miRNA-27b-3p, let-7f-5p and miRNA-142-5p can be Used in a Novel Serum Diagnostic Panel for Clear Cell Renal Cell Carcinoma

Original Research

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Abstract

Background: Clear cell renal cell carcinoma (ccRCC) is a prevalent malignant tumor affecting the urinary system. Due to its unfavorable prognosis, there is a pressing need to develop effective approaches for early diagnosis and treatment of ccRCC. Extensive research has consistently demonstrated the presence of stable microRNAs (miRNAs) in human serum. Accordingly, the objective of this study was to identify a specific panel of miRNAs in serum that can serve as a reliable and non-invasive biomarker for the early detection of ccRCC.

Methods: The study comprised of training and validation phases to identify potential biomarkers. In the training phase, a total of 10 miRNAs exhibiting the most significant differential expression among 28 ccRCC patients and 28 healthy controls (HCs) were identified using quantitative reverse transcription polymerase chain reaction (qRT-PCR). In the subsequent validation phase, these 10 miRNAs were assessed in serum samples obtained from an additional 80 ccRCC patients and 84 HCs using RT-qPCR. To construct a panel with optimal diagnostic capability, backward stepwise logistic regression analysis was conducted. Furthermore, bioinformatics analysis was performed on this selected miRNA panel. Results: In ccRCC patients, the serum expression level of miRNA-142-5p was found to be significantly elevated compared to healthy controls (HCs), whereas the expression levels of let-7f-5p, miRNA-27b-3p, miRNA-212-3p, and miRNA-216-5p were significantly reduced. To assess their diagnostic potential for ccRCC, receiver operating characteristic (ROC) curve analysis was performed. The analysis revealed that miRNA-27b-3p, let-7f-5p, and miRNA-142-5p exhibited moderate diagnostic capabilities for ccRCC, with area under the curve (AUC) values of 0.826, 0.828, and 0.643, respectively. To further enhance diagnostic accuracy, a final diagnostic panel consisting of these three miRNAs was constructed, demonstrating good diagnostic value with an AUC of 0.952.

Conclusions: The miRNA serum biomarker panel (miRNA-27b-3p, let-7f-5p, and miRNA-142-5p) identified in this study holds promise for early, non-invasive, and accurate diagnosis of ccRCC. This panel could potentially provide a valuable tool in clinical settings to aid in the timely detection and management of ccRCC.

Keywords: miRNA; panel; renal cell carcinoma; biomarker

1. Introduction

Clear cell renal cell carcinoma (ccRCC) is a frequent malignancy that arises from the urothelial system within the renal parenchyma. It is considered one of the most prevalent types of cancer affecting the urinary system [1]. ccRCC is a highly malignant tumor with very poor prognosis [2] and an etiology that is still unclear [3]. At present, the treatment methods for early ccRCC are mainly total nephrectomy, partial nephrectomy, and other surgical methods [4]. Although the prognosis for early ccRCC is good, rapid detection and treatment can improve the survival rate [5]. Indeed, the discovery of accurate biomarkers is crucial to further improve the survival rate of ccRCC patients. These biomarkers can play a vital role in early detection, prognostic evaluation, and personalized treatment selection for individuals diagnosed with ccRCC. By identifying reliable biomarkers, we can enhance patient outcomes and potentially develop novel therapeutic interventions tailored to specific molecular characteristics of ccRCC.

Large scale RNA sequencing (RNA seq) analysis reveals that more than two-thirds of the human genome is transcribed, but <2% is translated into protein [6]. These proteins have been widely studied and correlated with various human diseases [7], with some becoming therapeutic targets [8]. However, there is a lack of detailed research on transcribed non-coding RNAs (ncRNAs) [9], especially miRNAs, which are small small interfering RNA (siRNA)-like molecules are encoded by the genomes of higher eu-
karyotes and play significant regulatory roles in various biological processes [10]. By pairing with the mRNA of their target gene(s), miRNAs can hinder the translation of mRNA, or degrade it via the RNA-induced silencing complex (RISC) [11]. miRNAs are therefore highly conserved during the evolution of species. Many studies in animals, fungi and plants have revealed that miRNAs are expressed only in specific tissues and at certain development stages. The functional specificity of tissues and cells is determined by the timing and tissue specificity of miRNA expression, which reveals they can regulate the growth and development of cells [12].

Aberrant miRNA expression has been observed in a diverse array of malignant tumors, encompassing bladder cancer, colorectal carcinoma, gastric cancer, ccRCC, and breast cancer [13–18]. These dysregulated miRNAs play pivotal roles in driving tumorigenesis and tumor progression by influencing critical cellular processes, such as cell proliferation, apoptosis, angiogenesis, and metastasis. The identification and characterization of specific miRNA signatures associated with these malignancies hold great promise for their potential utilization as diagnostic biomarkers, prognostic indicators, and therapeutic targets. Continued research in this field will further enhance our comprehension of cancer biology and facilitate the development of innovative approaches in cancer diagnostics and therapeutics.

ccRCC represents a significant contributor to cancer-related mortality, with a 5-year survival rate of less than 20% [19]. While some miRNAs have been associated with the risk and prognosis of ccRCC, there still remains a lack of understanding regarding the impact of many other miRNAs on the development of this particular cancer type. The aim of this study was to identify a specific panel of miRNAs in serum that can serve as a reliable and non-invasive biomarker for the early detection of ccRCC. By focusing on miRNAs present in serum, we aimed to develop a diagnostic tool that can aid in the timely identification of ccRCC, leading to improved patient outcomes through early intervention and targeted treatment strategies.

2. Materials & Methods

2.1 Participants and Ethics Statement

The participants in this study included 108 ccRCC patients and 112 healthy control (HC) volunteers. These were recruited from patients attending Shenzhen People’s Hospital from October 2019 to February 2022. All ccRCC patients were confirmed by preoperative puncture or postoperative histopathology. This study specifically included patients diagnosed with early-stage ccRCC, with clinical stage I–II. No clinical therapy was performed prior to collection of the serum specimen. The enrolled patients had primary ccRCC, with no metastasis or other carcinomas. All HCs were participants who did not have any acute or chronic diseases, or a history of other tumors. The study was explained to all participants, and each gave signed informed consent. This research was reviewed and approved by the medical ethics committee of Shenzhen People’s Hospital. In addition, the relevant regulations of the medical ethics committee of our hospital were strictly adhered to for the collection of serum samples and for the conduct of other study processes.

2.2 Study Design

The research was conducted in four phases, as depicted in Fig. 1. Initially, differential expression analysis of miRNAs in renal cancer was performed using data from the GSE32960 database, available in the Gene Expression Omnibus. Based on the findings, a set of candidate biomarkers for ccRCC was selected. Subsequently, training and validation phases were carried out to further assess and validate these candidate biomarkers. In the training phase, the relative serum levels of the selected candidate miRNAs were evaluated using quantitative reverse transcription polymerase chain reaction (RT-qPCR) in a cohort of 28 ccRCC patients and 28 healthy controls (HCs). The top 10 miRNAs demonstrating the most significant differences during this phase were then chosen for further investigation. For the validation phase, the study expanded the sample size and repeated the above steps using serum samples collected from 80 ccRCC patients and 84 HCs. This enabled the identification of the top five miRNAs showing the most significant differences between the ccRCC and HC groups.

Fig. 1. Overview of the study design. RCC, Renal cell carcinoma; HCs, healthy controls. qRT-PCR, quantitative real-time reverse transcription polymerase chain reaction; miRNA, microRNA.
Table 1. Demographic characteristics of study participants.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Testing Phase (n = 56)</th>
<th>Validation Phase (n = 164)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ccRCC</td>
<td>HCs</td>
</tr>
<tr>
<td>Total number</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>49.8 ± 11.3</td>
<td>51.1 ± 16.6</td>
</tr>
<tr>
<td>Gender</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>Male</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>12</td>
</tr>
</tbody>
</table>

No statistically significant differences in terms of age or gender were observed between ccRCC and HC participants (Wilcoxon-Mann-Whitney test). Parameters are shown as numbers. ccRCC, Clear cell renal cell carcinoma; HCs, healthy controls.

2.3 Collection of Serum Samples and RNA Extraction

Serum specimens from participants were collected and stored at −20 °C until further use. Prior to the collection of serum samples, none of the participants received any treatment. For the RT-qPCR step, 2 µL of miRNA-54 (Cell-miRNA-54-5p; 10 nm/L, RiboBio) was added to each serum sample as an internal reference to account for variability during the RNA extraction process. The total RNA was extracted from the serum samples using the LS separation kit (Thermal Fisher Science, Wilmington, MA, USA). To assess the concentration and purity of the total RNA in each sample, a NanoDrop 2000c spectrophotometer (Thermal Science) was utilized.

2.4 RT-qPCR to Quantify the Levels of Candidate miRNAs

To measure the serum levels of the candidate miRNAs, reverse transcription-specific primers from the Bulge-Loop miRNA quantitative reverse transcription polymerase chain reaction (RT-qPCR) primer set (RiboBio) were used for amplification. The RT-qPCR procedure was conducted using Taqman probes and a Roche Diagnostics LightCycler480 Real-Time PCR system. The qPCR reaction consisted of 40 cycles at the following conditions: denaturation at 95 °C for 20 seconds, followed by annealing at 95 °C for 10 seconds, extension at 60 °C for 20 seconds, and a final step at 70 °C for 10 seconds. To evaluate the relative levels of each candidate miRNA, the \( 2^{-\Delta\Delta Cq} \) method was employed. This method allows for the comparison of miRNA expression levels between different groups, taking into account the internal reference (miRNA-54) and normalizing to a control group or baseline level [20].

2.5 Statistical Analysis

The serum samples obtained from a total of 220 study participants were divided into two parts: the training phase and the validation phase. Firstly, the Shapiro-Wilk normality test was used to test whether the continuous variables conformed to a normal distribution. Categorical variables in different groups were expressed as percentages, while continuous variables (in line with normal distribution) were presented as mean ± standard deviation. Statistical significance was defined as \( p \)-values less than 0.05. To compare the levels of miRNAs between ccRCC and HC samples, t-tests were used for continuous variables, and \( \chi^2 \) tests were employed for categorical variables. The Kruskal-Wallis or Mann-Whitney tests were utilized for multiple comparisons across different independent stages. The diagnostic performance of each candidate miRNA was evaluated using receiver operating characteristic (ROC) curves and the area under the ROC curve (AUC). These measures were used to assess the specificity, sensitivity, and overall diagnostic ability of each miRNA. Furthermore, the Youden index \((J = \text{sensitivity} + \text{specificity} – 1)\) was calculated to determine the combination of miRNAs that offered the highest sensitivity and specificity for diagnosis. For statistical analysis, SPSS software (version 26.0, Chicago, IL, USA), GraphPad Prism 8 (Graphpad Software Inc, La Jolla, CA, USA), and MedCalc (version 19, MedCalc Software BVBA, Ostend, Belgium) were employed. The clinical characteristics of each group were presented as percentages, means ± standard deviation, or numbers (percentages) for continuous variables.

2.6 Survival Analysis and Bioinformatic Analysis

To assess the relationship between candidate miRNAs and the prognosis of ccRCC, a survival analysis was conducted using log-rank \( p \)-values. This analysis aimed to determine if there was a significant association between the expression levels of candidate miRNAs and the survival outcomes of ccRCC patients. To gain insights into the potential functions of these candidate miRNAs in ccRCC, miRNA Walk2.0 (http://mirwalk.umm.uni-heidelberg.de/) was utilized. This platform enabled the prediction of a series of target genes that could potentially be regulated by the candidate miRNAs. Additionally, miRNA Walk was em-
employed to investigate and validate interactions between the miRNAs and their respective target genes [21]. For further functional annotation and analysis of the predicted target genes, the Enrichr database (http://amp.pharm.mssm.edu/Enrichr/) was employed. This database facilitated the prediction of functional annotations and concentration analysis of target genes using gene ontology (GO) annotation and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses [22]. These analyses provided valuable information about the potential biological processes and pathways associated with the candidate miRNAs in ccRCC.

3. Results

3.1 Clinical and Demographic Characteristics of Study Participants

The study included a total of 220 participants, consisting of 108 ccRCC patients and 112 healthy control (HC) volunteers. All ccRCC patients were diagnosed using the TNM pathology staging system, and the histological classification followed the World Health Organization (WHO) standard [23]. It is worth noting that the ccRCC patients included in the study were diagnosed with primary ccRCC and did not have other carcinomas or metastatic carcinoma. The HC group comprised healthy volunteers who did not have any acute or chronic diseases, nor a history of other tumors. Table 1 presents the demographic and clinical characteristics of the participants in both the training and validation phases, including 108 ccRCC patients and 112 HCs. The statistical analysis conducted using the Wilcoxon-Mann-Whitney test revealed no significant differences between the ccRCC and HC participants in terms of age and gender. This suggests that age and gender are unlikely to confound the results obtained from the study.
3.2 Screening for Candidate miRNAs

The gene expression dataset GSE32960, available on the Gene Expression Omnibus (GEO) platform (GPI14722), was downloaded for the initial analysis. To identify differentially expressed miRNAs in ccRCC, GEO2R (http://www.ncbi.nlm.nih.gov/geo/geo2r) was utilized. Differentially expressed miRNAs were screened based on an adjusted _p_-value threshold of less than 0.05 and a log fold change (logFC) greater than 1. In addition to the computational analysis, a literature review was conducted to further refine the selection of candidate miRNAs relevant to ccRCC. Combining the findings from the differential expression analysis and the literature review, a total of 10 miRNAs associated with ccRCC were chosen as candidate miRNAs for subsequent investigation in the study.

3.3 Confirmation of Candidate miRNAs

To assess the serum levels of the 10 selected candidate miRNAs, RT-qPCR was performed on a random subset of 28 ccRCC patients and 28 healthy controls (HCs). As depicted in Fig. 2, the levels of miRNA-27b-3p, miRNA-212-3p, let-7f-5p, miRNA-142-5p, and miRNA-216-5p exhibited significant differences between ccRCC patients and HCs. Based on these findings, further analyses focused specifically on these five miRNAs.
<table>
<thead>
<tr>
<th>miRNA</th>
<th>AUC</th>
<th>p value</th>
<th>95% CI</th>
<th>Associated criterion</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>let-7f-5p</td>
<td>0.826</td>
<td>&lt;0.001</td>
<td>0.760–0.881</td>
<td>≤1.18</td>
<td>98.75</td>
<td>55.95</td>
</tr>
<tr>
<td>miRNA-142-5p</td>
<td>0.643</td>
<td>&lt;0.001</td>
<td>0.564–0.716</td>
<td>&gt;0.6</td>
<td>83.75</td>
<td>41.67</td>
</tr>
<tr>
<td>miRNA-212-3p</td>
<td>0.607</td>
<td>0.0158</td>
<td>0.528–0.682</td>
<td>≤0.98</td>
<td>63.75</td>
<td>59.52</td>
</tr>
<tr>
<td>miRNA-216-5p</td>
<td>0.690</td>
<td>&lt;0.001</td>
<td>0.613–0.759</td>
<td>≤1.19</td>
<td>78.75</td>
<td>48.81</td>
</tr>
<tr>
<td>miRNA-27b-3p</td>
<td>0.828</td>
<td>&lt;0.001</td>
<td>0.761–0.882</td>
<td>≤1.05</td>
<td>87.50</td>
<td>67.86</td>
</tr>
<tr>
<td>Three-miRNA panel</td>
<td>0.952</td>
<td>&lt;0.001</td>
<td>0.907–0.979</td>
<td>&gt;0.43845</td>
<td>95.00</td>
<td>84.52</td>
</tr>
</tbody>
</table>

AUC, Area Under the Curve; CI, Confidence Interval.

### 3.4 Diagnostic Value of the Five miRNA Candidates in the Validation Phase

To further investigate the potential of the five selected miRNAs as serum biomarkers for ccRCC screening, we expanded the sample size. An additional 80 ccRCC patients and 84 healthy controls (HCs) were included in the study. RT-qPCR was used to determine the relative serum levels of the five miRNAs. As shown in Fig. 3, the relative level of miRNA-142-5p was significantly higher in ccRCC patients compared to HCs. In contrast, the relative levels of the other four miRNAs (miRNA-27b-3p, miRNA-212-3p, let-7f-5p, and miRNA-216-5p) were lower in ccRCC patients compared to HCs. To evaluate the diagnostic value of these five miRNAs, ROC curve analysis was performed. The area under the ROC curve (AUC) for each miRNA is presented in Fig. 3B,D,F,H,J. The AUC values with their corresponding 95% confidence intervals (95% CI) were as follows:

- let-7f-5p (0.826, 95% CI: 0.760–0.881), miRNA-27b-3p (0.828, 95% CI: 0.761–0.882), miRNA-142-5p (0.643, 95% CI: 0.564–0.716), miRNA-212-3p (0.607, 95% CI: 0.528–0.682), and miRNA-216-5p (0.690, 95% CI: 0.613–0.759). The Youden index was then utilized to calculate the optimal cut-off values, specificity, and sensitivity for the diagnosis of ccRCC using the five miRNAs (Table 2). From the ROC curves, it is evident that miRNA-27b-3p, let-7f-5p, and miRNA-142-5p exhibited good diagnostic potential for ccRCC, with AUCs of 0.828, 0.826, and 0.643, respectively.

### 3.5 Identification of the Best miRNA Panel for Detecting ccRCC

During the validation phase, miRNA-27b-3p, let-7f-5p and miRNA-142-5p were found to have good diagnostic ability for ccRCC. Therefore, we investigated whether a combination of several miRNAs had even higher diagnostic value for ccRCC. Using a stepwise logistic regression model, results obtained with the 5 miRNAs during the validation phase were used to identify the best combination for ccRCC diagnosis from amongst all of the possible miRNA combinations. The formula for this model was: Logit(P) = 8.403 + (–6.411 × let-7f-5p) + (–5.659 × miRNA-27b-3p) + (4.345 × miRNA-142-5p). As shown in Table 2, the ROC curve for the combined diagnostic panel comprising the three miRNAs revealed an AUC of 0.952 (95% CI: 0.907–0.979; specificity = 84.52%, sensitivity = 95.00%). This result was superior to that of each single miRNA, as shown in Fig. 4.

### 3.6 Survival Analysis for let-7f-5p, miRNA-27b-3p, and miRNA-142-5p

Fig. 5 presents the results of the survival analysis conducted for the three miRNAs in ccRCC patients. MiRNA-27b-3p, let-7f-5p, and miRNA-142-5p demonstrated prognostic value in ccRCC. Specifically, high serum levels of miRNA-27b-3p and let-7f-5p, as well as low serum levels of miRNA-142-5p, were associated with an improved 5-year survival rate in ccRCC patients. These findings indicate that these miRNAs are not only helpful in the diagnosis of ccRCC but are also closely related to the prognosis of ccRCC patients.
3.7 Bioinformatic Analyses for let-7f-5p, miRNA-27b-3p, and miRNA-142-5p

In order to explore the potential target genes of let-7f-5p, miRNA-27b-3p, and miRNA-142-5p, miRNAWalk2.0 was employed. This analysis predicted a total of 261 genes as possible targets for these miRNAs. Further analysis was conducted using the Enrichr database to perform KEGG pathway enrichment analysis and GO functional annotation. The top 10 significant biological processes, cellular components, molecular functions, and KEGG pathways were ranked based on their $p$-values (Fig. 6). These findings suggest that the target genes of let-7f-5p, miRNA-27b-3p, and miRNA-142-5p are involved in critical pathways and processes associated with cancer development and progression. The enrichment of these target genes in cancer pathways and the p53 signaling pathway reflects their potential role in modulating crucial cellular functions related to tumorigenesis. In the context of GO functional annotation, the enriched biological processes indicate the involvement of these miRNAs in essential cellular responses to oxygen levels, regulation of vascular endothelial cell proliferation, and peptidyl-serine modification. These processes are known to play key roles in cancer development and angiogenesis. The identified cell components highlight the potential subcellular localization of the target genes, such as intracellular membrane-bound organelles, endoplasmic reticulum membranes, and dendrite cytoplasm. These cellular compartments are known to be important for various cellular processes and signaling pathways, which may be relevant to ccRCC pathogenesis [24]. Furthermore, the molecular functions associated with the target genes suggest their involvement in transmembrane receptor protein kinase activation, 5S rRNA binding, and DNA-binding transcription factor interactions. These molecular functions have implications in signal transduction, protein synthesis, and gene regulation, which are critical processes contributing to cancer development and progression. Overall, these bioinformatics analyses provide insights into the potential biological functions and mechanisms through which let-7f-5p, miRNA-27b-3p, and miRNA-142-5p may exert their effects in ccRCC. Further experimental studies are warranted to validate these predictions and unravel the precise roles of these miRNAs and their target genes in ccRCC pathophysiology.

4. Discussion

miRNAs are important members of the ncRNA family that lack the ability to encode proteins and could be considered as “transcription noise” [25]. However, an increasing number of studies have reported that miRNAs take part in many tumor biological processes via the regulation of target genes [26]. miRNAs are known to play important roles in the differentiation, translation, proliferation and apoptosis of tumor cells [27].
The present study aimed to improve the diagnosis of ccRCC and explore potential molecular mechanisms for targeted therapy by investigating the role of miRNAs in this disease. miRNAs have been increasingly recognized as important players in various human cancers, including ccRCC [13]. Consistent with previous studies, our findings confirmed that the relative expression of miRNA-142-5p in ccRCC tissues was significantly higher than in adjacent normal tissue \((p < 0.05)\). On the other hand, the relative expression levels of miRNA-27b-3p, let-7f-5p, miRNA-212-3p, and miRNA-216-5p were lower in ccRCC tissues. These differential expression patterns suggest that these miRNAs may be involved in the development and progression of ccRCC.

In terms of diagnostic potential, ROC curve analysis demonstrated that serum levels of miRNA-27b-3p, let-7f-5p, and miRNA-142-5p exhibited moderate diagnostic ability for ccRCC. This indicates that these miRNAs hold promise as potential non-invasive biomarkers for early detection and diagnosis of ccRCC. Survival analysis revealed that serum levels of miRNA-27b-3p, let-7f-5p, and miRNA-142-5p were correlated with the prognosis of ccRCC, suggesting their potential prognostic value.

Additionally, bioinformatics analysis using miRNAWalk2.0 predicted potential downstream target genes for these miRNAs. Genes that were predicted by two or more miRNAs were selected as the target genes, resulting in a total of 261 predicted genes. KEGG pathway enrichment analysis demonstrated that these genes were mainly enriched in cancer pathways, the p53 signaling pathway, and parathyroid hormone synthesis, secretion, and action. Taken together, our findings provide further evidence for the involvement of miRNAs in ccRCC pathogenesis. The dysregulation of miRNA-27b-3p, let-7f-5p, and miRNA-142-5p in ccRCC suggests their potential roles as diagnostic and prognostic biomarkers for this disease.

Furthermore, the predicted target genes and enriched pathways offer valuable insights into the potential molecular mechanisms underlying ccRCC development. It is important to note that further experimental validations and functional studies are necessary to confirm the role of these miRNAs and their target genes in ccRCC. Moreover, future studies should explore the potential therapeutic implications of targeting these miRNAs or their downstream pathways for the development of novel treatment strategies for ccRCC.

In conclusion, the differential expression of miRNA-27b-3p, let-7f-5p, and miRNA-142-5p in ccRCC patients, along with their correlation with ccRCC prognosis, highlights their potential as valuable biomarkers for the early diagnosis and prognosis of ccRCC. The identification of reliable biomarkers is crucial for improving patient outcomes through early detection, personalized treatment strategies, and monitoring disease progression. The dysregulated expression of these miRNAs suggests their involvement in the molecular mechanisms underlying ccRCC development and progression. The bioinformatic analysis provides additional insights into their potential biological functions, revealing their relevance to cancer pathways, the p53 signaling pathway, and parathyroid hormone synthesis, secre-
tion, and action. These findings suggest that these miRNAs may play important roles in key cellular processes and signaling pathways related to ccRCC pathogenesis. The use of miRNA-based biomarkers offers several advantages, including their stability in serum samples, non-invasive detection, and potential for early diagnosis. The development of a panel consisting of miRNA-27b-3p, let-7f-5p, and miRNA-142-5p as diagnostic markers for ccRCC could contribute to improved patient management by enabling timely intervention and treatment decisions. However, further validation studies in larger cohorts and diverse populations are required to confirm the diagnostic accuracy and clinical utility of these miRNAs. Additionally, functional studies are needed to elucidate the precise molecular mechanisms by which these miRNAs regulate ccRCC pathogenesis and to explore their potential as therapeutic targets.

5. Conclusions

This research, conducted in three stages comprising bioinformatics analysis, a training cohort stage, and a validation cohort stage, has identified novel serum miRNA markers for ccRCC. The findings of this study lend support to the potential utility of miRNA-27b-3p, let-7f-5p, and miRNA-142-5p as promising biomarkers for the early diagnosis and prognosis of ccRCC. Ongoing investigations in this field are anticipated to contribute to the advancement of innovative management strategies for ccRCC, ultimately enhancing patient outcomes.

Availability of Data and Materials

All results are included in the manuscript, and the original data can be requested from the corresponding author if there is a legitimate reason.

Author Contributions

The study was conceived and designed by QL and YQL. TH, CL, and WG conducted the majority of the experiments and data analysis, as well as contributed to the writing of the manuscript. ZJG, RKL, XJL, and CS were involved in the collection of clinical samples and obtaining patient informed consent. WTL and QSL performed data compilation and conducted bioinformatics analysis. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was explained to all participants, and each gave signed informed consent. This research was reviewed and approved by the medical ethics committee of Shenzhen People’s Hospital (SYJCYJ202102). In addition, the relevant regulations of the medical ethics committee of our hospital were strictly adhered to for the collection of serum samples and for the conduct of other study processes.

Acknowledgment

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Conflict of Interest

The authors declare no conflict of interest.

References


