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Original article

Significance of CD105 Expression in Clear Cell Renal Cell Carcinoma (Immunohistochemical Study)

Nehal S. Zafer, Tagreed A. Abdel Aziz, Ghada A. Abd-Elfattah,
Sarah N. Nasif, Sarah H. Sherif

Abstract:

Background: Renal cell carcinoma (RCC) poses significant challenges due to its increasing incidence, mortality rates, and poor response to traditional therapies. Identifying diagnostic biomarkers and therapeutic targets- particularly in cancer stem cells (CSCs)- remains crucial. CD105, associated with tumor growth and angiogenesis, has emerged as a potential prognostic marker and CSC identifier in RCC. This study aimed to evaluate the role of CD105 expression in ccRcc and to correlate the findings with the available clinicopathological data. Material and **Methods:** Fifty cases of cc RCC and ten non-neoplastic renal tissue controls- were studied using archival blocks, processed between 2022 and February 2024. Histopathological classification followed the WHO 2022 guidelines, assessing nuclear grading, invasion, staging, and immunohistochemical staining for CD105 expression. A semiquantitative scoring system and H-score were employed to evaluate tumoral CD105 expression. Vascular density determined endothelial CD105 expression. **Results:** The study revealed associations between high endothelial CD105 expression and grade II/IV RCC, tumor necrosis, and lymph node invasion ($p<0.05$). No significant associations were found between tumoral CD105 expression and clinicopathological features, except for lymph node invasion($p=0.025$). Endothelial and Tumoral CD105 extent of expression showed significant relationship ($P=0.045$). High tumoral CD105 expression correlated with high endothelial expression (>75% positive cells; $p=0.045$).CD105 showed 31.6% sensitivity and 71% specificity for Stage of ccRcc. **Conclusion:** D105 expression in ccRcc demonstrated correlations with certain clinicopathological factors, primarily endothelial CD105 expression with higher grades and tumor aggressiveness. However, tumoral CD105 expression lacked significant associations, emphasizing the need for further exploration of CD105's role as a prognostic marker in RCC.

Keywords: CD105; Expression; Clear Cell; Renal Cell; Carcinoma.

Pathology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:
Dr. Sarah H. Sherif.
Pathology Department, Faculty of Medicine Benha University, Egypt.
Email:
sarahameed20244@gmail.com

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Introduction

Renal cell carcinoma (RCC) is the seventh most common tumor and is associated with high mortality. Several subtypes of RCC have been defined: clear cell RCC (ccRcc; 70% incidence), papillary RCC (pRCC; 10% incidence), chromophobe RCC (ChRCC; 5% incidence), and rare types of RCC where the frequency is less than 1% of each [(1).]

Renal cell carcinoma (RCC) is the most common type of malignancy of the kidney, accounts for 3–5 % of all malignancies in adults and its incidence and mortality are currently on the rise [(2).]

In Egypt, Renal cell carcinoma (RCC) represents 1,78% of total malignancies, 11.02% of malignant urinary system tumors, 81,7% of primary malignant renal tumors. The male to female ratio is about 2:1 and the incidence in men is about 1.53% representing the 10th most common cancers in male and in women is about 0.97% representing the 17th most common cancers in females [(3).] In the USA, RCC is the 6th leading cause of cancer-associated deaths in men and the 8th leading cause in women [(2).]

At present, surgery is the standard treatment for primary RCC, however, the treatment of RCC remains a huge challenge due to the generally poor response to chemotherapy and radiotherapy [(4).]

Cancer stem cells (CSCs) were first identified in 3 types of solid tumor in the early 2000s. Now, CSCs have been identified in various cancer types, including RCC. Targeting of CSCs has become an important strategy to treat cancer. RCC exhibits a poor response to chemotherapy and radiotherapy due to the survival of CSCs, and it is important to identify molecular markers to isolate and characterize the CSCs among the tumor cells; of note, targeting of CSCs in RCC has provided a novel treatment strategy, particularly for metastatic RCC [(5).]

Recently, CD105 has been described as a novel RCC CSC marker. Several studies have indicated that CD105 contributes to the development of blood vessels and angiogenesis, and is essential for tumor growth and the development of metastasis. In addition, CD105 is a prominent marker for mesenchymal stem cells (MSCs). In RCC, CD105 has been reported as a potential prognostic marker and CSC marker [(6).]

However, little is known about the role of CD105 in the prognosis and diagnosis of ccRcc. Therefore, the present study aimed to evaluate the role of CD105 expression in clear cell renal cell carcinoma and to correlate the findings with the available clinicopathological data.

Material and methods

This retrospective study was carried upon 50 selected Egyptian cases with clear cell renal cell carcinomas (ccRcc) with ten cases of non-neoplastic renal tissue (chronic glomerulonephritis)- were taken as a control. The material included archival formalin-fixed paraffin-embedded blocks processed during the years 2022 to February 2024. One block from the tumor area was available. These blocks were collected from Pathology Department, Early Cancer Detection Unit, Faculty of Medicine, Benha University, between May 2022 and February 2024. Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Medicine at Benha University, code number {M.S.4.2019}.

Cases were selected on the bases of availability of demographic data (age and sex) and clinical data (tumor size, renal vein invasion, grade, lymph node status, stage, presence of tumor necrosis). From each block 4um sections was cut, the slides were subjected to H&E staining, and immunohistochemical staining for detection and studying expression of CD105 in clear cell renal cell carcinoma following procedures done by manufacture laboratory role, **Table (2).**

Histopathological Study: Histologic sections, four microns (4um) thick, were

stained by Hematoxylin and Eosin (H&E) for histopathological study of clear cell renal cell carcinoma. The cases were classified according to WHO classification, 2022. The studied H&E sections were reviewed and were also used to select representative areas of the tumor for subsequent immunohistochemical study. Nuclear grading was done according to the WHO/ISUP grading system with the presence or absence of tumor necrosis [7].

Renal vein invasion how and staging of cases was done according to the 8th editions (TNM8) staging system [8].

Immunohistochemistry: The immunohistochemical study aimed to evaluate CD105 expression in clear cell renal cell carcinoma using the Avidin-Biotin Complex (ABC) technique. Tissue sections on glass slides underwent antigen retrieval by autoclave formalin-fixed paraffin-embedded tissue sections were cut at 4µm and mounted on positively charged glass slides (Fischer, USA). Non-representative areas of the tumor were scraped off the slide. • Slides were deparaffinized in xylene and rehydrated through graded series of ethanol. • Slides were washed with distilled water 3 times for 2 minutes each. • For antigen retrieval: A. Slides were put in a slide rack and placed in a Coplan jar containing 0.01M citrate buffer (pH 6). Coplan jar is placed in a water bath to keep a humid atmosphere inside the microwave oven. B. Slides were microwaved in a microwave oven (General Electric,1000 Watts) at power 650 for 15 minutes. The amount of fluid in the Coplan jar was checked and water was added if necessary to prevent slides from drying out. Material and Methods 57 C. The jar was removed from the oven and allowed to cool for 20 minutes. D. Slides were then washed in distilled water several times then placed in phosphate buffer saline (PBS) (pH 7.4) for 5 minutes. blocking of peroxidase activity, and incubation with CD105 monoclonal antibody at a dilution of 1:100 (NeoMarkers, LABVISION, USA). Slides were incubated horizontally at the room temperature for 90 minutes. Subsequent steps included the application of the Ultravision/HRP polyvalent system (Cat no. TP-060-HL), chromogen use, counterstaining, and mounting. Positive controls were included using normal renal tissue and negative control was processed with omitting the primary antibody and adding Tris-buffered saline with a similar dilution instead. A section of endometrial carcinoma tissue was used as external positive control [9].

Evaluation of immunohistochemical staining results: The immunohistochemical analysis utilized a semiquantitative system for evaluating tumoral cytoplasmic staining intensity (0 to 3) and categorizing the percentage of positive cells into four groups. An overall H-score, derived from the intensity and percentage, ranged from 0 to 300. A cutoff of 100 was chosen to classify samples as high or low in tumoral cytoplasmic CD105 expression based on the median H-score. Additionally, endothelial CD105 expression was determined by assessing vascular density, categorized into low, moderate, and high groups based on the number of vessels positive for CD105 antibody in each core [10].

Statistical analysis

Data analysis was performed by SPSS software, version 25 (SPSS Inc., PASW statistics for windows version 25. Chicago: SPSS Inc.).

In the statistical comparison between the different groups, the significance of difference was tested using: Qualitative data were described using number and percent. Significance of the obtained results was judged at the (≤0.05) level. ChiSquare, Fischer exact test (FET), Monte Carlo test (MC) were used to compare qualitative data between groups as appropriate. Receiver-operating characteristic (ROC) analysis is performed to evaluate the diagnostic accuracy of CD105 expression in distinguishing

between different groups or conditions, specifically assessing sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy rate (AC).

Results

Clinicopathological results:

This study was carried upon 50 cases of (ccRcc). Among studied cases there were 32 cases (64%) aged less than 60 years, regarding gender; 60% were males and 40% were females, also histopathological findings were reported, **Table (1)**.

Immunohistochemical results:

Concerning the pattern of CD105 expression in ccRcc cases has diverse expression, it is expressed in vascular endothelial cell (MVD) showed brownish cyto-membranous staining in endothelial cells and expressed in tumoral cytoplasm showed brownish cytoplasmic staining in ccRcc cases, (**Figure 1,2**).

Concerning the pattern of CD105 expression in the non-neoplastic renal tissue -that was taken as a control- the tissue showed brownish cyto-membranous staining in all endothelial cells, tubule capillaries, and glomerular endothelial cells, but no staining was shown in tubule cells **.**

Table (1): Age and Gender of the studied cases.

	n=50	%
Age/years		
<60	32	64.0
≥60	18	36.0
Gender		
Male	30	60.0
Female	20	40.0

Table (2): Demographics and Histopathological findings of the studied cases.

	n=50	**%**
Tumor size		
0-4 cm	10	**20.0**
4.1-7 cm	14	**28.0**
7.1-10 cm	19	**38.0**
>10cm	7	**14.0**
Grade		
Low	36	**72.0**
High	14	**28.0**
Stage		
Low	31	**62.0**
High	19	**38.0**
Microvascular invasion		
present	4	**8.0**
absent	46	**92.0**
Lymph node invasion (LNI)		
positive	2	**4.0**
negative	48	**96.0**
Renal vein invasion (RVI)		
present	2	**4.0**
absent	48	**96.0**
Tumor necrosis		
present	17	**34.0**
absent	33	**66.0**

Table (3): Relation between Endothelial CD105 expression and histopathological and tumoral CD105 expression (intensity, extent and H score of expression) and Endothelial CD105 expression in the studied cases:

	test of significance	**Endothelial CD105 expression (MVD)** high N=2(%)	moderate N=13(%)	low N=35(%)	**test of significance**
Tumor size					
0-4 cm	χ^{2MC}=5.11	0	2(15.4)	8(22.9)	**χ^{2MC}=5.11**
4.1-7 cm	P=0.529	1(50)	3(23.1)	10(28.6)	**P=0.529**
7.1-10 cm		0	7(53.8)	12(34.3)	
>10cm		1(50)	1(7.7)	5(14.3)	
Grade					
Low	χ^{2MC}=25.51	1(50)	10(76.9)	25(71.4)	**χ^{2MC}=25.51**
High	P<0.001*	1(50)	3(23.1)	10(28.6)	**P<0.001***
Stage					
Low	χ^{2MC}=0.134	1(50)	8(61.5)	22(62.8)	**χ^{2MC}=0.134**
High	P=0.935	1(50)	5(38.5)	13(37.2)	**P=0.935**
Microvascular invasion	P=0.07	0	3(23.1)	1(2.9)	**P=0.07**
present	χ^{2MC}=5.45	2(100)	10(76.9)	34(97.1)	**χ^{2MC}=5.45**
absent					
Lymph node invasion(LNI)	P=0.640	0	0	2(5.7)	**P=0.640**
Positive	χ^{2MC}=0.893	2(100)	13(100)	33(94.3)	**χ^{2MC}=0.893**
Negative					
Renal vein invasion(RVI)	P=0.052	0	2(15.4)	0	**P=0.052**
present	χ^{2MC}=5.93	2(100)	11(84.6)	35(100)	**χ^{2MC}=5.93**
absent					
Tumor necrosis					
present	P=0.003*	2(100)	8(61.5)	7(20)	**P=0.003***
absent	χ^{2MC}=11.33	0	5(38.5)	28(80)	**χ^{2MC}=11.33**

	test of significance	**tumoral CD105 intensity of expression** 3(strong)	2(moderate	1(weak)	**test of significance**
Endothelial CD105 of expression	χ^{2MC}=1.53			25(71.4)	**χ^{2MC}=1.53**
low	P=0.821	3(75)	7(63.6)	8(22.9)	**P=0.821**
moderate		1(25)	4(36.4)	2(5.7)	
high		0	0		

	test of significance	**tumoral CD105 extent of expression** Group4 (>75%positive cells) N=3(%)	Group3 (51-75%positive cells) N=11(%)	Group2 (25-50%positive cells) N=28(%)	Group1(<25% positive cells) N=8(%)	**test of significance**
Endothelial CD105 of expression	χ^{2MC}=12.90 P=0.045*					**χ^{2MC}=12.90 P=0.045***
low		0	8(72.7)	20(71.4)	7(87.5)	
moderate		3(100)	3(27.3)	7(25)	0	
high		0	0	1(3.6)	1(12.5)	

	test of significance	**tumoral CD105 H score of expression** High H score N=15(%)	Low H score N=35(%)	**test of significance**
EndothelialCD105 of expression	χ^{2MC}=1.33			**χ^{2MC}=1.33**
low	P=0.513	10(66.7)	25(71.4)	**P=0.513**
moderate		5(33.3)	8(22.9)	
high		0	2(5.7)	

MC: Monte Carlo test, FET: Fischer exact test χ2: Chi-Square test, *statistically significant.

Table (4): Relation between tumoral CD105 intensity and H score of expression and histopathological findings of the studied cases.

	tumoral CD105 intensity of expression			**test of significance**
	3(strong)	2(moderate)	1(weak)	
Tumor size				
0-4 cm	1(25)	2(18.2)	7(20)	**χ^{2MC}=2.17**
4.1-7 cm	0	4(36.4)	10(28.6)	**P=0.903**
7.1-10 cm	2(50)	4(36.4)	13(37.1)	
>10cm	1(25)	1(9.1)	5(14.3)	
Grade				
Low	2(50)	8(72.7)	26(75.7)	**χ^{2MC}=1.05**
High	2(50)	3(27.3)	9(24.3)	**P=0.590**
Stage				
Low	2(50)	6(54.5)	23(65.7)	**χ^{2MC}=0.709**
High	2(50)	5(45.5)	12(34.3)	**P=0.702**
Microvascular invasion				
Present	0	2(18.2)	2(5.7)	**P=0.342**
Absent	4(100)	9(81.8)	33(94.3)	**χ^{2MC}=2.15**
Lymph node invasion(LNI)				
Positive	0	2(18.2)	0	**P=0.025***
Negative	4(100)	9(81.8)	35(100)	**χ^{2MC}=7.38**
Renal vein invasion(RVI)				
Present	0	0	2(5.7)	**P=0.640**
absent	4(100)	11(100)	33(94.3)	**χ^{2MC}=0.893**
Tumor necrosis				
Present	2(50.0)	5(45.5)	10(28.6)	**P=0.459**
absent	2(50.0)	6(54.5)	25(71.4)	**χ^{2MC}=1.56**
	tumoral CD105 H score of expression			**test of significance**
	High H score N=15(%)	Low H score N=35(%)		
Tumour size				
0-4 cm	3(20)	7(20)		**χ^2=0.043**
4.1-7 cm	4(26.7)	10(28.6)		**P=0.998**
7.1-10 cm	6(40)	13(37.1)		
>10cm	2(13.3)	5(14.3)		
Grade				
Low	10(66.7)	26(74.3)		**χ^2=0.302**
High	5(33.3)	9(25.7)		**P=0.582**
Stage				
Low	8(53.3)	23(65.7)		**χ^2 =0.683**
High	7(46.7)	12(34.3)		**P=0.409**
Microvascular invasion				
present	2(13.3)	2(5.7)		**P=0.363**
absent	13(86.7)	33(94.3)		**χ^{2MC}=0.828**
Lymph node				
invasion(LNI)	2(13.3)	0		**P=0.086**
positive	13(86.7)	35(100)		**χ^{2FET}=4.86**
negative				
Renal vein invasion(RVI)				
present	0	2(5.7)		**P=1.0**
absent	15(100)	33(94.3)		**χ^{2FET}=0.893**
Tumor necrosis				
present	7(46.7)	10(28.6)		**P=0.216**
absent	8(53.3)	25(71.4)		**χ^2=1.53**

MC: Monte Carlo test, *statistically significant.

High Grade renal cell carcinoma showed high endothelial CD105 expression in 50% of cases which was statistically significant (P=0.001). Presence of tumor necrosis of renal cell carcinoma showed high endothelial CD105 expression in 100% of cases which was statistically significant (P=0.003), (**Table 3**) & (**Figure2**).

A non-statistically significant relation was detected between tumoral CD105 intensity of expression and Endothelial CD105 of expression among studied cases. A statistically significant relation was detected between tumoral CD105 extent of expression and endothelial CD105 of expression (P=0.045). Also, there is no statistically significant relation between tumoral CD105 H score of expression and endothelial CD105 of expression (P=0.513), (**Table 3**).

All positively invaded L.N of renal cell carcinoma cases showed moderate tumoral CD105 intensity of expression, which was statistically significant (P=0.025). There was no statistically significant relation between tumoral CD105 H score of expression and the following histopathological findings including; tumour size, grade, stage, microvascular invasion, lymph node invasion, renal vein invasion and necrosis, (**Table 4**).

The diagnostic accuracy of CD105 expression for ccRcc was determined by using ROC Curve. The curve shows **(table 6 and figure 3)**. Sensitivity and specificity of CD105 in ccRcc were 31.6% and 71% respectively, (**Table 5)**.

Table (5): The sensitivity, specificity, accuracy rate, positive predictive value, and negative predictive value of Endothelial CD105 to stage of ccRcc:

Stage	**Low Stage I+II**		**High Stage III+IV**	
Endothelial CD105	%	No	%	**No**
Moderate +high	29.0	9	31.6	**6**
Low	71.0	22	68.4	**13**
AUC	**0.515**			
Sensitivity	**31.6**			
Specificity	**71.0**			
PPV	**40.0**			
NPV	**62.9**			
Accuracy	**56.0**			

AUC, Area under the curve; PPV= positive predictive value; NPV=negative predictive value.

Table (6): The sensitivity, specificity, accuracy rate, positive predictive value, and negative predictive value of Endothelial CD105:

AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
0.515	31.6	71.0	40.0	62.9	56.0

AUC, Area under the curve; PPV= positive predictive value; NPV=negative predictive value

Endothelial Expression of CD105:

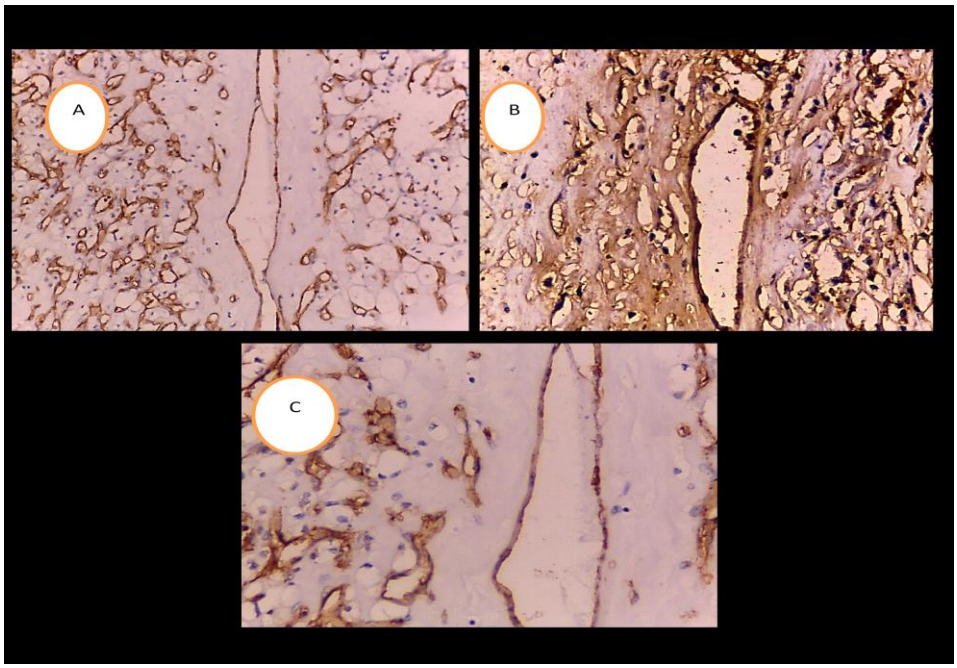

Figure 1: Clear cell renal cell carcinoma: showing high (A), moderate (B) and high (C) endothelial expression, grade 2 A, C (IHC, x200), B (IHC, x400).

Tumoral Cytoplasmic expression of CD105:

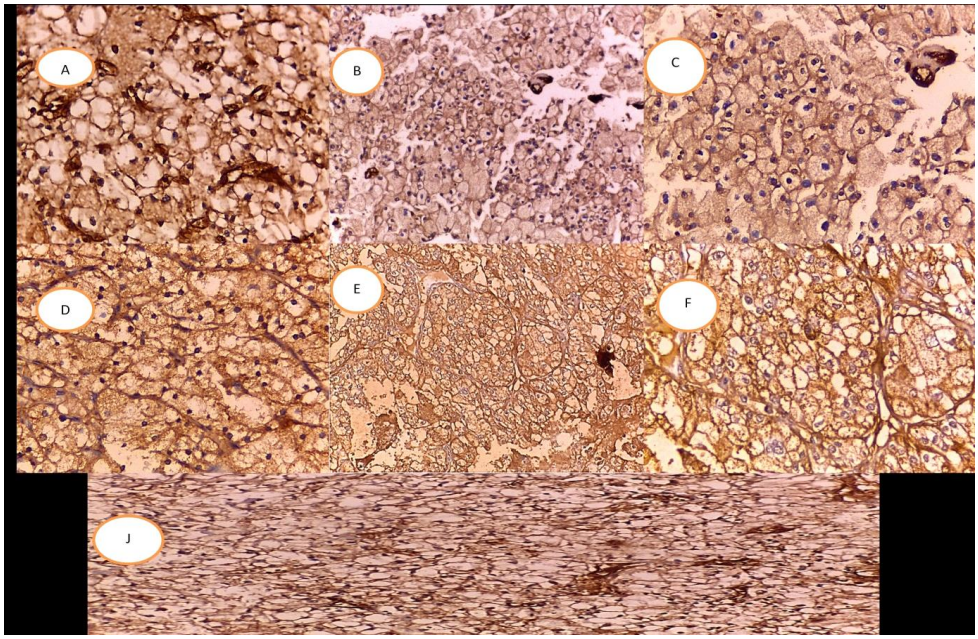

Figure 2: Clear cell renal cell carcinoma: showing tumoral Cytoplasmic expression H score low, grade 2 A :(IHC, x200), B :(IHC, x200) and score high, grade 2 C (IHC, x200) ,D,E(IHC, whx400) and score high, grade 3F (IHC x200), J(IHCx400).

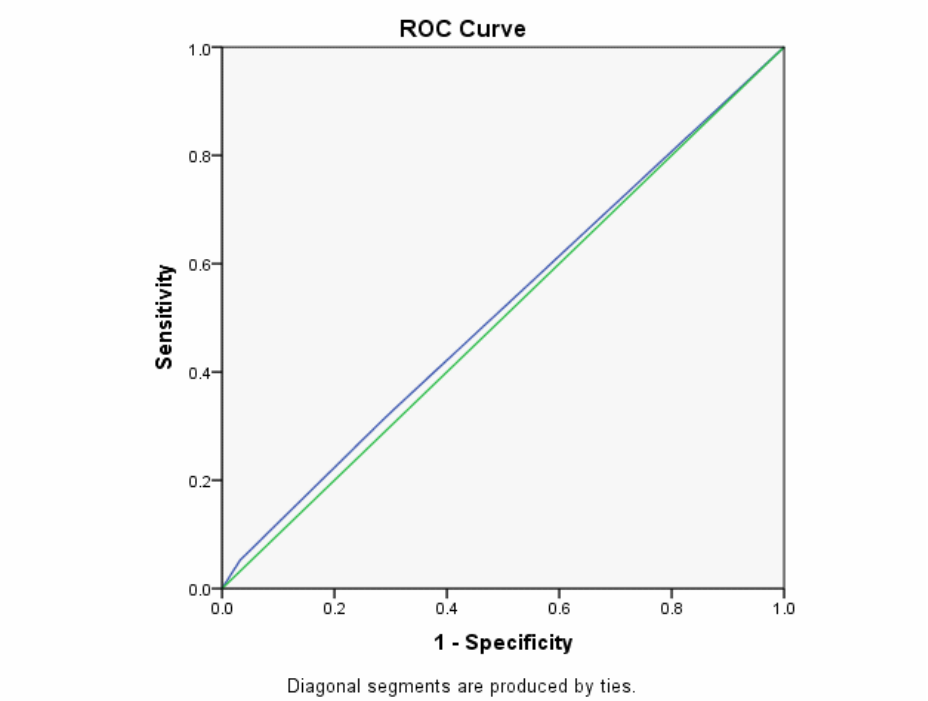

Figure (3): ROC curve for Endothelial CD105 expression, the area under the curve represents an optimal statistic for comparing the sensitivity and specificity of Endothelial CD105.

Discussion

Renal cell carcinoma (RCC) is the most common type of malignancy of the kidney, accounts for 4% of all malignancies in adults and its incidence and mortality are currently rising. This study was a retrospective one performed on selected biopsies of ccRcc.

Concerning the pattern of CD105 expression in the control cases studied, the tissue of non-neoplastic renal tissue that was taken as control showed brownish cyto-membranous staining in all endothelial cells, tubule capillaries, and glomerular endothelial cells, but no staining was shown in tubule cells**.**

In agreement with these results, Saeednejad Zanjani, L., and Fattahi, F., et al, who found that the expression of CD105 in non-neoplastic renal tissue was brownish cyto-membranous staining in all endothelial cells, tubule capillaries, and glomerular endothelial cells [10,11].

Moreover, it was found that the expression of CD105 in ccRcc tumor tissue was significantly higher compared with that of normal renal tissue (P=0.03) [3].

In this study, regarding the tumor size, 38% of the studied cases had tumor size from 7.1 to 10 cm, 28% from 4.1 to 7 cm and 20% from 0 to 4 cm. In the present study, there was no statistically significant relation between tumoral CD105 expression and tumor size. Also, there was no statistically significant relation between endothelial CD105 expression and tumor size. In contrast to, it was found that no significant association was detected between tumoral cytoplasmic expression of CD105 and other clinicopathological features in ccRcc patients.

However, there was a highly significant association between endothelial CD105 expression and tumor stage & tumor size and is significantly associated with risk of metastasis [10]. In the present study, regarding the immunohistochemical results of endothelial CD105 expression, there were (70%) cases had low endothelial CD105 expression, (26%) cases had moderate expression and (4%) cases had high expression. In the current study

regarding the immunohistochemical results of endothelial CD105 expression, the current study was in line with Saroufim, et al, who reported that three cases (6%) of RCC give negative expression versus (94%) showed positive staining, 60% of positive cases recorded low score while 40% of cases showed high score of expression [12]. In agreement with the current results, Saroufim, et al, evaluated the endothelial CD105 expression and reported that 34 cases had low expression, 33 cases had moderate expression, and 35 cases had high expression [13].

Regarding tumor grading according to other studies, 72% of cases classified as low grade and 28 % of cases classified as high grade. Moreover, high grade of renal cell carcinoma showed high endothelial CD105 expression in 50% of cases which was statistically significant (P=0.001) .while, The current results came in contrast with investigated the endothelial CD105 expression in different grades; there is a significant negative correlation between Fuhrman's nuclear grades and the endothelial CD105 expression in RCC (p-value=0.009). However, the highest expression was detected in lower Fuhrman's grades (I and II) [12, 14].

In this regard, Mohammed, et al, came in contrast with the present study, they reported that a high CD105-MVD was identified in a low Fuhrman's grade RCC ($p<0.01$). Also, Saroufim, et al, confirmed the same inverse significant relation between the tumor grade and the CD105 expression when it was evaluated as endothelial cell marker, but when it was evaluated as tumoral cytoplasmic marker of RCC, they reported a positive correlation. While, in another study Bauman, et al, found no correlation between endothelial CD105 expression and grades of RCC cases [12, 13, 15].

In agreement with the current results, Mohammed, et al, who found that CCRCCs had recorded in Fuhrman's nuclear grades; 91% of the conventional type were grade I&II, while all cases of CCRCC with sarcomatoid components by their name- were considered as grade VI [12].

In addition, stage distribution of the studied cases, there were 36% of cases were stage III, 32% were stage II, 30% were stage I and 2% were stage VI, with no statistically significant relation between tumoral and endothelial CD105 expression and stage.

Regarding stage distribution, our results were in contrast with Sandlund, and Shi, et al, observed that the tumoral cytoplasmic CD105 expression was higher in advanced stages (stage III and stage IV) in comparison with lower stages (stage I and stage II), which shows the association of cytoplasmic CD105 expression with tumor aggressiveness in ccRcc [10, 13, 14,16].

Previous studies in contrast with those finding, that showed a statistically significant association between tumoral cytoplasmic of CD105 expressions of tumor cells and TNM stage in Colo-Rectal Cancer (CRC) and ovarian cancers patients. There was a higher level of tumoral cytoplasmic CD105 expression in advanced stage that occurred distant metastasis [11].

According to results of the present study, microvascular invasion (MVI) was absent in (92%) cases and it was detected among (8%) cases. we did not find any association between tumoral and endothelial CD105 expression and MVI. Our results in contrast with that showed a statistically significant relationship between patients with MVI and worse OS [10, 17, 18]. Reported that tumor vasculature may have a role in supporting and maintaining cancer stem cells [19].

In the present study, renal vein invasion was absent in (96%) cases, and it was detected among (4%) cases. No statistically significant association was detected between tumoral and endothelial CD105 expression and renal vein invasion. Regarding renal vein invasion, our current findings are consistent with previous results. Specifically, among 102 cases of

clear cell renal cell carcinoma (ccRcc), twenty-four patients were found to have renal venous invasion [13].

Regarding lymph node invasion, the current study was in line with Zubac, et al who showed that LNI provided the strongest prognostic information for patients without MVI after radical nephrectomy [20].

The current study, in contrast to other studies, showed that MVD-CD105 expression and lymphatic invasion significantly correlated with patient outcomes in Small Cell Lung Carcinoma (SCLC). Specifically, it demonstrated positive correlations between increased MVD-CD105 expression and lymph node metastasis, which are indicative of a poor prognosis. This contrasts with Hepato-Cellular Carcinoma (HCC), where increased MVD-CD105 expression was also correlated with poor prognosis but mainly through blood spread rather than lymphatic spread [21, 22]. These differences might reflect the distinct modes of metastatic spread in SCLC and HCC—lymphatic spread being predominant in SCLC and blood spread being predominant in HCC.

The current results in contrast with Saeednejad, et al, whom, reported that there was no association between cytoplasmic expression of CD105 and LNI as well as survival outcomes [10, 13].

In the present study, tumor necrosis was absent in (66%) cases and it was detected among (34%) cases. There were statistically significant association between endothelial CD105 expression and tumor necrosis (P=0.003) and statistically significant association between tumoral cytoplasmic extent of CD105 expression (Group4) and tumor necrosis (P=0.007).

Regarding tumor necrosis, the current results were in contrast with Mohammed, and Sengupta, et al, who found that no statistically significant association was detected between the necrosis and the histopathological types [12, 23].

According to the current results, a study reported that endothelial CD105 expression levels were as follows: (24.2%) exhibited low expression, (19.2%) showed moderate expression, and (56.7%) displayed high expression (9).

Regarding tumoral CD105 expression in our results, among RCC samples stained for CD105, (8.1%) showed no staining, while weak, moderate, and strong staining intensities were observed in (60.2%), (23.1%), and (8.6%) cases, respectively. Evaluation of CD105 expression in RCC patients revealed that (74.2%) exhibited low expression, whereas (25.8%) showed high expression (10).

According to Saeednejad, et al, there were no significant associations between the levels of tumoral cytoplasmic and endothelial CD105 expression and any important histopathological parameters. This contrasts with the present study as it did not rely on different subtypes, the wide base data for more accurate staging and additional panel of angiogenic markers for comparison and confirmation [10].

Previous results in contrast with the current one, they reported that CD105 may serve as a useful prognostic molecular marker and potentially a target molecule for targeted therapy only in (ccRcc). Therefore, it was revealed that the high CD105 copy number group survived for longer and this trend was in accordance with high CD105 mRNA group. This contrast, due to that the current study did not rely on molecular genetic study

Using ROC curve analysis, the sensitivity and specificity of CD105 were 31.6% and 71% respectively, AUC for CD105 was 0.515 OF ccRcc based on CD105 expression levels. A previous study in contrast with the current results reported that the AUC for CD105 was 0.749 of ccRcc based on CD105 expression levels [24] according to ROC curve analysis. CD105 were prognostic markers in ccRcc.

Conclusion

High expression of endothelial or tumoral CD105 correlated with more favorable pathological features, including reduced rates of lymph node invasion and tumor necrosis, which are significant prognostic indicators. However, there was no statistically significant relationship found between the tumoral CD105 H score and various histopathological findings, such as tumor size, grade, stage, microvascular invasion, lymph node invasion, renal vein invasion, and necrosis. Interestingly, the extent of tumoral CD105 expression showed a significant association with endothelial CD105 expression levels.

High endothelial or tumoral CD105 was correlated with more favorable pathological features, including lymph node invasion and tumor necrosis, both of which are significant prognostic indicators. High CD105 endothelial was correlated with tumor grade. In the current study, regarding CD105 and tumor grades could not be used for diagnostic purpose only but also for a prognostic value.

Multiple studies confirmed that both mature differentiated vessels and immature undifferentiated ones of RCC could be stained by CD105, opposite to other angiogenic markers like CD34, CD31 that could be expressed only in mature differentiated vessels of RCC.

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Author contribution

Authors contributed equally in the study.

Conflicts of interest

No conflicts of interest

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