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# A FORENSIC STUDY OF CULTIVATING POSTMORTEM HEART BLOOD IN 131 AUTOPSIES SUSPECTED OF INFECTIOUS DISEASES

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**Abstract:** With the inception of evidence-based medicine in the 19th century, the value of postmortem microbial culture has been controversial. Even so, it still plays an important role in the diagnosis of infectious death in modern forensic medicine. In this study, we performed a retrospective study of postmortem heart blood microbial culture for 131 autopsies suspected of infectious diseases. We analyzed the correlations between the various influencing factors, blood culture results and pathological findings. The results showed that there were 79 (60.3%) positive cultures and 52 (39.7%) negative cultures. Except for gender (P=0.02), no significant difference between positive cultures and negative cultures for age (P=0.06), prior antibiotics therapy (P=0.49), leukocyte count (P=0.77), neutrophil percentage (P=0.86), survival time (P=0.10) and PMI (P=0.14) was found. The positive predictive value (PPV) was 75.9% (60/79) and the negative predictive value (NPV) was 36.5% (19/52) in our study. *Escherichia coli* (16 cases) had the largest numbers, followed by *Klebsiella pneumoniae* (8 cases), *Staphylococcus aureus* (6 cases) and *Streptococcus hemolyticus* (5 cases). Lungs (16 cases), intestines (11 cases) and wound (7 cases) were the most susceptible organs to infection in the body. Microorganism distribution results showed that *Escherichia coli*, *Klebsiella pneumonia*, *Staphylococcus aureus* and *Enterococcus faecium* were more active and often infected with multiple organs. These results strengthened our understanding of the postmortem microbial culture in diagnosing infectious diseases when combined with pathological findings.

**Keywords:** forensic medicine, postmortem blood culture, infectious diseases, cause of death.

## INTRODUCTION

Microbial infections have always been a high morbidity and mortality in the current medical process [1, 2]. Not merely is the constant discovery of new bacteria and viruses, the ceaselessly mutation of previous strains has also become a huge challenge for clinical medicine [3]. Compared with microbiology and lemology in clinical medicine, the cultivation of postmortem microorganisms is more concerned by forensic medicine and pathology [4-6]. Postmortem microbial culture is also a part of postmortem biochemistry what is an important method to auxiliary infer the cause of death in forensic medicine [7, 8].

O'Toole and his colleague firstly carried out their work on postmortem microbial culture in 1965, and then they re-studied the stability and practicability of culture conditions, trying to diagnose bacteremia and sepsis after death [9]. For a long time thereafter, the value of postmortem microbial cultivation has been a controversial topic in forensic field [6,10]. The differences in detection techniques and detection conditions might present different results. Besides, the transfer of microorganisms and postmortem blood contamination were also the important influencing factors [11]. We need understand the biological mechanism of blood culture to produce bacteria. In general, it is divided into four situations: (i) invasion in life: bacteria invade the target organs or body fluids with survival, and (ii) agonal spread: spreading during agonal stage (including exogenous bacteria invasion), and (iii) postmortem translocation: bacteria across the mucosal barriers and transfer into the surrounding tissue or bloodstream, and (iv) contamination: microorganisms come into samples at the time of collecting in autopsy [12,13]. For forensic examiner, the most important challenge is how to avoid the contamination of exogenous bacteria into blood, cerebrospinal fluid

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or organ samples during the autopsy. Although the postmortem blood culture results are often do not achieve an expectation, it is still a valuable method in the process of monitoring and identifying infectious diseases [14,15].

In this article, we performed a retrospective study of postmortem heart blood culture of 131 deaths that suspected of infectious diseases in our institution during the past 10 years. We collected the demographic characteristics, clinical laboratory results, survival time, postmortem interval (PMI), postmortem culture results of these cases. By analyzing the relationships between external influencing factors, blood culture results and pathological findings, we try to summarize the diagnosis value of postmortem medical cultures and explore the distribution laws of microorganisms in the body. We hope it can provide some basic research data and reference significance for forensic workers.

## MATERIALS AND METHODS

### *Materials*

Were performed the postmortem heart blood cultures in 131 autopsies in Chongqing Institute of Forensic Medicine from 2011 to 2020. All decedents were suspected with severe infectious diseases. The requirements for blood microbial culture were described as follows: (i) persistent fever > 38°C, or (ii) leukocyte counts $>10\times10^9$/L, or (iii) obviously severe local infection, or (iv) other features related to infectious diseases. Age, gender, prior antibiotics therapy history, clinical laboratory results (if any), survival time, PMI, blood culture results and pathological findings were carefully collected.

### *Postmortem investigation*

Complete autopsies were performed in our institution by at least two forensic pathologists in accordance with both local standards and international guidelines. Conventional haematoxylin and eosin (HE) staining of organ (or tissue) samples were subsequently performed. Final identification of the cause of death was determined by three forensic pathologists based on the results of macromorphological, micropathological, toxicological and other auxiliary examination.

### *Heart blood collection and cultivation*

The collection and culture of heart blood were performed in accordance with strict autopsy standards. A 20mL syringe with a 5-10 gauge needle was used to collect inferior venous blood after the chest opened. Heart surface (blood collecting site) and syringe needle should be strictly disinfected (Ethanol) before the action, and then the blood should be injected into a culture system (bioMe´ rieux, Hazelwood, MI, USA) immediately. The microorganism cultivation system included an aerobic culture, an anaerobic culture and a fungi culture. All specimens collected and cultured would be immediately transported to a same microbiology laboratory for detection. If there was no growth in the culture medium for 5-7 days, the result was considered negative. Gram staining and Gomori Methenamine Silver (GMS) staining were performed for susceptible infectious tissues to identify bacteria or fungi. Blood culture results and pathological findings were blindly reviewed by two pathologists, and the consistency of the above two results were carefully assessed. If there was a disagreement, a third pathologist would be invited for arbitration.

### *Statistical analysis*

All the statistical data were analyzed with SPSS 20.0. The centralized trend was expressed by the mean (± standard deviation (SD)) and the count data were expressed by the number of cases. Comparisons between two groups were performed by t-test and Chi-squared statistic test was performed to evaluate the univariate analysis (gender and prior antibiotics therapy). The statistical significance was defined of a P-value of less than 0.05.

### *Ethics*

Relevant ethical issues in this study were discussed and finally identified by the local Ethical Committee. In forensic investigation, blood, urine and cerebrospinal fluid were common biological samples which were routinely collected for auxiliary diagnosis of the cause of death. Therefore, it was unnecessary to perform an ethical approval in our study.

## RESULTS

Basic case information

In the study period, 131 cases were performed postmortem heart blood microbial culture from a total of 825 completed autopsies, with a 15.9% cultivate rates of total autopsies. Case profile was described as follow: 69 males and 62 females, 7 days-81 years of age, 1-380days of survival time and 4-48hours of PMIs. Among the 131 blood cultures, 79 cases were positive results and 52 cases were negative results. 95 cases were treated with antibiotics therapy in medical institution,

accounting for 72.5% of the total numbers. We did a statistical analysis of the influencing factors between positive cultures and negative cultures (Table 1). The results showed that except for gender (P=0.02), there was no significant difference between positive cultures and negative cultures for the remaining influencing factors such as age (P=0.06), prior antibiotics therapy (P=0.49), leukocyte count (P=0.77), neutrophil percentage (P=0.86), survival time (P=0.10) and PMI (P=0.14).

***Postmortem blood culture results***

The statistics of the postmortem blood culture results were shown in Table 2, and the correlations between blood culture results and pathological findings were analyzed. There were 79 cases (60.3%) showed positive results and 52 cases (39.7%) showed negative results, respectively. Among the 79 positive cultures, 60 cases (75.9%) showed that the culture results were consistent with the pathological findings, and the PPV was 75.9% (60/79). Among the 52 negative cultures, 19 cases (36.5%) showed that the culture results were consistent with the pathological findings, and the NPV was 36.5% (19/52). Among the identified microorganisms, *Escherichia coli* (16 cases) had the largest numbers, followed by *Klebsiella pneumoniae* (8 cases), *Staphylococcus aureus* (6 cases), *Streptococcus hemolyticus* (5 cases), Citrobacter freundii (4 cases) and *Enterococcus faecium* (4 cases), which accounted for 20.3%, 10.1%, 7.6%, 6.3%, 5.1% and 5.1% of the total cases, respectively. The blood culture results in six cases showed mixed bacterial growth, of which four cases were mixed growth of *Escherichia coli* and *Enterococcus faecium*, and one case was mixed growth of *Escherichia coli* and *Lactococcus garvieae,* and one case was mixed growth of *Escherichia coli* and *Candida tropicalis*.

***Statistics of infected sites and distribution of microorganisms***

The statistics of infection sites confirmed by pathological examination with positive cultures were shown in Table 3. We found that the lungs (16 cases) were the most susceptible organs to infection in the body, followed by intestinal infections (11 cases), multiple organ infection (9 cases), wound infection (7 cases), myocarditis (5 cases), purulent peritonitis (5 cases), brain infection (3 cases), uterus infection (3 cases) and kidney infection (1 case). Microorganism distribution results were shown in Figure 1. We found that *Escherichia coli* were more active in most infection sites of the body (lung, intestinal, wound, heart, peritoneum etc.), follow by Klebsiella pneumonia (lung, intestinal tract, wound etc.). Similar to *Klebsiella pneumoniae*, *Staphylococcus aureus* infections were also more common and could be found in multiple infection sites of the body. The appearance of *Enterococcus faecium* was often accompanied by *Escherichia coli*, especially when it infected in lung and intestinal. In addition, our research also found several rare bacterial infections, such as *Enterococcus gallinarum*, *Staphylococcus cohnii, Granulicatella adiacens, Comamonas acidovorans, Cryptococcus gattii, Clostridium difficile, Acinetobacter lwoffii, Aeromonas sobria* etc.

## DISCUSSION

Blood culture of patients is a stable and mature technology for the diagnosis of infectious diseases in clinical medicine. Due to the various influencing factors of death, the significance of the postmortem microbial culture in forensic medicine has been controversial [6]. Some researchers suggested that the collection of blood samples for postmortem microbial culture should be as far as possible within 48 hours, otherwise it would affect the detection effect [16,17]. However, Tsokos

**Table 1.** The influencing factors relate to postmortem heart blood cultures

| Influencing factors | Positive blood cultures | Negative blood cultures | P-value |
|---|---|---|---|
| Age (years) | 35.06±21.47 | 27.69±22.07 | 0.06 |
| Gender | | | |
| Male | 48 | 21 | 0.02 |
| Female | 31 | 31 | |
| Prior antibiotics therapy | | | |
| Yes | 59 | 36 | 0.49 |
| No | 20 | 16 | |
| Leukocyte count ($\times 10^9$/L) | 16.92±11.82 | 15.85±11.56 | 0.77 |
| Neutrophil percentage (%) | 77.43±16.87 | 78.96±16.76 | 0.86 |
| Survival time (d) | 16.81±47.14 | 5.83±10.35 | 0.10 |
| Postmortem interval (h) | 37.44±26.54 | 35.94±26.54 | 0.74 |

Note: Leukocyte count: clinical reference (4-10)×109/L , Neutrophil percentage: clinical reference 20%-40%.

**Table 2.** Correlations between postmortem blood culture results and pathological findings

| Heart blood culture results | Consistency between culture results and pathological findings | | Total n (%) |
|---|---|---|---|
| | Yes n (%) | No n (%) | |
| *Escherichia coli* | 10 (12.6) | 6 (7.6) | 16 (20.3) |
| *Klebsiella pneumoniae* | 5 (6.3) | 3 (3.8) | 8 (10.1) |
| *Staphylococcus aureus* | 4 (5.1) | 2 (2.5) | 6 (7.6) |
| *Streptococcus hemolyticus* | 4 (5.1) | 1 (1.3) | 5 (6.3) |
| *Citrobacter freundii* | 4 (5.1) | — | 4 (5.1) |
| *Enterococcus faecium* | 2 (2.5) | 2 (2.5) | 4 (5.1) |
| *Acinetobacter baumannii* | 3 (3.8) | — | 3 (3.8) |
| *Staphylococcus epidermidis* | 2 (2.5) | 1 (1.3) | 3 (3.8) |
| *Klebsiella oxytoca* | 2 (2.5) | — | 2 (2.5) |
| *Stenotrophomonas maltophilia* | 2 (2.5) | — | 2 (2.5) |
| *Leuconostoc mesenteroides* | 1 (1.3) | — | 1 (1.3) |
| *Enterococcus gallinarum* | 1 (1.3) | — | 1 (1.3) |
| *Staphylococcus cohnii* | 1 (1.3) | — | 1 (1.3) |
| *Granulicatella adiacens* | 1 (1.3) | — | 1 (1.3) |
| *Candida tropicalis* | 1 (1.3) | — | 1 (1.3) |
| *Comamonas acidovorans* | 1 (1.3) | — | 1 (1.3) |
| *Staphylococcus sciuri* | 1 (1.3) | — | 1 (1.3) |
| *Clostridium sordellii* | — | 1 (1.3) | 1 (1.3) |
| *Burkholderia cepacia* | 1 (1.3) | — | 1 (1.3) |
| *Cryptococcus gattii* | 1 (1.3) | — | 1 (1.3) |
| *Candida albicans* | 1 (1.3) | — | 1 (1.3) |
| *Streptococcus alactolyticus* | 1 (1.3) | — | 1 (1.3) |
| *Staphylococcus saprophyticus* | 1 (1.3) | — | 1 (1.3) |
| *Clostridium difficile* | 1 (1.3) | — | 1 (1.3) |
| *Candida krusei* | 1 (1.3) | — | 1 (1.3) |
| *Acinetobacter lwoffii* | 1 (1.3) | — | 1 (1.3) |
| *Proteus vulgaris* | 1 (1.3) | — | 1 (1.3) |
| *Pseudomonas aeruginosa* | 1 (1.3) | — | 1 (1.3) |
| *Aeromonas sobria* | 1 (1.3) | — | 1 (1.3) |
| *Enterobacter cloacae* | 1 (1.3) | — | 1 (1.3) |
| Mixed bacterium growth (≥2) | 3 (3.8) | 3 (3.8) | 6 (7.6) |
| Total n (%) | 60 (75.9) | 19 (24.1) | 79 (100) |
| Negative n (%) | 19 (36.5) | 33 (63.5) | 52 (100) |

Note: Of the six cases with mixed bacterium growth, four cases were mixed growth of *Escherichia coli* and *Enterococcus faecium*, and one case was mixed growth of *Escherichia coli* and *Lactococcus garvieae*, and one case was mixed growth of *Escherichia coli* and *Candida tropicalis*.

**Table 3.** Statistics of the infection sites with positive culture results.

| Infection sites | Total |
|---|---|
| Pulmonary infection | 16 |
| Intestinal infections | 11 |
| Multiple organ infection | 9 |
| Wound infection | 7 |
| Myocarditis | 5 |
| Purulent peritonitis | 5 |
| Brain infection | 3 |
| Uterus infection | 3 |
| Kidney infection | 1 |

[10] considered that the PMI had no effect on blood culture, and the instability of the detection results might relate to the detection technology. In general, different detection techniques and detection conditions might produce different results. Although there was no specific standard for postmortem microbial culture in the industry, it could still be used as an important auxiliary method to diagnose the cause of death in forensic [7].

Our results showed that there was no significant difference between the positive cultures and negative cultures in terms of survival time (P=0.10) and PMI (P=0.14). It indicated that the collection procedures and detection results of heart blood cultures with our current techniques were reliable, which was consistent with other study [18]. The positive cultures in male seemed to be higher than that in female (P=0.02). This was a peculiar phenomenon, because there was no report showed a significant difference in genders for blood culture [13,18]. Our results also showed that 72.5% of the decedents were treated with antibiotics before death, and there was no difference between antibiotics treatment and blood culture results (P=0.49). This was consistent with the results of

previous reports, indicating that the using of antibiotics would not reduce the positive rate of blood culture [19,20]. Leukocyte counts and neutrophil counts were important objective indicators for the performance of blood culture. Our results showed that there was no difference on leukocyte counts (P=0.77) and neutrophil counts (P=0.86) between positive cultures and negative cultures, but both of their values were greater than clinical reference. This indicated that we had a powerful data basis for suspecting the decedent with an infection while alive, though blood culture might not be able to detect a positive result for one reason or another.

As mentioned earlier, there are four main possibilities producing a positive blood culture result in theory: invasion in life, agonal spread, postmortem translocation and contamination [12,13]. Except for invasion in life, the remaining three conditions can produce false positive results in diagnosing the infectious diseases. Furthermore, the culture results of postmortem microbial translocation and contamination should be mixed bacteria growth. In our study, 60.3% of the total cases showed positive culture results, and the PPV was 75.9%, which was consistent with the results of previous studies [17]. However, the negative predictive value NPV in negative group was only 36.5% and the discrepancy rate reached at 63.5%. It indicated that a large number of cases were indeed with an infection before death, but the postmortem blood culture results were negative. This may because that some of the autopsies were frozen corpses in our institution, which may not be conducive to the growth of temperature-sensitive bacteria, such as *meningococci, pneumococcus*, and group B streptococcus [21,22]. What is more, those frozen corpses with a long PMI were also not conducive to the reproduction of microorganisms. Research showed that early blood cultures may produce more positive cultures for temperature-sensitive bacteria. Therefore, if we can obtain heart blood samples in early stage after death in medical institutions, the accuracy of blood culture will be greatly improved. In addition, we found that there were 16 cases of single bacteria and 3 cases of mixed not confirmed by pathological findings. It was not yet confirm whether this was caused by contamination during the autopsy. But, at least, our collection of heart blood of every autopsy was performed in accordance with a strict sterile standard.

According to the analysis of the infected sites based on pathological findings, we found lungs and intestines were the most commonly infected organs, followed by multiple organ infection and wound infection. This was consistent with the clinical research results, which was also determined by the special structure of the organs. Of course, many studies showed that blood cultures of lungs, intestines and brain were more likely to produce false positive results [23,24]. We also counted the types and numbers of the microorganisms. The results showed *Escherichia coli*, Klebsiella pneumonia, *Staphylococcus aureus* and *Streptococcus hemolyticus* were the most common isolate bacteria in our study, which was consistent with previous reports [6,25].

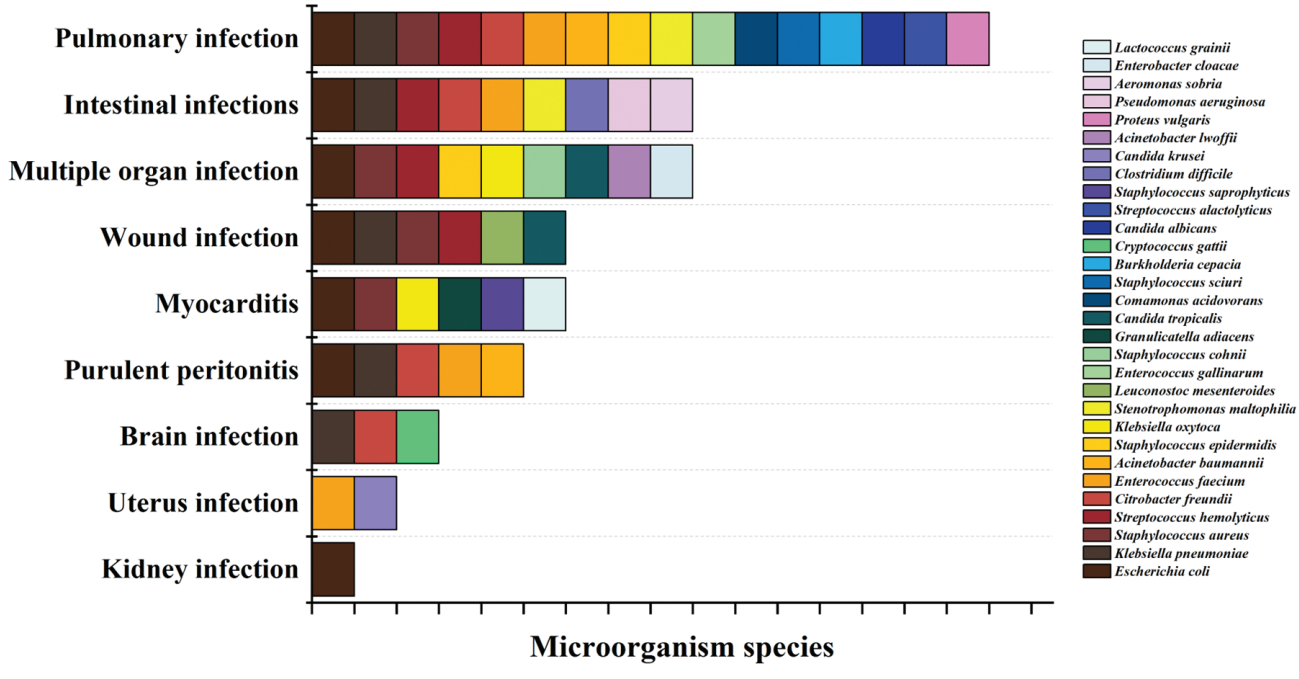


**Figure 1.** The microorganism species distribution in different infection sites.

These bacteria were more common in nosocomial infections by reviewing the hospital medical records of the decedent, which may be related to dysbacteriosis caused by antibiotic treatment [26,27]. Interestingly, *Enterococcus faecium* appeared more frequently in our research and often coexisted with *Escherichia coli* (4 cases). But we don't think these mixed bacterial were always related to contamination. On the contrary, we suspected that it may be caused by inappropriate antimicrobial therapy. In addition, we also studied the microorganism species distribution in different infection sites. *Escherichia coli*, Klebsiella pneumonia, *Staphylococcus aureus* and *Enterococcus faecium* were more active in multiple organ infections. The reason of this result was closely related to the blood transmission of microorganisms. Furthermore, we also found that the lungs also had the most types of bacteria, which was related to the most cases of lung infections. Research has shown that primary infections of the lungs can easily spread through blood transmission to multiple organs across the body. Of course, there were some rare strains and conditional pathogenic strains in our research, which were more likely to infect specific organs or tissues.

There are still some shortcomings and limitations in our study. Some researchers suggested that at least two biological samples (heart blood, cerebrospinal fluid, lung, spleen etc.) should be selected for postmortem microbial culture to ensure the accuracy of the results [10]. Our original intention for postmortem blood culture was to verify our conjecture about whether the decedent had a serious infection before his death. We regarded postmortem blood culture as a fast and efficient method to assist in inferring the cause of death. This study also lacks a control group where there was no suspicion of ante-mortem infection, which might lead to deviations in the results. In addition, the potential viral influence was not considered in our protocols. Therefore, this study still has some shortcomings as a systematic research, but it has important practical significance. We will intake both the case group and the control group in the follow-up study to enhance the scientific character of the research.

**In conclusion,** in this article, we performed a study of postmortem blood culture for 131 cases that of suspected infectious death. Although the detection rate of postmortem blood culture was not high, most of the positive results were credible. It may used to be a powerful auxiliary investigation tool in diagnosing infectious deaths, especially for undiagnosed infectious deaths in forensic medicine. The application of molecular technology to the detection of bacterial toxins, bacterial antigens and specific bacterial DNA or RNA will greatly improve the accuracy of microbial culture in the future.

**Conflict of interest**

The authors declare that they have no conflict of interest.

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