically higher than Khuzestan and Fars study (Masoompour et al., 2011; Roshandel et al., 2012). The role of *H. pylori* infection, gastro-esophageal reflux disease and dietary factors have been documented as risk factors for gastric malignancy (Tsugane, 2005; Babaei et al., 2010). The much lower incidence of gastric cancer malignancy in southern regions of the country (like Khuzestan and Fars) compared with Golestan, a northern province, maybe partly attributed to the lower prevalence of *H. pylori* infection in south of Iran (Japoni et al., 2010).

The higher incidence of colorectal malignancies is associated with economic development (Wang et al., 2012). It may be due to changing in lifestyle and eating habits, as a result, toward sedentary lifestyles and consuming less dietary fiber and more animal fat, adaptation of western type lifestyle, that have been shown could explain the increased incidence of colorectal cancer (Boffetta and Parkin, 1994; Roshandel et al., 2012). The ASRs for colorectal cancer in Khuzestan, Fars and Golestan are much less than of USA (34.1 and 25.0 per 100,000 for men and women respectively) confirming the mentioned idea that "the higher incidence of colorectal cancer is associated with economic development" (Masoompour et al., 2011; Roshandel et al., 2012; Wang et al., 2012).

The present data showed a substantial difference in

incidence of liver cancer between our region and other parts of the country. Sadjadi et al. study's reported ASR (in Ardabil 1996-1999) for liver cancer was about 23-46 times greater than ours (1.6 vs 0.07 in male and 2.3 vs 0.05 in women) (Sadjadi et al., 2003). reported ASR for liver cancer by Mohagheghi et al. study (1998-2001 in Tehran) and Masoompour (1998-2002 in Fars Province) study were dramatically greater than ours (Masoompour et al., 2011; Mohagheghi et al., 2009). The GLOBOCAN's estimated ASRs for liver cancer were substantially greater than that of us as well (Ferlay et al., 2010). The observed discrepancies could be explained by considering some facts; firstly it is possible that some metastatic liver cancers were misclassified as primary liver cancer in the process of cancer registration (Sen et al., 2002). Second, it was shown that the predominant cause of HCC, in southern Iran, is hepatitis B and C (Hajiani et al., 2005). On the other hand HBV prevalence has decreased substantially in Iranian population during the last decade as a result of national vaccination program from 1993. So the substantial decrease in HBV prevalence, the predominant cause of HCC in our region, may lead to observed lower incidence of HCC in our study. According to the American Cancer Society estimates (in 2007), the 3 most prevalent cancers in developing countries, in male gender, are lung, stomach, and liver cancers (Bener, Ayub, Kakil, and Ibrahim, 2008). But it seems the national vaccination program in our country has changed the estimated trend to the degree that there is no place for liver malignancy considering the five most frequent cancers in recently performed researches like Khuzestan, Golestan and Kohaladoodan et al. studies (Radmard, 2010; Roshandel et al., 2012).

According to the American Cancer Society estimates (2010), lung cancer is the second most common cancer in both genders (Jemal et al., 2010). However this pattern is not true for all countries and also for all races living in the USA as lung cancer is the third and fourth frequent malignancies in Hispanic men and women respectively (Siegel et al., 2012). In our study, lung cancer takes the respective sixth and seventh place in men and women with male and predominance (male/female ratio 2:1). The ASRs for lung cancer reported by Masoompour et al. and Sadjadi et al. studies were similar to ours (Sadjadi et al., 2003; Masoompour et al., 2011) However calculated ASRs for lung cancer in Golestan study is dramatically different from that of our and Fars studies (Roshandel et al., 2012). This discrepancy may be due to potential differences in smoking patterns and also probable variations in DNA repair capacity between different races as it was shown that lower lung cancer susceptibility among Hispanic Americans may be due to DNA repair gene variants (Chang et al., 2008; 2009).

Skin cancer, the most frequent cancer in our men and the second one in women has dramatically higher incidence rate in our region than some other parts of the country (Like Golestan, Fars, Tehran, Ardabil with respective ASRs as follow: 12.6 in male and 8.2 in female, 4.1 in male and 2.7 in female, 11.3 in men and 6.7 in female, 9.6 in males and 9.6 in female) (Sadjadi et al., 2003; Mohagheghi et al., 2009; Masoompour et al., 2011; Roshandel et al., 2012). This dramatic difference could be explained by the

fact that Khuzestan province location may be associated with higher ultraviolet radiation (UVR) exposure, the main known risk factor for skin cancer, than mentioned provinces. It should be emphasized that skin cancer is the most commonly diagnosed cancer in men living in the south-west Iran and it is in contrast with estimates made by GLOBOCAN study suggesting stomach cancer as a leading malignancy in Iranian men (Ferlay et al., 2010).

Breast cancer, the most common cancer in women in Khuzestan province, accounted for 31% of all malignancies in the female population. According to GLOBOCAN study (2008), breast cancer incidence rates range from 19.3 per 100,000 women (in underdeveloped region) to 89.9 (or maybe greater) per 100,000 women in developed countries (except Japan) (Ferlay et al., 2010). It seems the burden of breast cancer differs substantially based on differences in culture and consequently differences in reproductive patterns. For instance, ASRs for breast cancer in Hispanics are 30% to 40% lower than those in non-Hispanic whites mainly due to their reproductive characteristics including: younger age at first birth and higher parity (Siegel et al., 2012). Our calculated ASRs and that of Golestan study for breast cancer are worryingly higher than estimated rates by GLOBOCAN study (Table 2) (Ferlay et al., 2010; Roshandel et al., 2012). These findings together with a recent report concerning about an unusual peak of breast cancer in young women in northern-east of Iran may necessitate a revision of the age of starting screening programs in some parts of the country (Taheri et al., 2012).

The major etiology of cervical malignancy is chronic infection with human papillomavirus (HPV) (especially type 18 and 16) (Siegel et al., 2012). It was reported that the prevalence of HPV infection among southern Iranian females was lower than that observed worldwide. On the other hand, existence of cultural and religious factors like fewer number of polygamous relationships and higher rate of circumcision among men would lead to lower ASRs for cervix cancer in our setting than those reported by other parts of the world (9.6 and 5.7 per 100,000 in China and USA respectively) (Haghighi et al., 1971; Masoompour et al., 2011; Wang et al., 2012).

Bladder malignancy, the second and fifth most common cancer in men and women respectively, accounted for 11% of all cancers in men and 3% in women. There was a male to female predominance, considering ASRs, that was observed by other studies (Akbari et al., 2008; Ploeg et al., 2009; Chu et al., 2013). It was reported that bladder cancer was the 7th and the 17th most common cancer worldwide in men and women respectively (Burger et al., 2012). However in our region it is more frequent in both genders (the second and the fifth most common cancer in men and women respectively) (Table 2). Considering the incidence of lung malignancy in each region as a major indicator of smoking, suggested as the most common risk factor for bladder cancer, and knowing the fact that there is low incidence rate for lung cancer in Khuzestan province one might postulate that other important risk factors (e.g. occupational exposure to aromatic amines and polycyclic aromatic hydrocarbons) may be accounted for high incidence rate of bladder cancer in our region (Masoompour et al., 2011; Burger et al., 2012). The other factor that strengthens the mentioned hypothesis

is the fact that Khuzestan is an industrial province and consequently higher occupational exposure to potential carcinogenic agents could be expected. Hence bladder cancer might be job dependent in our province. Similar pattern was reported by an Isfahan study (other industrial province) (Mokarian et al., 2011).

Prostate cancer, the third most frequent cancer in men in Khuzestan province, accounted for 8% of all cancers in the male population in our region. But, it has been the most common cancer in American males since 1975 (Jemal et al., 2010) with an ASR of 85.6 in North America (Center et al., 2012). In the Sadjadi et al. study the total calculated ASR (based on collected data from 5 provinces from 1996 to 2000) was 5.1 per 100,000 persons (Sadjadi et al., 2007). Our calculated ASR for prostate cancer together with that of Golestan study are in line with GLOBOCAN estimated range (ASR between 5.4-11.4) but higher than those were reported by studies which were performed during early years of the last decade like Sadjadi et al. and Fars studies (Saalabian, 1989; Sadjadi et al., 2007; Ferlay et al., 2010; Masoompour et al., 2011; Roshandel et al., 2012). There was a steep rise in estimated ASRs for prostate cancer from 5.4 (in 2002) to 11.6 (in 2008) according to GLOBOCAN study (2002 and 2008) and a similar trend is observed when a comparison is made between recently performed studies and those that were performed in the past (Saalabian, 1989; Sadjadi et al., 2007; Ferlay et al., 2010; Masoompour et al., 2011; Roshandel et al., 2012). According to the existing evidence, the greatest contributor to the differences in prostate cancer incidence rates worldwide would be most likely international variation in diagnostic practices and screening programs (Center et al., 2012). PSA testing, which was introduced between the 1980 and 1990, has been proven to increase prostate cancer detection dramatically. Considering the ASRs for prostate cancer in America from 1975 till now, a steep increase in incidence rates could be recognized between 1980 to 1995 that was simultaneous with generalizing the use of PSA-based screening in the country (Jemal et al., 2010; Center et al., 2012). It seems similar pattern has been started in Iran and therefore by generalizing the prostate screening program throughout the country the incidence rate will increase in the future. It should be reminded that differences in PSA testing could not completely explain the international variations in prostate cancer incidence rates as about fifty-fold difference in ASRs worldwide was observed before introduction of this test (Center et al., 2012). Hence, some other factors like westernization of diet, sedentary lifestyle and greater levels of obesity may also account for the wide variations in prostate cancer incidence rate (Sadjadi et al., 2007; Center et al., 2012).

According to our results, lymphoma was not among the top ten cancers diagnosed in both men and women in Khuzestan province. ASRs of lymphomas were 1.97 per 100,000 and 1.44 per 100,000 in males and females respectively. Hence the reported male predominance by other studies was not observed in our population (Roshandel et al., 2011). The calculated ASRs for lymphoma were similar, to some extent, to those of Fars study (Masoompour et al., 2011) but dramatically lower than those of Golestan studies (1.97 vs 7.6 in male, 1.4 vs.

4.7 in female) (Roshandel et al., 2012) and (1.97 vs 8.4 in male, 1.4 vs 4.2 in female) (Roshandel et al., 2011). The basis of this disparity is thought to lie in differences in non-Hodgkin lymphoma incidence rates as the calculated ASRs for Hodgkin type in our population are similar to that of Golestan studies (Roshandel et al., 2011; 2012). Beside the probable variations in quality of medical reports and registration system in each cancer registry center and genetic susceptibility to a specific type of cancer among each population, some unknown environmental factors might account for the observed disparity. There are some evidence that supports the protective role of sun exposure and vitamin-D against the development of non-Hodgkin lymphoma (Armstrong and Krickler, 2007; Petridou et al., 2007). It seems high amount of sun exposure among our population, due to our province location, might account for low incidence of NHL in our region.

Leukemia, the most common blood malignancy in both genders in our population, has ASRs of 4.5 and 3.02 in men and women respectively. The reported ASRs for leukemia by Fars studies and several eastern Asian countries (e.g. China, Japan and Korea) are similar to ours but those of Golestan study, western European countries (France, Germany and UK), Canada and USA were dramatically higher than that of ours (Masoompour et al., 2011; Park et al., 2012; Roshandel et al., 2012; Saalabian, 1989). Knowing the fact that there are various risk factors involved in etiology of leukemia, it is difficult to identify the reasons for the observed substantial differences in incidence rate of leukemia worldwide. But one of the major contributors to the mentioned disparity might be occupational exposure as the National Institute for Occupational Safety and Health of the United States estimated that up to 40% of all cancers were as a result of occupational exposures (Mosavi-Jarrahi et al., 2009).

Being retrospective was one of the limitations of the present study. The other one was the low quality of medical record kept in public hospitals and medical centers. Despite mentioned and other possible limitations (that may potentially exist in cancer registry data base (Izquierdo and Schoenbach, 2000)), we did our best to avoid any systemic errors in our analysis. To the best of our knowledge it was the first population-based cancer registry research assessing the incidence rate of different cancers in Khuzestan province. The patterns observed from the analysis of Khuzestan cancer registry data provide comprehensive and valuable information on cancer incidence and will lead to better understanding of the epidemiology of various malignancies in our province and consequently provide a useful guide for authorities to make efficacious decisions about cancer control program and policies in south-west of Iran.

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