Age and gender related differences in renal tumors in southern Iran; a cross-sectional study

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Introduction
Renal cell carcinoma (RCC) accounts for the ninth most common cancer in men and the 14th most common cancer in women (1). RCC incidence has increased recently due to improvements in screening and registration programs (2). Some of risk factors for RCC include male gender, older ages, hypertension, diabetes, urinary tract infections, exposure to smoking, asbestos, radiation, and obesity (3). Currently, nephrectomy (partial or radical) is the only definitive strategy for treating RCC. Pathological stage, perinephric fat stranding, involvement of regional lymph nodes and distant metastasis are effective and important factors in determining the survival rate of patients (4).

Objectives
Considering the importance of prognostic factors in patient survival and the need to recognize the relationship between effective factors and pathological characteristics of the tumor, this study was performed to investigate renal tumors and the relationship between their pathological characteristics such as type and grade with various factors such as age and gender.

Patients and Methods
Study design
This retrospective cross-sectional study was conducted on patients who were candidate for partial or radical nephrectomy due to renal mass referred to Namazi and Ali Asghar hospitals in Shiraz (southern Iran) from April 2013 to March 2018.

Keywords: Renal tumor, Nephrectomy, Age, Gender
**Inclusion and exclusion criteria**
Inclusion criteria were all patients aged more than or equal to 18 years with renal mass, candidate for partial or radical nephrectomy.
Exclusion criteria were all patients with critical underlying diseases (hepatic, pulmonary or heart failure), other malignancy, distant metastasis, unresectable mass and incomplete medical records.

**Data collection**
In this retrospective cross-sectional study, we investigated the medical records related to eligible patients with renal mass who were candidate for partial or radical nephrectomy. Initially, demographic data such as age and gender were extracted and recorded in the data collection form. The patients underwent partial or radical nephrectomy and their specimens were sent to the laboratory for pathology examination. Pathological characteristics of the tumor include tumor type and subtype, size, grade and stage, benign or malignant status, capsular involvement, perinephric fat stranding, lymphovascular invasion, perineural invasion; lymph node involvement (N-stage) as well as T-stage tumor were extracted from files and recorded in the data collection form.

**Data analysis**
All statistical analysis was performed using IBM SPSS statistics 24 software (IBM Corporation, Armonk, NY, USA). Frequency, percentage, and mean ± SD were used to describe the data distributions. Tables were drawn to display the distribution of data. After assessing the normality of data distribution, chi-square ($\chi^2$), independent t-test, and Kruskal-Wallis test were used for comparing the variables in subgroups. In all analyses, $P < 0.05$ was considered statistically significant at a 95% confidence interval.

**Results**
A total of 381 patients with renal mass were analyzed. Around 63.8% of them were males and 36.2% were females. The mean age was 52.89 ± 4.26 years for women and 56.34 ± 5.12 years for men.

The major tumors were carcinomas (69%), that the clear cell type was more than all types of RCC (59%) (Figure 1). The frequency distribution of other renal masses is shown in Figure 2.

The highest distribution of tumor size is below 4 cm, and then, as the size increases, its distribution decreases. In all size groups, the percentage of tumor for patients under 50 years of age was higher than other age groups, however no statistically significant difference was found between age and tumor size ($P = 0.417$; Figure 3). At younger ages, the percentage of women was higher than men, and the age of onset of the disease in women is more common at younger ages, however men over the age of 50 years in all age groups had a higher percentage than women, which was not statistically significant ($P = 0.216$).

In the second age group, ie 50 to 60 years, the frequency of malignant masses has reached its peak and then decreased again, and the frequency of malignant masses in all age groups is significantly higher than benign masses, however no statistically significant difference was found between age and tumor type ($P = 0.73$; Figure 4).

In patients with tumor grades 1 and 2, a large percentage of patients are under 50 years of age, and with age,
Gender difference in renal tumors

The percentage of grades 1 and 2 decreases. In the two groups of grades 3 and 4, it seems that patients have a disproportionate distribution in terms of age, and in the first and third age groups, an increase in these two grades was observed, nevertheless no significant difference was observed between age and tumor grade ($P = 0.138$; Figure 5).

The distribution of masses in the women was more than 4 cm and higher sizes were less common in women, but no statistically significant difference was found between gender and tumor size ($P = 0.532$; Figure 6).

Malignant masses were more common among male patients that were statistically significant (85.9 versus 71.1; $P = 0.01$). No significant difference was observed between gender and tumor grade ($P = 0.501$). There was no significant difference between patients’ age and lymph node involvement ($P = 0.471$), type of nephrectomy ($P = 0.311$) and tumor stage ($P = 0.91$). Additionally, no significant difference between patients gender and lymph node involvement ($P = 0.309$) and tumor stage ($P = 0.315$) were detected, however a significant difference between patients’ gender and type of nephrectomy was found ($P = 0.043$) (partial nephrectomy was more in women).

**Discussion**

RCC has an aggressive behavior and if not diagnosed in time, it can metastasize to various other organs and severely affect a person’s health (4).

In the present study, patients who underwent partial or radical nephrectomy due to renal mass over five years were evaluated and factors such as age, gender, type of operation, and pathological characteristics such as tumor type, size, grade and stage were analyzed.

The results indicated that female patients had almost twice as many benign masses as male patients and the rate of malignant tumors was higher in male patients and a significant relationship was found between them. In a study by Aslan et al in Turkey, although benign tumors were more common in women, no significant relationship was found between the two variables (5). In another comparison, the age and type of surgery were evaluated, which showed

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**Figure 3.** Distribution of tumor size by age.

**Figure 4.** Distribution of tumor type by age.

**Figure 5.** Distribution of tumor grade by age.

**Figure 6.** Distribution of tumor size by age.
that the rate of partial nephrectomy decreased with age, while the rate of radical nephrectomy increased with age. However, this difference in statistical analysis was not significant. In a study conducted by Thomson et al in New York, the rate of partial nephrectomy decreased with age (6). In the comparison between age and tumor stage, with increasing age, tumor stage did not show a significant difference and no significant relationship was found between these two variables. A similar study by Hew et al on Dutch patients found that the frequency of high-grade tumors was less common in people over the age of 41 years (7), but in a study by Suh et al in the United States, higher stages of the tumor (stages 3 and 4) were less common in younger patients (18% versus 33%) (8).

In the present study, different RCC subtypes were also compared with the gender, which seemed to have differences between the gender groups in the frequency of RCC subtypes such as clear cell, papillary and chromophobe. In this study, the frequency of papillary RCC was significantly higher in men. In a study by Pierorazio et al in Colombia, this ratio was higher in men, while the frequency of chromophobe RCC was higher in women. Additionally, the frequency clear cell RCC was higher in women than men (9).

In another comparison, the size of the tumor was compared with the type of surgery which showed that in patients who underwent partial nephrectomy, the average size of the tumor was much lower than the size of tumors in patients with radical nephrectomy. Investigation of age and type of tumor also showed that a significant relationship was found only in three groups of patients with PNET (pyelonephritis, primitive neuroectodermal tumor), oncocytoma and transitional cell carcinoma (TCC). Accordingly, in the study of RCC subtypes, the frequency of clear cell RCC was significantly higher among patients older than 40 years than patients under 40 years. The tumor size was significantly associated with lymph node involvement and tumor stage, and also gender with type of tumor and type of surgery. Other results about degree and stage of the tumor showed that these parameters were significantly associated with the frequency of lymphovascular invasion, perineural invasion and perinephric fat stranding, which are expected findings according to reliable literature. Other findings about comparison of age with gender, degree of tumor, benign and malignant status, lymph node involvement, as well as tumor size with age and gender, also gender with tumor stage, tumor type and lymph node involvement that no significant relationship was found between these variables separately.

Conclusion
The results of this study showed that the frequency of benign renal masses in women is twice as high as in men. In addition, the type of tumors seen in men were significantly different from women. The rate of papillary RCC was higher in men than women. The distribution of tumors that occur at various ages will be different. The incidence of clear cell renal cell carcinoma (CCRCC), the most common type of RCC, was much higher at older ages than at younger ages. Tumors such as PNET have also been found in people under the age of 50 years, suggesting that PNET is a tumor in young people. Also, tumors such as TCC, which is an aggressive tumor, were much more common in those over 70 years of age than in younger people, but age cannot be a predictor of benign or malignant mass or tumor stage. Thus, these variables found an age-independent relationship. In the present study, the type of surgery was also examined, and it seems that the type of tumor and the extent of its aggressive behavior persuade the physician to perform more partial nephrectomy in women than men. Given the higher rate of malignant tumors in men, this result also seems reasonable and predictable. Tumor size was also a predictor of the type of choice operation. At higher sizes, the surgeon preferred to perform radical nephrectomy. Finally, the results were obtained indicating lymphovascular invasion, perineural invasion, and perinephric fat stranding as factors that affect the tumor stage, which of course were predictable results; since these factors are used in the staging of tumors, it can be concluded that the results of this study are reliable.

Limitations of the study
Further studies with larger sample size should evaluate and confirm our findings.

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Methodology: AA, KB.
Validation: KB, SYNO.
Formal analysis: AA, KB, SYNO.
Investigation: AA, SY.
Resources: KB.
Data curation: AA, KB.
Writing–original draft: AA, KB, SYNO.
Writing–review and editing: AA, KB, SYNO.
Visualization: KB, SYNO.
Supervision: KB, AA, SYNO.
Project administration: AA.

Conflicts of interest
The authors declare that they have no competing interests.

Ethical issues
The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Fasa University of Medical Sciences approved this study (IR.FUMS.REC.1398.070). Written informed consent was taken from all participants before any intervention. Additionally, this study was extracted from M.D of thesis of Shiva Yazdani Nasrabad Olia at this university (Thesis # 97301). Besides, ethical issues (including plagiarism, data fabrication, double publication) have
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