Review Article

Methods for detecting of cardiac troponin I biomarkers for myocardial infarction using biosensors: a narrative review of recent research

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Background and Objective: In cardiovascular diseases (CVDs), acute myocardial infarction (AMI) is considered one of the leading causes of human death, and its diagnosis mainly relies on the detection of the cardiac biomarker troponin I. Traditional detection methods have certain limitations, which has prompted the development of methods with higher sensitivity and specificity. In recent years, biosensors, as an emerging technology, have been widely applied in the clinical medicine and biodetection fields. We retrieved and reviewed relevant articles published over the past 3 years and subsequently summarized the research progress of different types of biosensors in detecting cardiac troponin I and the challenges faced in achieving simple, specific, and portable point-of-care testing (POCT) technology for bedside rapid detection. The aim of this review is to serve as reference for the early diagnosis and treatment of CVDs.

Methods: This study searched for relevant literature published from 2019 to 2022 in the PubMed database of the National Center for Biotechnology Information (NCBI). The keywords used were as follows: "cardiac troponin I", "biosensor", "point-of-care testing", "electrochemical detection", and "surface-enhanced Raman spectroscopy".

Key Content and Findings: The review found that biosensor technology has high specificity and sensitivity in the detection of cardiac troponin I and is simpler and more convenient than is traditional laboratory testing. Its vigorous development can facilitate the diagnosis of AMI earlier and faster.

Conclusions: This study reviewed the progress of cardiac troponin I detection based on biosensing strategies. We found that cardiac troponin I detection methods based on biosensing strategies have their own advantages and disadvantages in clinical applications, and their sensitivity has been constantly improved. In the future, the detection of cardiac troponin I using biosensing technology will be simpler, faster, more sensitive, and portable.

Keywords: Cardiac troponin I (cTn I); biosensor; point-of-care testing (POCT); electrochemical detection; surface-enhanced Raman spectroscopy (SERS)

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Introduction

Cardiovascular diseases (CVDs) constitute an increasingly serious epidemic with high morbidity and mortality rates worldwide. Acute myocardial infarction (AMI) is one of the leading causes of death related to CVDs, and thus the timely and accurate diagnosis of AMI is crucial (1,2).

Physicians mainly diagnose patients with AMI based on clinical manifestations, electrocardiography (ECG), and changes in cardiac biomarker levels (3). Among these strategies, the continuous measurement of cardiac biomarker troponin plays a key role. Troponin is composed of 3 regulatory proteins, including cardiac troponin C (cTn C), cardiac troponin I (cTn I), and cardiac troponin T (cTn T). cTn I, with its high specificity and sensitivity, has become the gold standard for diagnosing AMI (4). International guidelines recommend using high-sensitivity cardiac troponin (hs-cTn) detection and the 99th percentile upper limit as the threshold for diagnosing myocardial infarction (5).

Researchers have extensively explored methods for detecting troponin, including enzyme-linked immunosorbent assay (ELISA), chemiluminescence, fluorescence analysis, gold-labeled immunoassay, and immunoturbidimetry, each of which has a valuable role in detection. Over the past decade, many studies have combined biosensors, nanomaterials, and immunoassays to develop ultrasensitive sensing technologies, achieving higher sensitivity (6-9). Biosensors are an emerging molecular biotechnology with certain advantages, such as high analytical sensitivity, strong specificity, ease of use, and low cost. They are now widely applied in the clinical medicine and biodetection fields. This paper reviews the progress of cTn I detection based on biosensing strategies and discusses the challenges faced by portable point-of-care testing technology in achieving the early-as-possible diagnosis and treatment of CVDs. We present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1263/rc).

Methods

This study was conducted in the digital library of Nanjing Medical University in Jiangsu, China. Ethical approval or permission was not required, as the study did not directly involve animal or human subjects. Relevant literature on the definitions, types, and applications of biosensors in cardiac troponin I detection was collected. All data were obtained from the PubMed database of the National Center for Biotechnology Information (NCBI). For data collection, we used the following medical subject headings (MeSH) terms and their combinations in the title or abstract: "cardiac troponin I", "biosensor", "point-of-care testing", "electrochemical detection", and "surface-enhanced Raman spectroscopy". *Table 1* outlines the details of the search strategy.

Types of biosensors for detecting cardiac troponin I

Biosensors rely on biological molecules such as antibodies, aptamers, and enzymes as target recognition elements to convert the interaction between these elements and corresponding target molecules into quantifiable signals for detection by immobilizing them on transducers (10,11).

There are 2 main types of biological elements used to recognize cTn: antibodies and aptamers. Due to their high specificity and affinity, antibodies have become the mainstay of biological molecule recognition in practical applications (12). Aptamers, which are short single-stranded DNA or RNA molecules, are capable of binding to target molecules based on the diversity of single-stranded nucleic acid structures and spatial conformations. They also have advantages such as easy in vitro production, biocompatibility, convenient modification, and a broad range of potential targets (13,14).

Nanotechnology is an emerging, dynamic, multidisciplinary field. Nanomaterials possess unique mechanical, electrical, catalytic, thermal, magnetic, and imaging properties and come in various forms, such as nanoparticles, nanoflowers, nanofibers, and nanotubes. They have been used in cardiac troponin biosensor research to enhance biosensor performance (15).

Gold nanoparticles are the most commonly used nanoparticles, exhibiting surface plasmon resonance on the nanoscale. This prominent feature enables their wide application in chemical and biosensing (16). For example, Bai *et al.* developed citrate-capped trimetallic Au@Ag-Pt nanoparticles through seed growth and galvanic replacement reactions under convenient conditions. The bell-like structure endowed the Au@Ag-Pt nanoparticles with peroxidase-like activity while retaining plasmonic properties with strong colors in the visible range. This study successfully achieved the ultrasensitive colorimetric detection of human cTn I as low as 20 pg/mL (17). Khushai

Table 1 The search strategy summary

Item	Specification
Date of search	October 1, 2022, to January 31, 2023
Databases and other sources searched	NCBI, PubMed
Search terms used	"cardiac troponin I", "biosensor", "point-of-care testing", "electrochemical detection", and "surface-enhanced Raman spectroscopy"
Time frame	March 1, 2019, to January 31, 2023
Inclusion criteria	Literature published in English from March 1, 2019, to January 31, 2023, was collected. The literature was mainly related to the medical field, especially cardiovascular diseases
Selection process	Chen Q, Wu W, and Han Z jointly collected and collated the data. The information was then classified and analyzed by Chen Q

NCBI, National Center of Biotechnology Information.

et al. developed a FET-based biosensing technique by connecting solid-state devices and biorecognition elements with porous carbon nitride modified by gold nanoparticles, with indium, gallium, and zinc oxide serving as a suitable semiconductor channel. The biosensor had a detection limit of 6.6 pg/mL and a dynamic range of 10–10^6 pg/mL (18).

MoS_2, a 2D nanomaterial, is widely used due to its large surface area and numerous exposed active edges. Wang *et al.* established a sandwich-type ECL immunoassay for cTn I detection, in which molybdenum disulfide@cuprous oxide-silver nanoparticles (MoS_2@Cu_2O-Ag) immobilized cTn I as a capture antibody (Ab_1), and Ce-doped zinc oxide@nitro-embedded graphene quantum dots (Ce:ZnO@NGQDs) loaded signal antibody (Ab_2). The MoS_2@Cu_2O-Ag nanoparticles not only had good conductivity and biocompatibility but also a large specific surface area. Ce-doped zinc oxide acted as a c-reactant promoter, enabling the transformation of the $Ce^{4+}\leftrightarrow Ce^{3+}$ reaction and accelerating electron exchange, thus achieving signal enhancement. Under optimal conditions, the sensor had a detection limit of 0.0029 pg/mL (19).

However, MoS_2 has low conductivity, and van der Waals forces between layers tend to cause agglomeration. Reduced graphene oxide has active edge centers and excellent electrical properties, which can effective improve MoS_2's electrochemical activity and further amplify the signal. For example, Li *et al.* proposed a novel aptamer-based electrochemical sensor composed of silver nanoparticles, molybdenum disulfide, and graphene oxide. The combination of these three materials provided a synergistic effect for the stable immobilization of nucleic acid aptamers. The optimized aptamer sensor had a linear range of 0.3–200 pg/mL and a detection limit of 0.27 pg/mL for cTn I detection (20).

In order to develop sensors for cTn I with high sensitivity and specificity, antibodies, aptamers and a variety of nanomaterials have been used in various sensors, including electrochemical, chemiluminescence, colorimetric, surface plasmon resonance, surface-enhanced Raman spectroscopy (SERS), and fluorescence biosensors (21).

Electrochemical biosensors

Electrochemical biosensors have advantages, such as easy handling, portability, and good integration, and are easily self-assembled with antibodies and aptamers as recognition elements. Electrochemical biosensors can be divided into several types, including voltammetric, potentiometric, electrochemical impedance spectroscopy, electrochemical luminescence, and field-effect transistors signal sensors (21,22).

The working principle of voltammetric biosensors is to apply voltage to the working electrode as a signal input and then to detect the signal output by measuring the current (22). For example, Villalonga *et al.* constructed a novel amperometric aptasensor for specific detection of cTn I using a carboxyethylsilanetriol-modified graphene oxide as the sensing element, which can easily and highly load aminated DNA aptamers on the electrode surface, forming a sandwich structure with a novel aptamer-peroxidase conjugate as the signal element. The detection range of the sensor is 1–10^6 pg/mL, with a detection limit of 0.6 pg/mL. The authors also tested the sensor on voluntary donor

serum samples and compared it to a chemiluminescent procedure assay, achieving a low relative error of 9.2%. It was shown that the sensor is also highly reliable and accurate in the analysis of real samples (23).

The working principle of potentiometric biosensors is to record the potential accumulated on the working electrode. For example, Ni *et al.* reported a new 1-step potentiometric immunoassay. First, cTn I biomolecules were immobilized on the surface of gold nanoparticles (AuNPs) functionalized screen-printed graphite electrodes (SPGEs); then, rabbit anti-cTn I polyclonal antibodies were covalently coupled to di-dimethylmethylphenol dendrimers via a typical carbodiimide coupling method. As the target cTn I increased, the dendrimers were captured by the immunosensor decrease, resulting in a change in electrode potential. The potentiometric immunosensor has a good potential response to cTn I, with a linear detection range of 1–10^5 pg/mL and a detection limit of 7.3 pg/mL. Serum specimens from patients with cardio-cerebrovascular diseases were tested using this sensor and a commercial cTnI ELISA kit, respectively. The RSD of both was less than 12% (7).

Electrochemical impedance spectroscopy (EIS) is a highly sensitive technique that relies on the amount and conductivity of surface-adsorbed materials (24). Palanisamy *et al.* constructed a 3D immunosensor based on a metal-organic framework (MOF)-loaded nickel foam (NF). The biosensor was prepared by modifying the substrate with MOF material to achieve amine-functionalized electrodes, with a detection limit of 0.013 pg/mL and high specificity (8).

Electrochemiluminescence (ECL) detection of cTn I has certain advantages, such as high luminescence intensity, simple operation, low cost, and low background signal, and has become a new technology for clinical diagnosis. For example, Wang *et al.* constructed a solid-state ECL immunobiosensor based on a sandwich-type silica nanofilm, using a new electrochemiluminescence signal amplification strategy based on photonic crystal nanofilm light-scattering enhancement. A novel tightly packed monolayer silica film was fabricated as a solid-state electroluminescent electrode to achieve signal amplification. Under optimal conditions, the immunosensor had a detection limit of 0.0056 pg/mL for cTnI (25). Additionally, Du *et al.* established a label-free differential electrochemiluminescence immunosensor, which effectively eliminated cumulative errors, showing higher sensitivity, selectivity, and accuracy, with a detection limit of 0.00501 pg/mL and a detection range of 0.01–10^3 pg/mL (9).

Field-effect transistor (FET) biosensors are based on metal oxide field-effect transistors, with gate control induced by the response of biomolecules to changes in surface charge. For example, Chang *et al.* developed a silicon nanowire (SiNW) FET (SiNW-FET) biosensor device using a top-down fabrication process compatible with metal oxide semiconductor (MOS) technology. After fabrication, the SiNW surface was modified with cTn I monoclonal antibody (Mab-cTn I) to covalently immobilize the cTn I antigen. The device had a minimum detection limit of 16 pg/mL and a detection range of 25–500 pg/mL (26).

In summary, electrochemical biosensors have high sensitivity, high specificity, good stability, wide linear range, and low detection limits. However, they also face a few challenges, such as a time-consuming fabrication processes and difficulties in clinical application. In the future, by combining these methods with new technologies, their performance in clinical testing can be further improved.

Colorimetry

Colorimetry is a technique that uses color changes of indicators to determine the concentration of a target in a solution (27). Enzyme-linked immunosorbent assay (ELISA) is one of the traditional colorimetric immunoassays and uses enzyme-coupled antibodies to directly or indirectly catalyze color reactions for quantification. Commonly used enzymes include horseradish peroxidase (HRP), alkaline phosphatase (ALP), and β-galactosidase.

However, traditional ELISA methods have limited sensitivity, complex operations, and high costs, and thus efforts to improve this method have been made. For example, Wen *et al.* constructed a 3-dimensional nanoenzyme-catalyzed nanoreactor by confining MOF-818 nanoenzyme within the pores of mesoporous tungsten trioxide (p-WO_3) for the selective colorimetric detection of cTn I, with a linear range of 0.05–10^5 pg/mL and a detection limit of 0.018 pg/mL. The spiked healthy human serum samples were tested by the proposed aptasensor. The assay results were in good agreement with commercial ELISA kits (28).

Zhang *et al.* proposed an electrochemical-colorimetric dual-mode imprinting sensing strategy. First, they constructed an aptamer-functionalized Fe^{3+}-polydopamine (Apt@Fe^{3+}-PDA) as a sacrificial beacon for the preparation of recognition-site magnetic molecularly imprinted polymers for cTn I. Once cTn I was captured, the beacon formed a sandwich-like complex through binding with the aptamer. Under acidic conditions, Apt@Fe^{3+}-PDA dissociated, releasing a large amount of Fe^{3+} ions, which

then converted to Prussian blue. Using this sensor, the limit of detection values of the electrochemical method and colorimetry were 3.2 and 7.4 pg/mL, respectively (29).

Chemiluminescence

Chemiluminescence is a detection technique that relies on the generation of photons triggered by various redox or hydrolysis reactions from substrates and does not require incident excitation light, providing a higher signal-to-noise ratio and a broader dynamic range (30).

To improve detection sensitivity, signal enhancers can be used as electron transfer mediators, including substituted phenols, substituted boronic acids, indoxyl, N-alkyl phenothiazine, 4-dialkyl aminopyridine, Co(II), Co single-atom catalysts, and poly[(N-isopropylacrylamide)-co(methacrylic acid)] (21). For example, Zhao *et al.* reported a novel enhanced chemiluminescent immunoassay (CLIA) for the determination of cTn I, which fully utilized poly[(N-isopropyl acrylamide)-co-(methacrylic acid)] [P(NIPAM-co-MAA)] microspheres as a new potential signal enhancer, using magnetic fluorescent nanoparticles as an internal standard to improve the precision of the method. In this sandwich method, the antigen in the sample was captured by the antibody immobilized on the surface of the magnetic fluorescent beads and recognized by another antibody labeled with acridine ester (AE) on the P(NIPAM-co-MAA) microspheres. This method yielded a detection limit of 0.116 pg/mL, which is significantly higher than that of traditional chemiluminescent immunoassays (31).

Additionally, nanomaterials, such as gold, silica, and silver nanoparticles, can be used as catalysts or chemical carriers to enhance chemiluminescent signals. These particles have strong catalytic properties that can increase the specific surface area and electron density. For example, Han *et al.* reported the development of a highly sensitive chemiluminescent lateral-flow assay (LFA) involving gold nanoparticles coupled with aldehyde-activated HRP and antibody molecules (i.e., AuNP-(ald)HRP-Ab) as a new conjugation scheme for high-performance LFA testing, which achieved a detection limit of 5.6 pg/mL (32).

Fluorescence methods

Fluorescence-based sensors use fluorescent dyes or nanostructured markers to capture molecules for efficient detection of cardiac biomarkers. It has the advantages of high sensitivity and a clinically relevant linear dynamic range. Nevertheless, the quantum yield of fluorophores is low and the sensitivity of fluorescent sensors depends on the stability of light. Based on the mechanism of fluorescence signal transmission, fluorescence methods for cTn I analysis are mainly divided into 3 categories: coupling single fluorescent labels, coupling multiple fluorescent labels, and generating fluorescent labels through enzyme coupling (33). Single fluorescent labels refer to the analysis of fluorescent labels directly bound to detection antibodies or added to detection antibodies during binding events. Many studies have improved labeling and enzyme packaging and explored the use of multiple fluorescent labels that can be immobilized on highly porous substrates.

For example, Liu *et al.* constructed a direct, in situ, high-performance HRP-labeled fluorescent immunoassay platform based on the rapid in situ fluorescence reaction of polyethyleneimine (PEI) and p-phenylenediamine (PPD) analogs to generate fluorescent copolymer nanoparticles (FCNPs). By introducing different substituents in the PPD structure, the fluorescence wavelength of the FCNPs was adjusted. Using cTn I as the model antigen, a fluorescent enzyme-linked immunosorbent assay for cTn I was established. Compared to traditional ELISAs, this reaction platform not only reduces interference from background signals but also has good stability, adjustable wavelengths, and a high fluorescence quantum yield (34).

Digital immunoassay

Digital immunoassays calculate single molecules bound to antibodies using plasma imaging technology, offering higher sensitivity and precision compared to traditional ELISAs. For example, Jing *et al.* reported a gradient-based digital immunoassay method by designing a multizone microfluidic channel with specific troponin capture antibodies. This method quantifies concentration gradients by optically imaging gold nanoparticles conjugated to detection antibodies bound to different test zones. Differential counting between zones eliminates the most common noise and nonspecific binding. This method requires only 1 μL of plasma sample for troponin detection, with an analysis time of 30 minutes and a detection limit of 6.2 pg/mL. It features a simple design, high sensitivity, and real-time digital counting of recorded images (35).

Surface-enhanced Raman scattering (SERS)

In recent years, SERS has been developed, which can

detect template molecules adsorbed on SERS substrates and produce significant Raman enhancement signals. The perfect SERS substrate has excellent detection performance, reaching extremely high detection limits, and possesses label-free recognition and rapid detection capabilities (36). Usually, noble metals (e.g., gold or silver nanoparticles) are used as Raman-active signals. Under appropriate laser wavelength excitation, the enhanced local electromagnetic field around noble metal nanoparticles is the main driving force for SERS (37). Tu *et al.* developed an aptamer-based SERS test strip for detecting cTn I, using silica, malachite green isothiocyanate (MGITC), and gold nanoparticles to provide strong and stable SERS signals at a 638-nm excitation wavelength. The lateral flow strip design was used to construct the paper fluidics strip. In the presence of cTn I, the aptamer/silica/MGITC/AuNPs, cTn I, and aptamer formed a sandwich binding on the test line. The SERS signal on the test line increased with increasing cTn I concentration, with a detection limit of 16 pg/mL (38). Lin *et al.* prepared coral-shaped silver-coated magnetic nanoparticles as substrates using aptamer-modified Fe_3O_4@PEI/Ag NC-Apt as a magnetic capture probe. This method combined the bicinchoninic acid assay method and SERS detection technology, successfully constructing an Apt-SERS detection platform. With cTn I as the detection target, the detection range was 1–10^5 pg/mL, and the lowest detection limit was 0.23 pg/mL (39). While SERS has obvious merits, it also has some drawbacks that cannot be ignored. Raman measurement can be performed in solution or statically on the surface of the substrate. When we chose the solution, due to the continuous movement of the plasmonic material, the reproducibility of the experiment can be low. If we select static operation, some steps in the analysis process can make the proposal more complex. Therefore, we still need to continuously improve in these aspects (40).

Surface plasmon resonance (SPR)

SPR biosensors are label-free. It is capable of detecting cTn I in a simple and rapid manner. Despite significant progress in development, the sensitivity of the SPR biosensor assay needs to be improved to reach values sufficient for clinical diagnosis. SPR biosensors mainly include long-range surface plasmon polaritons (LRSPPs), gold nanoparticle SPR, SPR fluorescence spectroscopy, surface plasmon-enhanced scattering, and ultrasensitive plasmonic biosensors. For example, Hua *et al.* reported a fiber-based SPR biosensor with DNA aptamers specific to cTn I. By optimizing its surface concentration, the sensor had a detection limit of 0.0575 pg/mL for cTn I (41).

We have summarized the characteristics of various biosensing strategies for detecting cTn I in *Table 2*, which includes performance parameters.

Clinical translation

Currently, cTn detection is mainly laboratory-based, and there is an urgent need to shorten turnaround times for the clinical diagnosis of AMI. Point-of-care testing (POCT) is a specific form of diagnostic testing that can be performed without accompanying infrastructure or complex instruments (42). POCT devices, small benchtop instruments, and handheld devices have become emerging development targets for biosensors in bedside cardiac biomarker testing. Some recent bedside cTn I testings include gate-controlled FET biosensors, colorimetric immunosensors, and paper-based lateral-flow immunoassays (LFIA).

Sinha *et al.* designed an integrated microfluidic chip with immobilized highly specific aptamer probes and an FET sensor array for detecting 4 cardiovascular protein biomarkers (C-reactive protein, N-terminal pro-B-type natriuretic peptide, cTn I, and fibrinogen). This low-power, FET-based system required no sample preparation and enabled fully automatic detection of clinical samples (~4 μL) within 5 minutes through microfluidic and portable controllers. It had an area of only 4.0 cm × 3.3 cm and was proved suitable for large-scale production, with a detection range of 1–10^4 pg/mL and a detection limit of 0.394 pg/mL (43).

Fluorescent or colorimetric immunosensors based on dry chemistry have been widely used in bedside testing. For example, Zhan *et al.* designed a dry chemistry- and lateral-flow analysis-based, closed bipolar electrode ECL (CBP-ECL) immunosensor. The sensor, consisting of a fibrous material chip and a shell, could be easily manufactured through screen printing and 3D printing. Ru(II)-L-cysteine composite materials were used as self-enhanced ECL probes. The ECL signals generated by antibody-functionalized Ru(II)-L-Cys allowed for the sensitive quantification of cTn I. The immunosensor had a wide linear range (1–10^5 pg/mL) and acceptable sensitivity (0.4416 pg/mL). Furthermore, testing of cTnI clinical serum/plasma samples has shown a strong correlation with high-end laboratory equipment and can be used in real-world situations (44).

Table 2 Comparison of biosensing-based strategies for detecting cardiac troponin I

Type	Materials	Detection limit (pg/mL)	Detection range (pg/mL)	Reference
Electrochemical biosensor				
Voltammetric type	Apt-CES-GO/SPE	0.6	$1–10^6$	(23)
Potentiometric type	Ab-DE-COOH/cTn I/AuNP/SPGE	7.3	$1–10^5$	(7)
EIS	Ab-NH_2-MIL-88B(Fe_2Co)-MOF/NF	0.013	$10^{-4}–10^5$	(8)
ECL method	BSA/Ab-AgNPs/CdS@MOF-5/PDDA/FTO	0.005	$0.01–10^3$	(9)
FET	APTES/glutaraldehyde-modified SiNW-FET	16	25–500	(26)
Colorimetric method	GP/MOF-818@p-WO_3/c-DNA/apt-glu aptasensor	0.018	$0.05–10^5$	(28)
Chemiluminescence method	AuNP-(ald)HRP-Ab conjugate	5.6	$1–10^4$	(32)
Fluorescence method	PEI-PPD FCNPs	190	$5×10^3–1.8×10^5$	(34)
Digital immunoassay method	AuNPs/microfluidic chip	6.2		(35)
SERS	Fe_3O_4@PEI/Ag NC-Apt	0.23	$1–10^5$	(39)
SPR	chromium film/gold film/fiber	0.0575		(41)

EIS, electrochemical impedance spectroscopy; ECL, electrochemiluminescence; FET, field-effect transistor; SERS, surface-enhanced Raman scattering; SPR, surface plasmon resonance.

Table 3 Comparison of POCT equipment for detecting cardiac troponin I

Type	Materials	Detection time (min)	Detection limit (pg/mL)	Detection range (pg/mL)	Reference
Field effect transistor	HEMT-microfluidic chip/Apt	5	0.394	$1–10^4$	(43)
Colorimetric method	Ru(II)-L-Cys/GQDs-AuNPs/Ab/CBP-ECL	7	0.4416	$1–10^5$	(44)
Paper-based lateral-flow analysis	AuNP-polyHRP-Ab Conjugate	20	0.84	10–48,310	(45)

POCT, point-of-care testing.

Paper-based lateral flow assays (LFAs) is one of the most widely applied medical device detection biosensing platforms. For example, Han *et al.* developed a highly sensitive, automated LFA biosensing platform that incorporated gold nanoparticles into a polymer network of HRP conjugated with antibodies, enhancing enzyme coupling. This overcame the limitations of traditional colloidal gold-labeling methods, such as low sensitivity and limited quantification capabilities. The platform integrated a time-programmable amplification section based on water-soluble polymers for automated immunoanalysis and sequential reactions in signal amplification. The simple operation steps requiring no user intervention. It could automatically detect human cTn I in serum samples within 20 minutes, with a detection limit of 0.84 pg/mL. In addition, it costs only $0.66 per test. In summary, it has been proved to be practical and cost-effective (45).

Table 3 compares the performance parameters of the aforementioned POCT devices. These three POCT devices use different integration methods and can be detected automatically. The detection time ranged from a few minutes to tens of minutes. Each has its own advantages in terms of instrument volume and detection cost. In addition, we note that in (43) the authors used an integrated microfluidic chip. In recent years, microfluidics has gained much attention due to its functional characteristics such as high efficiency. Microfluidic systems, such as microfluidic chips, which are small in size, consume less samples, and are portable, are an important direction for the development of new-generation POCT instruments (46). By combining microfluidic systems with different types of biosensors, we are able to overcome some of the complexity problems of

fluid handling (47).

While POCT devices have many advantages, they also have certain limitations that need further improvement, such as enhanced stability, the ability to detect different biomarkers simultaneously, and a greater degree of automated signal acquisition and analysis. Manufacturing microfluidic systems that are safe and economical, more easily scalable and can be effectively cleaned and reused, and combining them with sensors are also not negligible. In the future, POCT should be developed to be highly integrated, miniaturized, cost-effective, and easy-to-operate detection systems.

Conclusions

This paper reviews the current state of research on cTn I biosensor technology, summarizing the characteristics of biosensors based on electrochemical, colorimetric, fluorescent, chemiluminescent, and SERS techniques. Most biosensors use immunoassay technology for detection, with antibodies as the biological components. In recent years, aptamer sensors have emerged as a viable alternative to immunosensors, offering advantages such as ease of chemical modification, flexibility, and high affinity. Sensing strategies based on nanoparticles and nanomaterials can amplify detection signals, further improving the sensitivity and performance of sensors. The goal is to develop portable, stable, sensitive, and rapid analysis detection devices. To meet these needs, future development directions may include developing more novel biorecognition elements (such as artificial receptors) and not simply traditional antibodies; developing composite biosensors for multiplex detection, allowing for the timely and cost-effective simultaneous measurement of multiple analytes; and developing in vivo sensors to continuously and track changes in biomarker concentrations real-time. In summary, cTn I detection methods based on biosensors will become increasingly simple, sensitive, and stable, enabling the early diagnosis and treatment of AMI.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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