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Enhancing early diagnosis and monitoring of wound infections caused by multiple bacteria in tissues through digital PCR integration with cutaneous infection biomarkers

Zhi Wang[1*], Cheng Feng[1], Guojing Chang[1], Hao Liu[1] and Wenchao Zhang[1]

Abstract

Background This study explores the potential of combining digital polymerase chain reaction (PCR) with cutaneous infection biomarkers for the early diagnosis and monitoring of wound infections caused by multiple bacteria.

Methods We selected a cohort of 276 patients with wounds who were admitted to our hospital from July 2022 to July 2023. These patients were categorized into 46 infection cases and 230 non-infection cases based on clinical evaluation. Clinical data, including routine blood tests [Red Blood Cell count (RBC), Hemoglobin (Hb), White Blood Cell count (WBC), Platelets (PLT)], D-dimer (D-D), and blood biochemistry parameters (liver function, lipid profile, blood glucose, renal function), were collected from both groups. Bacterial cultures were obtained from the infection group, and digital PCR targeting multiple bacteria (*Pseudomonas aeruginosa, Staphylococcus aureus, Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae*) was performed. Logistic regression analysis was conducted to identify risk factors for wound infection, and receiver operating characteristic (ROC) curves were generated to assess the diagnostic performance of digital PCR in conjunction with cutaneous infection biomarkers.

Results No significant differences were observed between the infection and non-infection groups regarding age, gender, body mass index (BMI), or wound characteristics ($P > 0.05$). However, the infection group exhibited significantly higher levels of RBC, Hb, WBC, PLT, and D-D ($P < 0.05$). Key factors influencing wound infections included WBC, PLT, glycosylated hemoglobin, and the specific bacteria identified. ROC curve analysis revealed area under the curve (AUC) values for individual markers, with a combined AUC of 0.899, demonstrating excellent diagnostic performance.

Conclusion Digital PCR, when combined with cutaneous infection biomarkers, proves to be an effective diagnostic tool for wound infections. This approach shows great promise in clinical applications, with the potential to significantly improve patient outcomes.

Keywords Digital PCR, Wound infections, Cutaneous infection biomarkers, Bacterial identification, Early diagnosis

Background

Wound afflictions affect approximately 2% of the population in the United States, 1.04% in Germany, and wound infections associated with trauma account for 67.48% of total patients in China [1, 2]. Over recent years, there has been a notable increase in the incidence of wounds, coinciding with the rise of highly drug-resistant bacteria,

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such as *Acinetobacter baumannii*, *Staphylococcus aureus*, and *Klebsiella pneumoniae* [3]. Wound infection occurs when bacteria or other pathogens enter a wound, leading to infection in conditions such as surgical procedures, trauma, burns, and other traumatic damage to the skin and mucosal surfaces. Contributing factors to wound infections include bacterial invasion, pathogen colonization, inadequate hygiene practices, and compromised immune function [4]. Early-stage wound infections often lack specific symptoms, and the stress response associated with underlying diseases can obscure early signs of infection. In clinical practice, routine laboratory indicators may not always reflect infection, inflammation, or disease progression directly. Thus, identifying reliable markers for wound infections is critical.

Inflammatory cytokines, known infection markers, can assist in the early diagnosis and assessment of infection severity. Elevated levels of RBC, Hb, WBC, and PLT in the blood indicate an inflammatory response [5–7]. However, the use of these parameters as indicators for evaluating wound infections has not been widely reported in the literature.

Current clinical practice faces challenges surrounding the pathological characteristics and bacterial spectrum of chronic wounds. Moreover, the lack of standardized guidelines for antibiotic treatment of wound-related infections remains a significant issue. Treatment practices vary across hospitals and departments, posing challenges in pathogen detection, especially within outpatient populations. Effective infection control is essential in managing infected wounds, where early pathogen identification coupled with timely intervention is critical [8, 9]. Consequently, an accurate assessment of the infection, timely identification of pathogen characteristics and drug susceptibility, appropriate antibiotic guidance, and minimizing the emergence of drug-resistant bacteria are essential. Such an approach not only helps control the spread of infections and improves wound conditions but also promotes wound healing. Therefore, this study aims to explore the potential of digital PCR in combination with cutaneous infection biomarkers for the early diagnosis and monitoring of wound infections.

Methods and materials

Clinical data

This study enrolled a total of 276 patients with wounds who were admitted to our hospital between July 2022 and July 2023. These patients were divided into two groups: 46 cases in the infection group and 230 cases in the non-infection group, based on infection status [10]. The infection group comprised 26 males and 20 females, aged between 23 and 73 years, with a mean age of 56.91 ± 9.76 years. The non-infection group included 110 males and 220 females, aged between 22 and 75 years, with a mean age of 56.34 ± 9.83 years. No significant differences in general characteristics were observed between the two groups ($P > 0.05$).

Selection criteria

Inclusion criteria

1) Wound bacterial culture was a key criterion for diagnosing wound infection, with clinical symptoms such as redness, swelling, pain, secretion, odor, and necrotic tissue considered significant indicators. This included various soft tissue injuries that led to skin defects, including cases with exposed bones or implants, which subsequently developed wound infections despite early treatment [11, 12].
2) Wounds presenting substantial exudate, necrosis, and tissue decay.
3) Clear consciousness and effective communication abilities.
4) Good compliance with treatment, demonstrating the ability to complete the entire treatment regimen cooperatively.

Exclusion criteria

1) Recent use of antibiotics within 7 days prior to admission.
2) Presence of multiple organ failure.
3) Diagnosis of malignant tumors.
4) Blood system disorders.
5) Known allergic constitution.
6) Severe mental or sensory impairments.
7) Rheumatic immune diseases with recent use of immunosuppressive agents within the past month.
8) Lactating women.

Methods

Clinical data

Clinical data were collected for both patient groups, including age, gender, body mass index (BMI), duration of illness, smoking and alcohol habits, history of hypertension, diabetes, peripheral vascular disease, blood pressure, blood glucose levels, glycosylated hemoglobin, and wound characteristics (type, location, depth, and causative factors).

Routine blood tests and blood biochemistry

A hematology analyzer (Mindray, Model: BC-6800) was used to assess various parameters, including RBC, Hb, WBC, PLT, D-dimer (D-D), liver function tests (aspartate aminotransferase [AST], alanine aminotransferase

[ALT], albumin [ALB]), lipid profile (total cholesterol [TC], triglycerides [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C]), renal function tests (homocysteine [Hcy], serum creatinine [SCr], blood urea nitrogen [BUN]), uric acid, creatine kinase isoenzyme (CK-MB), and lactate dehydrogenase (LDH).

Digital PCR of multiple bacteria in wound tissues

Bacterial cultures were obtained from the wound infections in the infection group and subjected to digital PCR targeting multiple bacteria. Bacterial culture and identification were performed using the BioMérieux microbiological analysis system from BioMérieux, France. Pathogen species were identified, and supporting reagents and consumables were obtained from BioMérieux. Bacterial susceptibility testing was carried out using the K-B paper disk method, with results interpreted according to the Clinical and Laboratory Standards Institute (CLSI M02) 2024 edition. Quality control strains, including *Staphylococcus aureus* ATCC25923, *Klebsiella pneumoniae* ATCC 700603, *Pseudomonas aeruginosa* ATCC 27853, and *Escherichia coli* ATCC25922, were sourced from the Clinical Laboratory Center of the Ministry of Health.

Univariate/Multivariate logistic regression analysis of risk factors for wound infection

Determining the application value of digital PCR combined with cutaneous infection biomarkers through ROC curve analysis

Statistical analysis

Data were analyzed using SPSS 21.0 software, and a database was established using Excel. Metric data conforming to a normal distribution were presented as means ± standard deviation. Overall comparison of data between groups was performed using one-way analysis of variance (ANOVA), with pairwise comparisons carried out using the LSD method. Count data were expressed as percentages (%), and comparisons were made using the chi-square (χ^2) test. Univariate and multivariate logistic regression analyses were used to assess the risk factors for wound infection. ROC curve analysis was performed to determine the application value of digital PCR combined with cutaneous infection biomarkers in patients with wound infections. Differences were considered statistically significant at $P<0.05$.

Results

General data comparison

No significant differences were found between the two groups in terms of age, gender, BMI, duration of illness, smoking habits, alcohol consumption, history of hypertension, history of diabetes, history of peripheral vascular disease, blood pressure, blood glucose levels, glycosylated hemoglobin levels, or wound characteristics (type, location, depth, and causative factors) ($P>0.05$), as shown in Table 1.

Comparison of digital PCR results for multiple bacteria in wound tissues

The bacterial flora identified in the wounds of the infection group included *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi, as detailed in Table 2.

Comparison of routine blood tests and blood biochemistry parameters between the two groups

In the infection group, levels of RBC, Hb, WBC, PLT, and D-D were significantly higher than those in the non-infection group ($P<0.05$). However, no significant differences were found between the two groups in terms of AST, ALT, ALB, TC, TG, HDL-C, LDL-C, SCr, Hcy, BUN, LDH, CK-MB, and SUA ($P>0.05$), as illustrated in Table 3.

Univariate analysis of risk factors for wound infection

Univariate logistic regression analysis was conducted using variables with notable differences in general data, including RBC, Hb, WBC, PLT, D-D, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi as independent variables, and wound infection occurrence as the dependent variable. The results revealed that factors influencing the occurrence of wound infections included WBC, PLT, glycosylated hemoglobin, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi, as outlined in Table 4.

Multivariate analysis of risk factors for wound infection

Multivariate logistic regression analysis was conducted using variables with significant differences in general data, including WBC, PLT, D-D, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi as independent variables, and wound infection occurrence as the dependent variable. The findings emphasized that WBC, PLT, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi were influential factors in the occurrence of wound infections, as shown in Table 5.

Table 1 General data comparison

Parameter	Infection group ($n=46$)	Non-infection group ($n=230$)	t/χ^2	P
Age (years)	56.98 ± 10.37	54.38 ± 11.23	−1.451	0.147
Gender (n)			1.837	0.175
Male	20	110		
Female	26	220		
BMI (kg/m^2)	22.39 ± 3.57	22.42 ± 3.24	0.056	0.955
Disease duration (days)	2.38 ± 0.73	2.21 ± 0.69	−1.511	0.132
Smoking (n)	5	26	0.007	0.933
Drinking (n)	7	23	0.049	0.825
History of Hypertension	3	17	0.019	0.890
History of diabetes	4	19	0.009	0.924
History of peripheral Vascular disease	2	14	0.212	0.645
Blood pressure (mmHg)				
Systolic pressure	82.19 ± 7.27	81.98 ± 8.32	−0.159	0.874
Diastolic pressure	123.87 ± 10.38	122.71 ± 11.02	−0.658	0.511
Wound type (n)			1.027	0.598
Postoperative wound non-healing	16	85		
Diabetic foot	20	109		
Burn	10	36		
Wound location (n)			0.159	0.984
Anterior tibia	15	79		
Ankle	14	73		
Buttock	9	41		
Anterior chest	8	37		
Wound depth (n)			0.056	0.972
Superficial and deep dermis	27	139		
Subcutaneous tissue and muscle	15	71		
Involving bone	4	20		

Table 2 Comparison of digital PCR results for multiple bacteria in wound tissues

Pathogen	Infection group ($n=46$)	
	Number of Strains	Percentage (%)
Gram-negative bacteria		
Pseudomonas aeruginosa	6	13.04
Klebsiella pneumoniae	7	8.70
Escherichia coli	4	19.57
Acinetobacter baumannii	13	28.26
Gram-positive bacteria		
Staphylococcus aureus	9	19.57
Staphylococcus epidermidis	6	13.04
Fungi	1	2.17

Application value of digital PCR combined with cutaneous infection biomarkers in wound infections, as determined by ROC curve analysis

ROC curve analysis was performed using wound infection occurrence as positive samples and non-infection as negative samples. ROC curves for RBC, WBC, PLT, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi were constructed to predict wound infection outcomes in patients. The results indicated that the area under the curve (AUC) for each marker was as follows: 0.748, 0.715, 0.768, 0.857, 0.703, 0.793, 0.782, 0.801, 0.653, and 0.689, respectively. Additionally, the combined prediction of all indicators yielded an AUC of 0.899, demonstrating optimal performance in terms of AUC, specificity, and sensitivity (Table 6 and Fig. 1).

Table 3 Comparison of routine blood tests and blood biochemistry parameters

Index	Infection group ($n=46$)	Non-infection group ($n=230$)	t	P
RBC ($\times 10^{12}$/L)	4.56 ± 0.49	4.41 ± 0.43	−2.109	0.036
Hb (g/L)	119.29 ± 19.83	112.34 ± 20.04	−2.151	0.032
WBC ($\times 10^{9}$/L)	14.94 ± 1.41	9.32 ± 1.47	−23.827	< 0.001
PLT ($\times 10^{9}$/L)	201.23 ± 18.29	213.29 ± 19.34	3.895	0.001
AST (U/L)	46.93 ± 8.29	46.46 ± 8.48	−0.994	0.321
ALT (U/L)	45.37 ± 5.18	45.64 ± 5.27	0.318	0.751
ALB (g/L)	39.78 ± 3.26	39.01 ± 3.34	−1.433	0.153
TC (mmol/L)	1.82 ± 0.46	1.76 ± 0.52	−0.728	0.468
TG (mmol/L)	4.13 ± 0.53	4.27 ± 0.59	1.493	0.137
HDL-C (mmol/L)	1.09 ± 0.23	1.12 ± 0.29	0.661	0.509
LDL-C (mmol/L)	2.02 ± 0.36	1.92 ± 0.32	−1.894	0.059
SCr (μmol/L)	70.39 ± 8.34	71.28 ± 9.93	0.569	0.570
Hcy (mmol/L)	0.87 ± 0.25	0.92 ± 0.23	1.221	0.223
BUN (mol/L)	6.57 ± 1.62	6.83 ± 1.67	0.969	0.334
CK-MB (IU/L)	21.09 ± 4.19	20.18 ± 4.34	−1.305	0.193
LDH (U/ml)	205.19 ± 23.24	201.28 ± 20.13	−1.171	0.243
SUA (μmol/L)	321.28 ± 28.91	319.29 ± 26.87	−0.453	0.651
FPG (mmol/L)	4.58 ± 0.34	4.51 ± 0.42	−1.062	0.289
2hPG (mmol/L)	6.32 ± 0.45	6.26 ± 0.48	−0.782	0.435
Glycated hemoglobin (%)	6.23 ± 1.03	6.29 ± 1.09	0.344	0.731

Table 4 Univariate analysis of risk factors for wound infection

Variable	β-value	$s_{\bar{x}}$	Wald χ^2	*P*-value	OR value (95%CI)
RBC	0.137	0.121	1.327	0.706	1.152 (0.916–1.352)
Hb	0.489	2.026	3.978	0.152	1.539 (0.978–3.183)
WBC	1.456	0.532	6.978	0.008	3.278 (1.518–8.869)
PLT	0.023	0.015	9.867	0.002	1.016 (0.821–1.659)
Glycated hemoglobin	0.936	0.338	6.712	0.005	2.716 (1.023–4.398)
Acinetobacter	1.107	0.246	21.293	< 0.001	2.395 (1.272–3.379)
Staphylococcus	1.519	0.348	17.831	< 0.001	1.276 (0.138–1.898)
Klebsiella	0.349	0.131	7.033	0.007	1.379 (1.004–1.793)
Pseudomonas	1.029	0.429	5.023	0.028	1.004 (0.705–1.533)
Escherichia	0.833	2.217	9.871	0.001	2.196 (1.527–2.873)
Staphylococcus epidermidis	0.525	0.179	2.833	0.003	1.651 (1.162–2.359)
Fungi	0.387	0.161	2.443	0.027	1.448 (1.026–2.009)

Discussion

Wound infection, a common post-surgical or post-traumatic complication, significantly hampers wound healing and diminishes patients' quality of life [13, 14]. Infection-induced inflammatory responses escalate tissue damage, hinder wound repair, and prolong patient recovery time. Symptoms such as pain, redness, swelling, and local exudate around the wound contribute to patient distress [15]. Moreover, unchecked wound infections can extend to adjacent tissues or deeper organs, culminating in severe complications like deep tissue infections and abscess formation. Wound infections disrupt the normal healing process, leading to suboptimal wound closure and complications such as wound dehiscence and hypertrophic scarring. In severe cases, wound infection can precipitate life-threatening conditions such as sepsis and organ failure, escalating the risk of patient mortality [16]. Hence, the prevention and management of wound infections are

Table 5 Multivariate analysis of risk factors for wound infection

Variable	β-value	$s_{\bar{x}}$	Wald χ^2	*P*-value	OR value (95%CI)
WBC	0.023	0.001	2.449	< 0.001	1.029 (1.018–1.048)
PLT	0.268	0.128	4.467	0.028	1.238 (0.981–1.951)
Glycated hemoglobin	25.831	9.923	8.091	0.013	1.293 (0.897–1.287)
Acinetobacter	0.581	0.117	22.651	0.001	1.652 (1.002–2.2561)
Staphylococcus	0.658	0.307	4.651	0.023	1.927 (1.062–3.091)
Klebsiella	0.783	0.306	6.761	0.007	2.091 (1.211–3.871)
Pseudomonas	0.893	0.176	21.082	< 0.001	0.537 (0.291–0.891)
Escherichia	0.829	0.326	6.198	0.008	2.198 (1.218–4.091)
Staphylococcus epidermidis	0.978	0.389	6.876	0.007	2.187 (1.371–4.876)
Fungi	1.290	0.376	11.871	< 0.001	3.198 (1.276–7.098)

Table 6 Application value of digital PCR combined with cutaneous infection biomarkers in patients with wound infections as determined by ROC curve analysis

Indicator	AUC	*P*-value	Specificity	Sensitivity
RBC	0.748	0.011	84.02	80.03
WBC	0.715	0.025	81.92	81.23
PLT	0.768	0.031	80.93	85.39
Acinetobacter	0.857	0.002	83.02	78.27
Staphylococcus	0.703	< 0.001	81.76	62.87
Klebsiella	0.793	< 0.001	67.39	76.39
Pseudomonas	0.782	< 0.001	63.29	81.29
Escherichia	0.801	< 0.001	82.39	70.98
Staphylococcus epidermidis	0.653	< 0.001	77.73	64.39
Fungi	0.689	< 0.001	67.91	78.93
Combined diagnosis	0.899	< 0.001	89.34	94.39

paramount. Utilizing sensitive indicators to assess the specific nature of wound infections and promptly initiating effective interventions are crucial for facilitating patient recovery.

Currently, conventional detection techniques for wound infections include colorimetric culture-based methods, quantitative fluorescence PCR detection, colloidal gold techniques, immunochromatographic test strips, and Southern blot hybridization techniques, among others. Each of these methods possesses its advantages and disadvantages, and none effectively achieve absolute quantification [17]. Digital PCR (dPCR) technology, a next-generation PCR approach, facilitates single-molecule absolute quantification. By subjecting the sample to limited dilution, it uniformly distributes the sample across microreaction units, reads the final fluorescence signal of each unit post-amplification, and, based on the Poisson distribution statistical principle, achieves absolute quantification of initial template molecules. dPCR

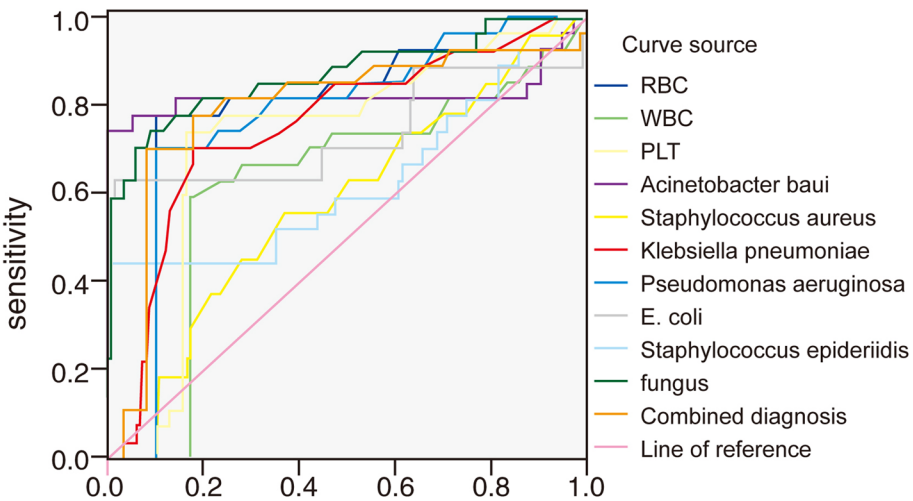

Fig. 1 ROC curve analysis of wound infection prediction using digital PCR and clinical biomarkers

has found widespread applications in virus detection, cancer diagnosis, and treatment monitoring, among other fields [18]. When applied to wound infection, digital PCR can detect multiple bacterial species in wound tissues, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi. Previous studies have indicated that post-open fracture infections predominantly stem from Gram-negative bacteria, such as *Pseudomonas aeruginosa*, while Gram-positive bacteria like *Staphylococcus aureus* are also common pathogens [19].

Zhu et al. [20] reported that the most frequently isolated bacteria from wounds included *Klebsiella pneumoniae* (15.10%), *Pseudomonas aeruginosa* (13.54%), and *Staphylococcus aureus* (10.94%). Révész et al. [21] demonstrated a relatively high prevalence of *Staphylococcus aureus* in wound microbiota. Abdulbaqi et al. [22] also identified a high detection rate of *Staphylococcus aureus* in wound samples. Macedo-Viñas et al. [23] highlighted that *Staphylococcus aureus* was frequently isolated from burn wounds. Research by Jia et al. [24] demonstrated that the bacterial flora in wounds of severely burned patients infected with bacteria predominantly includes *Pseudomonas aeruginosa*, followed by *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Spindler et al. [25] reported that wound infections following cardiac surgery are often associated with an increased prevalence of *Staphylococcus aureus*. The findings from this study, which identified a bacterial flora of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus epidermidis*, and fungi, align with these prior research outcomes, supporting the utility of dPCR in detecting a wide range of bacterial pathogens in infected wound tissues.

WBC count serves as a critical diagnostic marker for bacterial infections in routine blood tests. Research by Chang et al. [26] suggested a strong correlation between elevated WBC levels and bacterial infections following intervertebral disc herniation surgery, a finding echoed in other studies on tibial plateau fractures [27] and femoral neck fractures [28]. D-Dimer (D-D), an early indicator of coagulation dysfunction, has been recognized as a sensitive marker for the pre-state of disseminated intravascular coagulation (DIC) and hyperfibrinolysis [29]. D-Dimer levels have been associated with wound infection complications, especially in critically ill patients [30], where they serve as a useful tool for predicting deep vein thrombosis (DVT) [31]. Elevated RBC levels, although primarily studied in the context of cardiovascular disease, may also contribute to wound infection-related complications by increasing blood viscosity and susceptibility to vessel blockages [32]. Platelets (PLT) are involved in the immune response against infection, as they can identify microorganisms and produce antimicrobial molecules [33].

The findings of this study revealed that RBC, Hb, WBC, and PLT levels were significantly higher in the infection group compared to the non-infection group ($P<0.05$), aligning with previous literature. Elevated WBC levels, for instance, have been consistently associated with bacterial infections in surgical wounds [34]. Similarly, elevated Hb and PLT have been reported as contributing factors for infections after surgeries, including cesarean sections [35] and gastrointestinal surgeries [36].

Chen et al. [37] pinpointed RBC as a significant influencing factor for wound infections following osteosarcoma resection surgery. Increased WBC levels were found in patients with orthopedic wound infections, which subsequently decreased post-treatment [34]. Cramm et al. [38] suggested that WBC data are valuable for identifying the risk of postoperative infections following appendectomy for complicated appendicitis. Wang et al. [39] reported that a D-dimer level > 1.81 mg/L can predict the occurrence of preoperative deep vein thrombosis (DVT). Kocaaslan et al. [40] indicated that the platelet-to-lymphocyte ratio (PLR) can serve as a marker for urinary tract infections in neonates. Wang et al. [36] identified that Hb is a risk factor for postoperative incisional infection in patients undergoing gastrointestinal surgery. Qi et al. [41] reported that the bacterial distribution in wound exudates of hospitalized patients includes Staphylococcus aureus. Diao et al. [42] indicated that *Escherichia coli, Pseudomonas aeruginosa,* and other Gram-negative bacteria, as well as *Staphylococcus aureus*, are the primary pathogens causing wound infections. Abbas et al. [43] identified pathogens causing postoperative wound infections, including *Acinetobacter baumannii, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli*, and *Candida albicans*. Yang et al. [44] identified that during postoperative pulmonary infections following gastric cancer surgery, the levels of *Klebsiella pneumoniae* and *Escherichia coli* are significantly elevated. The data in this study confirm these findings, identifying these bacteria as key contributors to wound infection, along with fungi. Moreover, the elevated levels of WBC, PLT, and RBC, combined with the detection of these pathogens, underline the multifactorial nature of wound infections.

In clinical practice, there is a dearth of research exploring the application of digital PCR combined with wound infection biomarkers for early detection of various bacteria in wound tissues. Feng et al. [45] noted elevated WBC levels in cases of wound infections. Zheng et al. [46] identified bacterial distribution in mixed bacterial

infections of elderly diabetic foot ulcers, highlighting the presence of *Staphylococcus aureus, Escherichia coli, Staphylococcus epidermidis*, and *Pseudomonas aeruginosa*, alongside elevated HbA1c levels. The study's findings revealed AUC values for predicting wound infection occurrence in patients, with RBC at 0.748, WBC at 0.715, PLT at 0.768, *Acinetobacter baumannii* at 0.857, *Staphylococcus aureus* at 0.703, *Klebsiella pneumoniae* at 0.793, *Pseudomonas aeruginosa* at 0.782, *Escherichia coli* at 0.801, *Staphylococcus epidermidis* at 0.653, and *fungi* at 0.689. Combining all indicators resulted in an AUC value of 0.899, indicating the efficacy of amalgamating various indicators in predicting wound infections. Furthermore, the combined prediction of AUC, specificity, and sensitivity for each indicator was optimal, underscoring the effectiveness of this composite approach in predicting wound infections. O'Dell et al. [47] reported that PLT is not an independent risk factor for nosocomial infections in trauma patients, which is inconsistent with the findings of this study. This discrepancy may be attributed to differences in the study populations included.

Despite the promising findings, there are limitations in this study that should be acknowledged. Currently, there is scarce research on the utilization of digital PCR combined with wound infection biomarkers in wound infections, and the sample size in this study is limited, not to mention the absence of foundational research. Future research endeavors should focus on enlarging the sample size to validate the findings further, and explore the potential correlation between wound location and the type of microbes present, which may provide valuable insights into the pathogenesis of wound infections and guide targeted therapeutic strategies. If feasible, animal studies should be conducted to delve into the underlying mechanisms.

Conclusion

In conclusion, this study demonstrates that digital PCR analysis, in combination with clinical biomarkers such as WBC, PLT, and D-D, offers a promising approach for diagnosing wound infections. The presence of key pathogens like *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*, alongside elevated levels of RBC, Hb, WBC, and PLT, were found to be significant factors associated with wound infections. The integration of digital PCR with these biomarkers improves diagnostic sensitivity and specificity, thereby aiding in early detection and intervention. Clinicians should remain vigilant in monitoring these comprehensive indicators to effectively manage wound infections and improve patient outcomes. However, future studies with larger sample sizes and further validation of the combined diagnostic approach are necessary to fully integrate this methodology into clinical practice.

Abbreviations

PCR	Polymerase chain reaction
RBC	Red blood cell count
Hb	Hemoglobin
WBC	White Blood cell
PLT	Platelet
D-D	D-dimer
ROC	Receiver operating characteristic curve
AUC	Area under curve
BMI	Body mass index
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
ALB	Albumin
TC	Total cholesterol
TG	Triglycerides
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
Hcy	Homocysteine
SCr	Serum creatinine
BUN	Blood urea nitrogen
CK-MB	Creatine kinase isoenzyme
LDH	Lactate dehydrogenase
DIC	Disseminated intravascular coagulation
DVT	Deep vein thrombosis
PLR	Platelet-to-lymphocyte ratio

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Authors' contributions

Conceptualization, ZW and CF; Methodology, ZW, CF and GC; Software, ZW and HL; Formal Analysis, ZW, CF and WZ; Investigation, ZW and HL; Data Curation, ZW and CF; Writing – Original Draft Preparation, ZW; Writing – Review & Editing, CF, GC, HL and WZ; All authors approve the submission.

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Data availability

Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate

This study adhered to the Declaration of Helsinki and was obtained from the Peking Union Medical College Hospital Institutional Review Board. All participants provided written informed consent before study participation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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