Lungs Cancer Detection through Biosensors: Current Scopes and Limitations

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Abstract

It is evident that saliva contains many biomarkers that may help in noninvasive diagnosis of many diseases. There is also a direct contact between saliva and oral cancer lesions that may be helpful in the early detection of lung cancer. This review represents different biosensors that are in use for various medical applications, which can be further utilized to detect cancers. However, specific, accurate, and high sensitive biosensors are required because the cancer biomarkers have less concentration in saliva. Patients suffering from lung cancer have some biomarkers that are not found in healthy patients and can be useful in the early detection of disease. Currently, a single method is not enough to detect lung cancer from saliva. So, in order to get true positive results, some considerations must be taken while interpreting results from biosensors. Moreover, a combination of other technologies and comparing results with healthy persons will allow us to diagnose lung cancer in the future.

Keywords: Cancer biomarkers, Types of biosensors, Sensor based limitations

1. Introduction

In humans, oral fluid originates mainly from three pairs of major salivary glands (parotid, sublingual, and submandibular) and a large number of minor salivary glands are used for the detection of gland-specific pathology such as infection and obstruction [1]. Due to easy sampling, risk free transportation and non-invasiveness, saliva is in research to detect other pathologies particularly cancer. R. S. P. Malon et al., discussed that saliva can provide very useful information for clinical diagnosis and prognosis of cancers. In order or detect biomarkers

from body fluids ELISA and biosensor based techniques are common. Low levels of biomarkers can be measured by them in physiological samples which can assist in the diagnosis of cancer at an early stage because of their lower minimum detection limits [5].

Biosensors are already in use medical filed they can detect blood-glucose level, Urinary tract infections, pathogens, cardiovascular diseases, and many types of cancer. The presence or absence or change in the level of the specific biomarkers in a cell often indicate cancer development [9]. Early detection of lung cancer biomarkers from saliva can be helpful to treat the patient on early basis.

In this study different biomarkers related to cancer, and other pathologies were discussed and try to find the ability of biosensors to detect lungs cancer from currently known biomarkers. Wong et at., discussed that CCNI, EGFR, LZTS, BRAF, FRS2, ANXA1 and combination with others biomarkers differentiate the health persons form patients. It was also found that some fluorescence biosensors have ability to detect these biomarkers from saliva.

Questions

Can biomarkers in saliva be helpful in the early detection of lung cancer?

How will biosensors improve the detection of cancer?

2. Method

2.1 Level of Details

Pubmed and google scholar database were used to search the literature.

2.2 Inclusion and Exclusion Criteria

Studies which carry cancer biomarkers details particularly saliva biomarkers were included. Only studies that were conducted from 2012 to 2020 and reported in the English language were included. Then studies related to the detection of disease by biosensors were also added in the group. Studies with copyright or permission issues were excluded.

2.3 Search Strategy

Targeted literature was searched with specific keywords such as “biomarkers, saliva early detection, and lung cancer”. No experts, scientists, engineers, or researchers were added externally. Single researcher solely did it. Only published papers were included in the whole review.

2.4 Selecting Appropriate Sources

Citations were downloaded into the endnote library to keep track of them. Some studies were excluded i.e. related to manufacturing of biosensor and not containing saliva as per determined criteria. Full-text manuscripts were included in the study. The database showed 50 papers references, a total of nine were included.

2.5 Quality Assessment

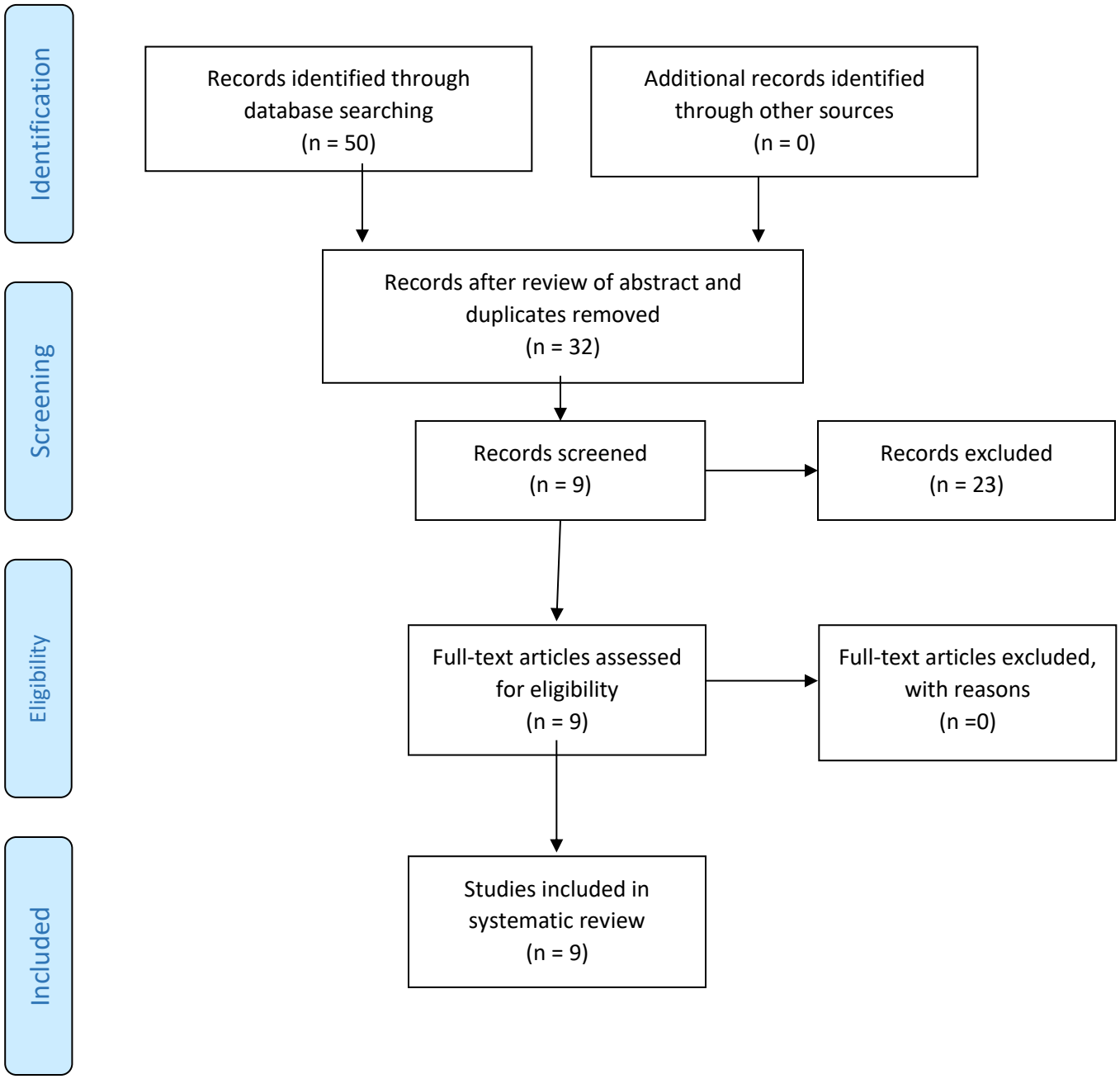
Critical appraisal skills programme (CASP) checklist was used as criteria to eliminate biasness and include relevance.

2.6 Data Extraction

Data was directly extracted on MS Word. Some information was truly based on the cancer biomarkers, and other encompassing biomarkers in different fluids of body. Finally,

saliva biomarkers were extracted and enlisted in the excel sheet. Data was grouped into one category and present it into tabulated form.

Figure1. PRISMA Flow Diagram



3. Results

I found 50 articles combining PubMed and google scholar. After screening and finding eligibility 9 articles were selected and included in the review. Data was systemized (see Table 1.) that represents researchers, source, biomarkers, and the biosensors used to detect specific biomarkers. Topics of areas related to biosensors in saliva detection, biomarkers in saliva, and cancer biomarkers detection were included.

3.1 Biomarkers in Saliva

Two studies were evident that saliva contains many biomarkers that may help in noninvasive diagnosis of many diseases. If the full potential of saliva biomarkers detection is achieved, it will provide better management, fast and risk-free diagnosis.

3.1.1 Cancer Biomarkers

Two studies (see Table 1.) suggested that in cancer diagnosis, there is direct contact between saliva and oral cancer lesions, IL-8, tumor necrosis factor-alpha, and salivary transferrin. For head neck squamous cell carcinoma, CD44 Ag is in use as a biomarker. One study indicated that saliva also contains lung cancer biomarkers. It was confirmed that salivary protein, the product of oncogene c-erbB-2, and cancer Ag 15-3 is useful for early detection of breast cancer, and patient response towards treatment [1].

3.1.2 Other Biomarkers

Malon et al in separate studies described the common biomarkers in saliva i.e. glucose, lactate, phosphate, alpha-amylase, hormones, and antibodies.

It was evident that there are certain biomarkers in saliva that can be related to cancer (see Table 1.).

3.2 Early Detection of Biomarkers

Two studies suggested that the devices based on saliva biomarker detection will ease the healthcare services domestically, as no expertise will be required to operate them. One study gives clear results that the logistic regression model combining five of the mRNA biomarkers (CCNI, EGFR, FGF19, FRS2, and GREB1) could differentiate lung cancer patients from normal control subjects [8]. It was confirmed that salivary mRNA biomarkers possess the discriminatory power for the detection of lung cancer [8].

3.2.1 Development of Biomarkers

Several biosensors including SPR, surface-immobilized optical protein sensor, label-free fluorescent biosensor(see Table 1.) are in use that detect cancer biomarkers, but specific, accurate and high sensitive biosensors are required because the cancer biomarkers have less concentration in saliva"[1].

3.2.2 Methods of Detection

Comparison of the novel and current methods of biomarkers detection gave clear evidence that conventional techniques like ELISA and PCR are manual, time-consuming, and require reagents, which makes the diagnosis so laborious one study confirms cancer. Three studies suggested that different biosensors (electrochemical, optical, mass-based, and calorimetric) are used to detect biomarkers to diagnosis different diseases as they have fast and labor free detection method.

It was observed that saliva of lungs cancer patients has some biomarkers that are not found in healthy patients, and biosensors can be useful in early detection of biomarkers.

3.3 Role of Biosensors In Cancer Detection

Two studies assessed that biomarker-based detection plays a significant role in prompt diagnosis and subsequent treatment. Various studies assessed that biosensors are being used in healthcare areas related to cardiovascular, diabetes, wound healing, cancer, artificial limbs, bio manufacturing, organ-on-chip, and regenerative medicines.

3.3.1 Different Types of Biosensors

One study described the types and structure of biosensors. Biosensors' core components include bio receptors and transducers. Bio receptors either enzymatic based or affinity-based when interacted with specific analyte produces electrical activity. Different transducers (electrochemical, optical, and piezoelectric) are used to get quantifiable data from the biological organs.

It was found that different biosensors are already in use in medical application, which can be further utilized to detect cancers.

3.3.2 Selectivity and Specificity of Biosensors

Data from two studies suggested that biosensors are evaluated on different factors i.e. sensitivity, measurement range, response time, accuracy, precision, resolution, reproducibility, the limit of detection, and hysteresis. Glucose biosensors are used to regulate the production in saccharification and fermentation in the fermentation process. Tissue-based biosensors are used to detect the biosynthesis of proteins and quite helpful in biological applications. For example, the HfO2 sensor is employed to detect antigens [2].

3.3.2.1 Biosensors Ability to Detect Biomarkers

Genomic and proteomic profiling, as well as next-generation sequencing [4] is helpful to detect new biomarkers by biosensors. It has been demonstrated that biosensors have the potential for continuous measurement and detection of cancer biomarkers. Efficient biosensors will detect the change in cell structure quickly and precisely which will help to detect cancer at developmental stages. Moreover, multiplex detection is essential for the proper diagnosis of cancer. However, some of the biosensors e.g. electrochemical possessed the capability to quantify biomarkers in a wide range from fg mL-1 –ng mL-1[4].Different biosensors are mentioned in Table 1. that are in use to detect different cancers.

3.3.2.2 Advantages of Biosensors over Older Techniques

One study showed that biosensors have a major advantage that they can simultaneously detect many biomarkers. Furthermore, Optical biosensors can detect P53, EGFR, ALCAM, CA 19-9, TAGLN2; Mass-based biosensors can detect CA125, PSA, P53 mutation; electrochemical biosensors can detect HER2, PNA, VEGF, PSA; and colorimetric biosensors can detect HER2/neu.

Biosensors detects cancer biomarkers automatically, but they must be specific and should have required selectivity.

3.4 Limitations in Detecting Biomarkers of Lung Cancer

There can be benefits of detecting biomarkers to diagnose cancer but one study clarifies those complications and normal processes that can lead to false-positive results. In order to get true positive results, some considerations must be taken while interpreting results from biosensors. If errors are there in readings than results will be inaccurate so what are common factors that may lead to false results should be known before research that this article discussed.

3.4.1 Biomarker Based Limitations

In contrast to four studies one study states that saliva might not be the ideal material for a cfDNA quantitative test, and scfDNA concentration is not applicable for NSCLC diagnostics [8].

3.4.2 Technical Limitations Related To Biosensors

One study referred that other diseases may also lead to bad and false-positive results. However, their commercialization is still in the process due to limited sensitivity, selectivity, real-time analysis, and significant costs.

One study disapproved the exactness of lungs cancer detection by current biosensors, but combination of other technologies and comparing detection results of patients with healthy persons, will allow to detect lungs cancer in future.

Table 1. Biomarkers and Biosensors

Reference	Source	Biomarker	Biomarker Type	Biosensor
R. S. P. Malon	Saliva	Il8,tumor necrosis factor-alpha,salivary transferrin,cyfra 21-1	Oral cancer	Surface immobilised optical protein sensor
R. S. P. Malon	Saliva	Cd44 ag	Head and neck squamous cell carcinoma	Not mentioned in study
R. S. P. Malon	Saliva	Tissue polypeptide ag,cancer ag 125,salivary zinc finger protein 510 peptide	Oral cancer	Not mentioned in study
R. S. P. Malon	Saliva	Kras, mbd3l2, acrv1, and dpm1	Pancreatic cancer	Not mentioned in study
R. S. P. Malon	Saliva	C-erbb-2 and cancer ag 15-3 (ca15-3)	Breast cancer	Spr biosensor based on thin film au/zinc oxide
R. S. P. Malon	Saliva	Glucose	Other	Electrochemical & optical

R. S. P. Malon	Saliva	Lactate	Other	Electrochemical & electrochemiluminescent
R. S. P. Malon	Saliva	Phosphate	Other	Electrochemical
R. S. P. Malon	Saliva	Alpha-amylase	Other	Electrochemical ‹electrochemiluminescent & optical
Wong et al	Saliva	CCNI,EGFR,LZTS,BRAF,FRS2,ANXA1 + combination with others	Lung Cancer	Not mentioned in study
P. Patel	Other	Ca 125	Ovarian cancer	Mass-based biosensors
P. Patel	Other	Ca 19-9	Colon and pancreatic cancer	Optical biosensors
P. Patel	Other	Rcas1	Gastric cancer	Optical biosensors

4. Discussion

The purpose of this study was to find that if it is possible to diagnose lung cancer through biosensors using human saliva. Different types of biosensors and their current role was studied, and biomarkers in saliva were extensively extracted.

4.1 Analysis of lungs cancer biomarkers in Saliva

It was hypothesized that there will be a large number of lungs cancer biomarkers in saliva as lung's air directly passes by contacting mouth saliva. But reality is that only one study discussed that biomarkers of lung cancer are found in the saliva (see Table 1).

4.2 Biosensors to detect lungs cancer from saliva

Studies discussed different bio sensors that are already in use to diagnose cancers for example FERT, biosensor, enzymatic biosensors and many others. Mostly electrochemical biosensors are effective in finding pathologies in saliva.

4.3 Conclusion

Some studies lead me to very tentative conclusion that there will be many biomarkers in saliva that will surely help in diagnosing lungs cancer. But it was found there is gap in literature to relate lung cancer biomarkers and their detection by biosensors. Collectively different types of biosensors, saliva biomarkers and cancer biomarkers were found effective in early diagnosis of cancers. But there are some limitations at that moment only a single method to detect cancer from lungs is not effective. By combining conventional techniques with biosensor based techniques can only help to detect lungs cancer.

Major References

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