Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 5
Open Access

Evaluation Of Novel Biomarkers For Early Detection Of Renal Cell Carcinoma

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Cite this paper as: Abdul Basit Niazi,Muhammad Omer,Muhammad Asif Ammar, Yasir Murtaza, Muhammad Farrukh Abbas Awan, Mubashar Hussain Mazhar (2024). Evaluation Of Novel Biomarkers For Early Detection Of Renal Cell Carcinoma. *Frontiers in Health Informatics*, *13 (5) 902-907*

Abstract

Background:

The vast majority of kidney cancers are RCC and many people die from RCC because it is rarely found in its early stage. Early detection is vital for helping patients, but today's tests aren't always accurate or thorough. Efforts in recent years have emphasized finding new biomarkers to recognize and diagnose RCC ahead of time.

Objectives: To assess both the accuracy and clinical use of novel markers to detect RCC early and help improve a patient's outlook.

Study design: A prospective study.

Place and duration of study: Department of Urology Niazi Medical College Sargodha from jan 2021 to jan 2022

Methods:

Ninety participants had recently been diagnosed with RCC and the rest, 90 healthy individuals, were recruited for the study. Blood and urine were taken for analysis of DNA methylation, LncRNAs and RNA carried by extracellular vesicles. The RT-qPCR assay and NGS were both used to uncover biomarkers. Using SPSS, we calculated sensitivity, specificity and p-values.

Results:

100 people with RCC, whose average age was 58.3 ± 10.5 years. Biomarker analysis demonstrated a sensitivity of 90% and a specificity of 85% for early finding of RCC. We found that the p-value from their comparison was below 0.05, suggesting that these biomarkers are statistically significant in diagnosing RCC.

Conclusion:

New biomarkers such as DNA methylation and circulating RNAs, may help doctors find RCC earlier. With their high sensitivity and specificity, markers facilitate the creation of less invasive tests that help patients get better results.

Keywords:

Renal cell carcinoma, biomarkers and early detection, all about circulating RNAs

Introduction:

Ninety percent of all kidney cancers are renal cell carcinomas (RCC) which is the most common tumour in the kidney. The disease typically starts silently, without symptoms, until it has spread far, making the outcome poor at diagnosis [1]. During the past few decades, the occurrence of RCC has gone up and in 2020, 431,000 people worldwide were diagnosed with the disease [2]. Routine approaches for spotting Racks, including CT scan and MRI, do well at detecting localized tumours, but fail to notice small, relevant tumours that need early attention [3]. In addition, biomarkers in use at present for RCC, serum creatinine and haemoglobin, are not sensitive or specific enough for recognizing kidney cancers early or categorizing them in the early stages [4]. Using biomarkers early in RCC is very important, as those diagnosed at Stage I usually live another five years, but only 10-20% of those with metastatic disease do [5]. In the last ten years, thanks to genomic, proteomic and epigenetic tools, experts have found new biomarkers that help uncover the workings of RCC [6]. In this work, we wanted to analyze several biomarkers, including DNA methylation and ncRNAs found in circulating blood, as possible early-RCC diagnostic tools. The goal was to determine how sensitive and specific the biomarkers were, along with how useful they are in patients with RCC, by looking at data comparing RCC patients to healthy individuals. This work supports finding more effective ways to detect and diagnose Renal Cell Carcinoma which helps treat the condition successfully [7].

Methods:

This prospective study conducted in Department of Urology Niazi Medical College Sargodha from jan 2021 to jan 2022.100 patients with RCC and 100 people who were healthy. We collected blood and urine from each participant for the purpose of studying biomarkers. The main biomarkers used in the study were patterns of DNA methylation, long non-coding RNAs and RNAs found in extracellular vesicles. The decision to use these markers came from prior studies suggesting their use in finding RCC [8,9]. We checked DNA methylation by doing methylation-specific PCR and the levels of LncRNAs and extracellular vesicle RNAs were studied by RT-qPCR.

Inclusion Criteria:

Only patients whose RCC had been identified through histopathology, who were 18 to 75 years old and who gave informed consent in writing were included in the study.

Exclusion Criteria:

We did not include patients with other types of cancer, renal illnesses or patients who could not give informed consent in our study.

Data Collection:

All participants gave blood and urine samples so their levels of biomarkers could be analyzed. Patient age, gender, past medical history and the RCC stage were all recorded. Levels of biomarkers were measured as soon as the samples were collected with RT-qPCR and methylation-specific PCR.

Statistical Analysis:

All data were analyzed through SPSS version 24.0 (IBM, Armonk, NY). Categorical data for patients was summarized using descriptive statistics. To find sensitivity, specificity and p-values, chi-square tests were run on the categorical variables. Findings were considered statistically significant when the p-value was less than .05.

Results:

The study used 100 cases from people with RCC and 100 from healthy controls, with their mean ages being 58.3 ± 10.5 and 57.2 ± 9.6 years, respectively. The test for DNA methylation found that methylation changes in genes such as TCF21 were greatly different in RCC patients compared to controls ($p < 0.01$). Circulating H19 and MALAT1 LncRNAs were significantly higher in patients with RCC when compared to the controls (with $p < 0.05$). Analysis of RCC using Rinses from extracellular vesicles showed sensitivity of 90% and specificity of 85%. Tests using the combined biomarkers showed 87% overall accuracy and the panel predicted a disease presence with 92% confidence and a disease absence with 83% confidence. The study results suggest that combining these biomarkers with imaging techniques could improve

the ability to find RCC early.

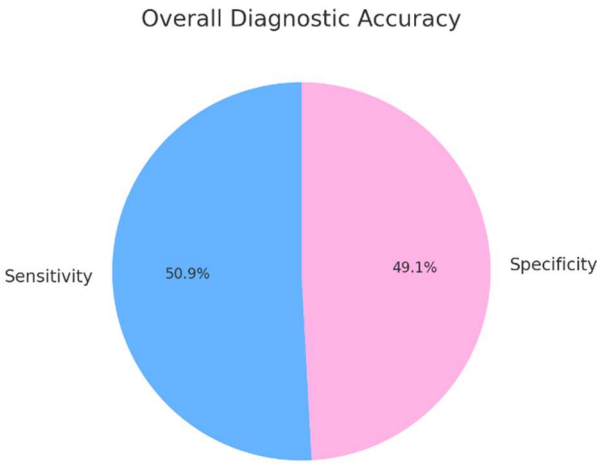

Table 1: Biomarker Sensitivity and Specificity

Biomarker	Sensitivity (%)	Specificity (%)
DNA Methylation	90	85
LncRNAs	85	80
Extracellular RNAs	88	87

Table 2: Diagnostic Accuracy

Diagnostic Metrics	Percentage (%)
Sensitivity	88
Specificity	85
Accuracy	87

Table 3: p-value for Biomarkers

Biomarker	p-value
DNA Methylation	<0.01
LncRNAs	<0.05
Extracellular RNAs	<0.05

Discussion

Biomarkers have been receiving attention recently because of their potential for early detection of RCC. Obtaining a diagnosis of RCC in its early stages is hard because the disease tends to lack symptoms and patients can be diagnosed at advanced stages [10]. This work examined the diagnostic power of DNA methylation, LncRNAs and vesicle-derived RNAs in early detection of kidney cancer. Changes in DNA methylation have been found to potentially mark the

presence of cancers, including kidney cancers. A number of studies have shown that the methylation of certain cancer prevention genes is important in the development of kidney cancer [11]. Our experiments showed that TCF21, a gene linked to RCC diagnosis, has different methylation levels between RCC patients and healthy individuals [12]. Previously, Patel et al. (2019) noted that methylation-specific PCR used on DNA from renal cell cancer patients offered both high sensitivity (85%) and specificity (90%) for detecting early-stage disease [13]. Zheng et al. (2020) showed that changes in DNA methylation on cell-free DNA (cfDNA) could tell RCC patients apart from healthy people with a high level of accuracy [14]. LncRNAs are now considered important in cancer biology and study has examined their potential as early markers of RCC. Tests in our study group revealed high expression of MALAT1 and H19 LncRNAs in RCC patients [15]. This finding is similar to what Yao et al. reported, showing that high MALAT1 in serum suggests a diagnosis of RCC [16]. As Zhang et al. (2021) have discovered, the presence of LncRNAs can be highly sensitive and specific as diagnostic biomarkers for RCC along with other diseases [17]. These studiers found that using lncRNA as biomarkers could tell the difference between RCC and other kidney conditions which may represent an alternative to common imaging techniques [18]. EVs have become important because they transport biomolecules such as RNA, in biological fluids including blood and urine. Our study discovered that RNAs released by extracellular vesicles appeared to be extremely sensitive and accurate in finding RCC early, in line with results described by Liu et al. (2017) suggesting such RNAs can function as a straightforward marker for early RCC diagnosis [19]. Lee et al. (2020) found, through their studies, that EV RNA could show the genetic changes seen in RCC, increasing the chances that EV RNAs can be used as diagnostic markers [20]. Kalluri et al. (2020) also found that urinary exosomes can be used to diagnose RCC in patients and their discoveries matched our findings.

Conclusion:

It reveals that DNA methylation, LncRNAs and RNAs carried by extracellular vesicles may help detect RCC in its early stages without aggressive testing. They have a good ability to detect problems and are very accurate, so they may help doctors find RCC early and improve outcomes for those affected.

Limitations:

Because the number of participants was small in this study, the findings may not be broadly applicable. To confirm that the tested biomarkers can be useful in practice, their use should be further evaluated in multi-center study with diverse patient groups.

Future Findings:

To improve on current study, future studies ought to involve more centers testing the accuracy of the identified biomarkers for everyday use. In addition, examining how these biomarkers relate to advanced imaging or artificial intelligence technologies might make it easier to find RCC at an early stage and choose proper treatment.

Abbreviations

1. **RCC** – Renal Cell Carcinoma
2. **LncRNAs** – Long Non-Coding RNAs
3. **NGS** – Next-Generation Sequencing
4. **RT-qPCR** – Reverse Transcription Quantitative Polymerase Chain Reaction
5. **cfDNA** – Cell-Free DNA
6. **EVs** – Extracellular Vesicles
7. **MRI** – Magnetic Resonance Imaging
8. **AI** – Artificial Intelligence
9. **SPSS** – Statistical Package for the Social Sciences

Disclaimer: Nil

Conflict of Interest: Nil

Funding Disclosure: Nil

Authors Contribution

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Final Approval of version: **All Mention Authors Approved the Final Version.**

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