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Personalized Medicine-Based Microbiology Management of Infectious Diseases

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Abstract:
This study identified pathogenic variables associated with increased mortality risk in infectious diseases using predictive analysis and a combination of genotypic, phenotypic, and medical data. The quick nucleic acid-based clinical assessment might affect the spread of hospital-acquired illnesses, and we argue that such life-saving operations should be carried out closer to the individual, preferably in 24/7 medical facilities' specialized labs. Personalized medicine notions are relevant in infections for the rapid characterization of a disease-causing microbial community and perseverance of its antibiotic susceptibility characteristic to guide a suitable antibiotic therapy for the proper care of the individual. Personalized medicine aims to interrogate a patient's genetic data as well as pharmacodynamic polymorphisms, and guide drug options and dosage. This work demonstrates the potential use of fundamental genetic analysis in treating infectious diseases and theoretically justifies the value of customized therapy.

INTRODUCTION

Antibiotic usage allows selectively eliminating infectious germs with minor adverse effects on the host cells (1). Every antibiotic therapy is developed based on an individual assessment of the patient (2). Antimicrobial stewardship initiatives to stop the spread of antibiotic resistance have received great attention in recent years (3). Due to the scarcity of novel antibiotic classes, this is especially crucial (4). Antibiotic medications are classified as either empiric (without microbiological inquiry) or definitive (based on the finding of relevant bacterial etiologies and, optionally, in vitro susceptibility testing) (5).

Antibiotics may also be used to prevent atherosclerosis during dental treatments or as preventive medication in various surgical operations (6). Antimicrobial therapy can also be given as a preventative measure to more susceptible patients, such as those with solid or stem cell transplants and blood levels of cytomegalovirus (CMV), those with candida colonization in intensive care units (ICUs), or those with cystic fibrosis (CF) and sporadic Pseudomonas aeruginosa colonization of their airways (7, 8). These are antibacterial drug therapies based on detecting bacteria without clinical signs of infection in the patient populations (9). The threat of colonization with a specific microorganism commonly leads to real infectious disorders with the same pathogen, which are difficult to eliminate, and has thus been an incentive for preventive antimicrobial treatment (10).

A severe illness that causes substantial mortality and morbidity is staphylococcus aureus bacteremia (SAB) (11, 12). The number of cases is now approximately 20% which depends on host and infection variables (13). Age and the existence of concomitant conditions are two host-related characteristics that have repeatedly been proven to be determinants of death in patients with SAB (14). In contrast, the diversity and variability of disease pathogenesis make it challenging to fully understand the involvement of pathogen-specific variables. To resolve this information gap, researchers phenotyped a collection of sequenced medical S.

aureus isolates from SAB patients (11, 15). The researchers discovered pathogen-specific characteristics associated with an increased mortality risk by applying predictive analysis to genotypic and phenotypic information on microorganisms and comparing it to 30-day death certificates (15, 16). This research reveals that an infecting microorganism's genetic make-up may be more relevant to infection progress than previously thought (17). Furthermore, this work presents a model for discovering host-pathogen relationships, where the highest performing predictive algorithm is the one that includes all available information, including clinical data, conceptually proving the advantages of person-centered therapy (18). Further investigation into the effectiveness of targeted medicines or interventions may be sparked by the discovery of significant pathogen-specific characteristics, according to scientists (19).

Personalized Medicine for Infectious Diseases

To offer the proper treatment, at the correct dose, to the particular patient, personalized medicine is a field that employs a patient's genetic information to advise the administration of a suitable treatment protocol in light of the patient's predicted response to a particular drug or mixture of therapies. Personalized medicine ideas have historically been centered on planning genetic conditions, where polymorphisms in genes that control phase are rationally construed against expanding datasets of known medicinal interactions with modified functions to mentor drug medication and dosage (15–19). The value of biomarkers linked to the immune reaction, infection risk, host-microbiota relationships, or sensitivity to antibacterial medication therapy is being established, which is progressively shifting this perspective (19, 20). Use of personalized medicine for infectious illnesses to direct molecular pathogen treatment has clear benefits. The use of a personalized medicine strategy could be conceptualized as a bimodal process for interpreting clinically relevant genomic modules of the patient and the disease-associated pathogen(s) to choose and as well as the treatment regimen for acute life-threatening illnesses. The molecular microbiome provides techniques that enable rapid identification and recognition of microbial cells. This molecular microbiome technique is essential knowledge that a doctor can quickly use to focus the first (critical) hours of a patient's treatment protocol and substantially speed up infectious disease management (21).

Infectious Disease Management in the Molecular Medicine Era

When a feverish, possibly infectious patient enters the healthcare center, a screening cycle including numerous time-consuming processes is initiated. Although, the quantitative phase of the process for traditional phenotypic bacteriology identification techniques represents the most activity occurs constraint, there are also significant delays related to the pre-and post-analytical stages, such as sample transportation, batching procedures, and result transmission, which inevitably lengthen the delivery time (15, 18, 22).

Molecular Tools for POC or near POC Diagnostics of Infectious Diseases

Point-of-care (POC) screening is characterized by medical samples analyzed at or near the individual with the expectation where the test findings will be provided instantaneously or in a very short timescale to aid caregivers with prompt diagnosis and therapeutic action (15-20). This description clearly states that time and space are critical factors on which technology specialists and medical system administrators should work to shorten the detection process and make biological POC screening possible (22). The ultimate aim may be bedside screening, but the creation of near point-of-care laboratories would undoubtedly shorten the detection process and boost the effectiveness of infectious disease treatment by expanding access to highly efficient nucleic acid-based assays (23). In the market for bacterial infections, point-of-care screening is ruled by rapid microscopic examination which can be performed outside medical laboratories but frequently lacks responsiveness and sensitivity (21-23); a frequently updated list of CLIA-waived assessments can be accessed via the Internet (24). Procalcitonin, a potential biomarker utilized in medical care in certain countries, detects the existence and intensity of infectious diseases such as community-acquired pneumonitis and septic (25). Although not particular, and despite some conflicting studies about its reliability and utility as a septic predictive biomarker, it has been proposed that serum prolactin serum concentrations might be utilized as an antimicrobial stewardship strategy (26).

Applications and Anticipated Impact of POC or near POC Diagnostics of Infectious Diseases Increased use of quick diagnostic procedures for infections in healthcare systems in developed and developing nations ensures speedier treatment strategies, more suitable antimicrobial medicine, better human and laboratory asset allocation, as well as decreased mortality, morbidity, and costs (18-21). Depending on the type of health service, the (administrative) modularity of healthcare facility budget procedures is a significant impediment to the implementation of rapid diagnostic techniques when test costs are considered without considering the mid-to-long-term effects of technological advancement on client health and organizational effectiveness (22-25). In this era of rapidly rising medical costs, adopting new technologies and systematic procedures requires careful planning so that the reasoned preliminary choices prove cost

efficiency and clinical usefulness as well as encourage further advancement within microbial identification and infection care organizations (26). This section contains examples of therapeutically meaningful uses of point-of-care or near-point-of-care diagnostic techniques that may act as a standard for customized infection control therapy (27).

A)Bloodstream Infections and Sepsis

Infections caused circulated by the bloodstream are potentially fatal circumstances with a crucial period for timely treatment of fewer than 6 hours. Furthermore, it has been proven that for every hour gained in initiating proper antibiotic medication in individuals infected, the likelihood of survivability improves dramatically (28, 29). The gold standard approach, blood culture, has a very high positive predictive value; however, due to the number and culture-ability conditions of microbial and pathogenic fungi, the overall positive emotion percentage for the prognosis of sepsis is approximated to be 30-40% (30), and possibly as low as 20% (31). Theoretically, detecting MRSA on positive blood samples is quicker than current culture-based approaches. However, the timing of PCR-based diagnosis of MRSA may be far more relevant if the diagnosis was performed straight from blood. Thus, blood culture from each person and checking the microbial density can be a strong point of personalized medicine for treating and managing sepsis in hospitals.

B)Influenza and Severe Respiratory Tract Infections

The treatment of influenza is an ongoing issue in the health service, as diagnostic symptom assessment seldom results in unneeded and inefficient antimicrobial medication (28-31). Antiviral therapy is more efficient than viral therapy when initiated within 48 hours of the onset of symptoms. Nucleic acid-based experiments (reverse transcription PCR) are faster than culture and more sensitive than advertising antigen-based experiments; promoting a non-empirical strategic plan that provides the most significant advantages would seem logical. Similarly, while influenza molecular techniques may offer rapid findings and minimize medication use and hospitalizations, an experimental antiviral medication approach, which costs about the same as RT-PCR, would lead to the medication of 5-15 individuals without influenza for each positive argument (30-32). In a recent publication, molecular analysis has detected other respiratory tract virus pneumonia caused by at least 15 distinct pathogens. The Infectious Diseases Society of North America has underscored the importance of faster molecular diagnostics in this clinical sector (30-32).

C)Hospital-Acquired Infections

Hospital-acquired infectious diseases have become a fundamental problem in medical facilities, with their monitoring being immensely muddled by antibiotic-resistant emergence. It was projected with 1.7 million people having an illness and hospitalized, and nearly 100,000 died. As a result, it led to at least $6.5 billion in medical costs (20-23). Researchers have discussed the significance of reducing the possibility of adverse effects and medication interaction as well as the timing of potential antibiotic therapies in Gram-negative hospital-acquired bacterial meningitis. Rapid computed tomographic molecular techniques might be essential given that nosocomial infection is the second most common illness among hospitalized patients worldwide. That improper first antibiotic treatment has been linked to lower survival rates (32). Fast computed tomography molecular techniques can be a huge step in personalized medicine by choosing the right drugs for patients.

Whole-genome sequencing (WGS) and infectious diseases

The potential use of whole-genome sequencing (WGS) in treating infectious diseases and implementing customized therapy, as shown by this research, is of great interest. WGS will most likely be restricted, given the abovementioned warnings on bacterial pathogenicity's complexity (20, 21, 32).

We predict that, at least shortly, the primary goal of sequence analysis will be quick, ideally culture-free characterization of infectious diseases (22, 33). Time to proper treatment is critical in determining a patient's probability of recuperation for high-burden diseases, such as septicemia. At the moment, screening techniques depend on blood cultures, and further analysis is required to determine the bacterium responsible for the disease and the tolerance pattern, with a turnaround time of two to three days (23, 33). Through sequencing microorganisms directly from a patient's blood specimen, a different diagnostic strategy that uses WGS might be used. In this method, microorganisms from a patient's specimen would be condensed, the Genome would be isolated, and MinI ON equipment would be used for whole-molecule sequencing as genetic analysis (Oxford Nanopore Technologies). The microbial pathogen (including lineage) and the resistance genotype might be identified using sequence data using a well-designed computational laboratory. Additional patient treatment targeting may be made possible by discovering pathogen-specific variables in conjunction with clinical information of medical laboratory during one shift (24, 25, 33).

Dosing patterns for antibiotics and personalized medicine

The positive result for individuals and the antibacterial spectrum has long been understood to be significantly dependent on medication dosage (26, 34). Dosing

Table 1. list a description of several terminologies related to sequencing.

Uses case	Description
Adapter	Any little bit of known-sequence DNA that one attaches to the ends of their unidentified DNA is of interest, often to ultimately enable a sequencing primer to hybridize at this place.
Amplicon sequencing	Analysis of genetic variants using ultra-deep sequencing of PCR products
ANI	An analytical technique that measures the nucleotide identity between genomic areas shared by two isolates is called average nucleotide identity.
Assembly	Genome assembly is assembling a representation of the original genomic sequence from several small DNA sequence fragments, such as those produced by next-generation sequencers.
Bridge amplification	a PCR method where DNA is encased on a solid surface before sequencing. Platforms from Illumina employ it.
Contig	a consensus sequence created by assembling many brief, overlapping DNA segments
cgMLST	Core genome multi-locus sequence typing—an analysis method that detects variation in genes that are present in the majority (>97%) of strains of a given species
Coverage (read depth)	The average number of reads that include a given nucleotide in the reconstructed sequence
Draft genome	Sequencing of genomic DNA is less accurate than the final sequence; some segments are missing, in the wrong order, or are oriented incorrectly.
Emulsion PCR	A polymerase chain reaction (PCR) method on a bead's surface inside of tiny water bubbles floating atop an oil solution. Platforms for IonTorrent take advantage of it.

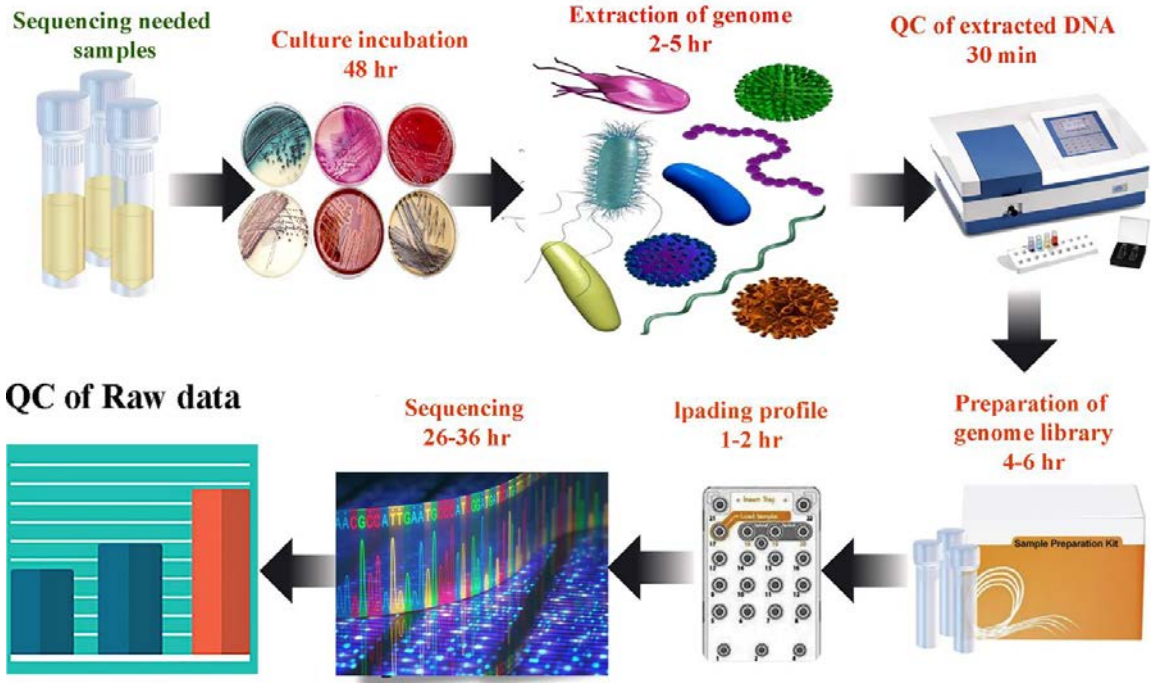

Fig 1. Methodology for full genome sequencing often used in clinical or health promotion labs.

should consider whether the antimicrobial effect is mainly based on duration above the MIC, area-under-the-curve (AUC) above the MIC, or peak dosage above the MIC to achieve the best impact of microbial death or inhibition of microbial contamination (27, 28, 34). The guidelines of current dosage regimens consider this and advocate frequent administration (time-dependent killing), once-daily dosing (mainly density killing), or frequently twice-day dosing (AUC above MIC killing) (29, 30, 34). Most often, if the best antibacterial activities are not considered when deciding on dosage reductions, incorrect dosing with compromised functional status occurs (31, 34).

While altered perfusion and the volume of distribution have received less attention, dosage reductions caused by reduced organ functions are the main focus of pharmacokinetic investigations of critically sick patients. Due to stringent exclusion and inclusion criteria, randomized, controlled clinical trials risk not accurately reflecting the types of patients who will ultimately receive daily treatment with the medicine under investigation (33, 35). Thus, only 13%

of the 187 patients who received tigecycline outside the procedure could have been randomly assigned to the clinical research. Those individuals were noticeably worse than those who had been randomized (32-34).

Quantify level of variety and find mutations that encode tolerance to antibiotics based on personalized medicine

It is crucial to remember that another advantage of such a work process is the capacity to avoid any possible growth "bias" when germs are identified from labeled clinical specimen bottles (34, 35). When cultured under non-selective circumstances (i.e., without medications), this occurs when wild-type populations outcompete specific sub-populations (33-35). These are not only sub-populations probably "hidden," but if separated, they typically occur at a regularity that falls below the detection limit of existing predisposing testing procedures (i.e., less than 1×10^6 organisms). Population diversification has been well-established for viral diseases, with diverse populations linked to worse reactions and outcomes in HIV and hepatitis C infectious diseases (35, 36). Recent investigations have also shown comparable variety in certain SAB cases, which is not unexpected given the development of WGS (36). This finding is important, mainly if the variability that has been recognized is related to the existence of resistant sub-populations since patients who fail preliminary antibiotic treatment typically have persistent septicemia and worse outcomes than patient populations who complete their preliminary SAB. In these situations, WGS would make it easier to quantify the level of variety and find mutations that encode tolerance to many medicines, including daptomycin, and help choose the best course of treatment (37).

CONCLUSION

In this article, we have proposed a personalized medicine method where patients could benefit enormously from optimized infection control influenced by clinically-relevant genomics data derived from microbiota. Genomics data derived from microbiota in specialized POC devices and tests performed near patients or nearby POC research labs and quickly recounted to the attending physician to ameliorate time-consuming and error-prone initiatives occurring in the pre-and post-analytical stages. In addition to the possibilities listed above, it is also feasible that a meta-genomics approach may focus on both host and pathogens variables (from a patient's blood sample), expanding the range of potential treatment targets. A more profound comprehension of mediated activation would be necessary for this and other sequencing technological developments. The following is probably necessary before applying WGS in treating SAB (and maybe other disease types). First, a deeper understanding of the processes behind bacterial resistance is required such as the contribution of a larger genetic context. Regarding the latter, such comprehension may also assist in determining the best kind of treatment (i.e., could predict resistance development). Secondly, further study is needed to understand the extent of bacterial variety that results in clinical failure regarding tolerance.

Ultimately, advances in customized treatment and the control of infectious diseases have saved patients' time, money, and lives. It improves the technologies that enable reliable bacterial DNA recovery (from plasma or tissue specimens) for WGS. In conclusion, despite these factors, WGS is likely to play a significant role.

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