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Original article

Evaluation of the BD PhoenixTM CPO Detect Test for the detection of carbapenemase producers

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ABSTRACT

Objectives: Becton-Dickinson recently developed the PhoenixTM CPO (carbapenemase-producing organism) Detect Test, a growth-based test embedded in Gram-negative (GN) panels for the detection and confirmation of bacteria producing class A, B and D carbapenemases. This study aimed to (a) determine the performance of the CPO test, and (b) assess its added value in routine diagnostic workflows.

Methods: The performance of the BD Phoenix CPO test was analysed retrospectively on a collection of 185 molecularly characterized strains, including 92 CPOs, and prospectively on 135 and 160 routine isolates with and without CPO suspicion, respectively.

Results: In the retrospective study the CPO test exhibited 92.4% accuracy (95%CI 87.6-95.8), 97.8% sensitivity (95%CI 92.4-99.7) and 87.1% specificity (95%CI 78.6-93.2) for carbapenemase detection. The CPO test provided a classification to class A, B, and D for 81.3% of detected carbapenemases with 94.6% accuracy (95%CI 86.7-98.5). In the prospective study the CPO test detection performance showed 77.8% accuracy (95%CI 68.8-84.5), 100% sensitivity (95%CI 91.2-100) and 67.8% specificity (95%CI 57.3-77.1) with 135 CPO-suspicious isolates and 98.8% accuracy and specificity (95%CI 95.6-99.9) with 160 non-CPO-suspicious isolates. Compared to routine testing, the implementation of the CPO test allowed a mean reduction of 21.3 h (95%CI 17.6-25) in turnaround time, 16.8 min (95%CI 13.4-20.2) in hands-on time, and 20.6 CHF (95%CI 16.5-24.8) in costs.

Conclusions: The CPO test is reliable for the detection of CPO with a high sensitivity. However, the relatively low detection specificity required the use of additional confirmatory methods. The carbapenemase classification accuracy is robust in providing preliminary results before molecular characterization. Finally, the implementation of the test in routine workflows allowed a significant reduction in turnaround time, hands-on time and cost compared to the conventional approach. A. Croxatto, Clin Microbiol Infect 2019: 1

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Introduction

The emergence of carbapenemase-producing organisms (CPOs) has triggered the development of new reliable and rapid diagnostic tools. Upon suspicion of isolates being CPOs following initial antibiotic susceptibility testing (AST), phenotypic or molecular-based methods can be used to detect and/or characterize the presence of carbapenemases. Phenotypic tests include, among others, the Carba NP test [1-4], the Hodge test [5,6], the carbapenem inactivation

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method (CIM) [7], matrix-assisted laser desorption/ionization timeof-flight mass spectrometry (MALDI-TOF) [8-11], lateral flow immunoassay tests [12,13] and carbapenem disk diffusion or E-test with and without carbapenemase inhibitors [14–17]. Depending on the phenotypic test, the turnaround time varies from 15 min to 24 h. Some of these phenotypic tests—such as the NG-test Carba 5 (NG Biotech, Guipry, France) and Carba NP test—can be applied directly from positive blood cultures, allowing a rapid turnaround time for antibiotic regimen guidance [18]. Usually, the number of tests required, turnaround time, hands-on time and costs are significantly higher to exclude the presence of a carbapenemase with a high sensitivity rather than to demonstrate its activity.

The use of nucleic acid amplification tests (NAATs) to rapidly identify CPOs from samples such as positive blood culture and

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stools is an alternative approach to rapidly establishing an optimal empirical antibiotic therapy or for infectious control management [19,20]. Most carbapenemase NAAT panels detect the most frequent gene variants encoding carbapenemases, including KPC, NDM, OXA-48, VIM and IMP. However, these tests cannot exclude the presence of a gene encoding another carbapenemase type, and they are relatively expensive, preventing their use in systematic screening of some specimen types or bacterial isolates with CPO suspicion, especially in countries where CPO prevalence is low to very low.

Becton-Dickinson (BD, Sparks, USA) recently developed the Phoenix CPO Detect Test, a growth-based method embedded in Gram-negative (GN) panels for the detection and confirmation of carbapenemases of classes A, B and D [21]. This study aimed to determine the performance of the CPO test and to investigate its added value in routine diagnostic workflows. The performance of the BD Phoenix CPO test was retrospectively and prospectively analysed on a collection of 185 molecularly characterized strains and on 295 routine isolates, respectively. The prospective phase comparing the CPO test to routine testing was performed to further determine the performance of the test and differences in turnaround time, hands-on time and costs, including (a) 135 strains with CPO suspicion representing an extreme diagnostic challenge, and (b) 156 strains with no CPO suspicion representing conventional isolates encountered mostly in countries with low CPO prevalence.

Methods

Strains

The performance of the Phoenix CPO Detect Test was tested on a collection of 92 molecularly characterized CPOs and 93 non-CPOs (Supplementary material Table S1). The collection included 27 non-fermentative bacteria and 158 members of the Enter-obacterales. In addition, 295 clinical isolates, including 135 isolates suspected of carbapenemase production, were prospectively but not consecutively isolated from various de-identified clinical specimens during a 10-month period ranging from January to October 2018 (Supplementary material Table S2).

Phenotypic tests

All phenotypic tests were performed from bacterial colonies growing on Columbia agar with 5% sheep blood (BD, Cat. No. 254071) or Mueller—Hinton agar (Oxoid Ltd, Hampshire, UK, Cat. No. CM0337). The Carba NP test was performed as described by Dortet et al. [4]. The CIM test was carried out as described by van der Zwaluw et al. [7] using the susceptible *Escherichia coli* indicator strain (ATCC 25922) and a 10-µg meropenem disk (Oxoid Ltd). Our evaluation of these two phenotypic tests demonstrated an 83.9% sensitivity and 100% specificity for the Carba NP test and a 100% sensitivity and 100% specificity for the CIM test.

MALDI-TOF

MALDI-TOF was used as an additional phenotypic test to exclude the presence of carbapenamase activity in Phoenix CPO Detect Test false positives. Hydrolysis of the meropenem test was performed as described previously [9] except that meropenem (Labtech, Sorisole, Italy) was used at a final concentration of 0.5 mM. Each isolate was tested in duplicate by spotting twice 1 μ L of each replicate on a 96-well target plate (MFX μ Focus MALDI plate 96 circles, Hudson Surface Technology, Fort Lee, USA). The matrix was composed of 1 μ L of α -cyano-4-hydroxycinnamic acid (HCCA, Bruker Daltonik,

Bremen, Germany) resuspended in 125 μL of acetonitrile + 125 μL of water. The MALDI-TOF was performed on a Bruker Daltonik Microflex LT mass spectrometer. (A detailed description of the spectra analysis is provided in Supplementary material.)

Phoenix CPO Detect Test

The Phoenix CPO Detect Test (BD) is a qualitative confirmatory growth-based test embedded in Gram-negative (GN) panels (NMIC-502, NMIC-505) for detection and confirmation of class A, B and D carbapenemases. The Phoenix CPO Detect Test utilizes meropenem, doripenem, temocillin and cloxacillin, alone and in combination with various chelators and β -lactamase inhibitors in amounts required for the detection and classification of CPO. The Phoenix CPO Detect Test was applied as described by the manufacturer.

Nucleic acid amplification test (NAAT)

All false-positive results of the Phoenix CPO Detect Test from the prospective study were verified by NAAT testing using the BD MAXTM Check-Points CPO test as described by the manufacturer (Cat. No. 278102). As described in the package insert, variants of the carbapenemases KPC, OXA-48-like, NDM and IMP should be detected by the BD MAX Check-Points CPO test.

Whole-genome sequencing and analysis

Bacterial strains were sub-inoculated onto BD Columbia agar with 5% sheep blood (Cat. No. 254071), and genomic DNA was extracted from bacterial colonies using the Wizard Genomic DNA Purification kit (Promega, Madison, USA, Cat. No. A1120) as described by the manufacturer. Libraries were prepared with the Nextera XT kit (Illumina, San Diego, USA, Cat. No. FC-131-1096) as described by the manufacturer, and the sequencing was performed on MiSeq (Illumina) with a paired-end 250 cycles protocol. (A detailed description of the bioinformatics analysis is provided in the Supplementary material.)

Laboratory workflow with and without Phoenix CPO Detect Test upon suspicion of CPO

A description of the conventional routine and Phoenix CPO Detect Test laboratory workflows upon CPO suspicion is provided in Fig. 1. Upon CPO suspicion, the Carba NP test with an 83.9% sensitivity and short turnaround time (around 2 h) was performed first, and the CIM test with a 100% sensitivity but a longer turnaround time (around 1 day) was performed second to increase the sensitivity of the detection.

Turnaround time, hands-on time and cost

The turnaround time, hands-on time and cost were evaluated on the first 114 of the 135 isolates with CPO suspicion. The total turnaround time, hands-on time and cost for each analytical workflow were obtained by summing the respective turnaround time, hands-on time and costs of the initial AST tests and the successive phenotypic tests that were initiated upon CPO suspicion. The laboratory costs of the various consumables were the following: Vitek card (AST N290 and AST N240): 8.75 CHF (7.80 EUR, 8.72 USD); Phoenix panel (NMIC-502): 8.75 CHF (7.80 EUR, 8.72 USD); carbapenems disks: 0.94 CHF (0.84 EUR, 0.94 USD); carbapenems E-tests: 17.30 CHF (15.41 EUR, 17.24 USD); Carba NP test: 0.90 CHF (0.80 EUR, 0.90 USD); CIM test: 0.85 CHF (0.76 EUR, 0.85 USD).

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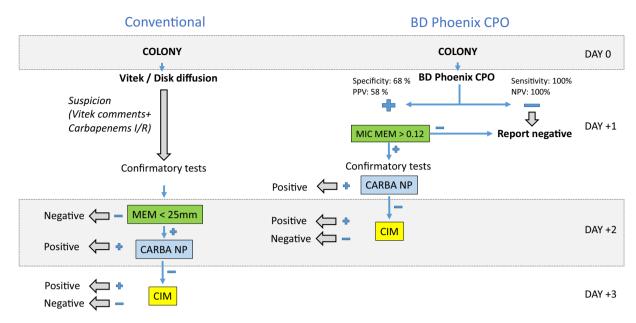


Fig. 1. Conventional and Phoenix CPO (carbapenemase-producing organism) Detect Test laboratory workflows. Conventional workflow: at day 0, an antibiotic sensitivity test (AST) was performed on an automated Vitek system (bioMérieux, Marcy-l'Etoile, France) with a MacConkey agar purity plate. When a CPO was suspected 1 day later (day +1) due to documented decreased susceptibility to at least one carbapenem drug, a subculture on blood agar of the putative CPO strain and a meropenem disk diffusion test on Mueller—Hinton agar were performed and incubated 18−24 h. At day +2, a Carba NP test was done when the meropenem disk diffusion diameter was ≤25 mm. A CIM test was initiated and incubated 18−24 h following a negative Carba NP test. The CIM test was read at day +3. Phoenix CPO Detect Test workflow: At day 0, an AST was performed on the automated Phoenix M50 system with the Phoenix CPO Detect Test (panel NMIC-502) using a blood agar purity plate. At day +1, a negative Phoenix CPO Detect Test result was directly reported thanks to 100% sensitivity as observed in the evaluation of the performance of the Phoenix CPO Detect Test in the prospective study. When the Phoenix CPO Detect Test was positive, a panel of confirmatory tests similar to the conventional laboratory workflow was initiated, including reading of the Carba NP test at day +1 and the CIM test at day +2. MEM, meropenem; CARBA NP, Carba NP test; CIM, CIM test.

Results

Retrospective performance analysis

The performance of the Phoenix CPO Detect Test to detect and to classify carbapenemases was analysed on a collection of 185 strains, including 92 molecularly characterized CPOs and 93 non-CPOs (Supplementary material Table S1). The Phoenix CPO Detect Test exhibited a total detection performance of 92.4% accuracy (95%CI 87.6–95.8), 97.8% sensitivity (95%CI 92.4–99.7) and 87.1% specificity (95%CI 78.6-93.2) (Table 1). Two false negatives and 12 false positives were documented (Supplementary material Table S3). The two false negatives included an Acinetobacter pittii strain carrying an IMP-5-encoding gene and an E. coli strain carrying a gene encoding OXA-181. The A. pitti IMP-5 was positive in both Carba NP and CIM tests, whereas the E. coli OXA-181 was 'doubtful' in the Carba NP and positive in the CIM tests. The genomes of the 12 falsepositive strains were sequenced and confirmed to be non-CPOs, but they contained other β-lactamase-encoding genes such as extended-spectrum β-lactamase (ESBL) (CTX-M), AmpC cephalosporinases and other β-lactamase types (SHV, TEM, OXA) (Supplementary material Table S4).

The performance of the Phoenix CPO Detect Test for carbapenemase classification was assessed on the 90 detected carbapenemases. Among these strains, 74 were classified (82.2%) and 16

(17.8%) were detected but not classified (Table 2). Unclassified CPOs included strains carrying genes encoding KPC, NDM, VIM and OXA variants (Supplementary material Table S5).

Among the 74 classified carbapenemases, four misclassifications were observed, giving an overall accuracy of 94.6% (95%Cl 86.7–98.5) (Table 3 and Supplementary material Table S6). The genomes of the four misclassified carbapenemase isolates were sequenced; they all encoded carbapenemases of one or more different classes and other β -lactamase-encoding genes (Supplementary material Table S7).

Prospective performance analysis

The performance of the CPO detection test was evaluated prospectively on 135 and 160 routine strains with and without CPO suspicion (Supplementary material Table S2). CPO suspicion was based on reduced susceptibility to one or more carbapenems following routine initial AST with either automated or disk-diffusion assays. Among the 135 routine strains with CPO suspicion, 42 isolates (31.1%) were characterized as CPO strains based on a positive Carba NP test (37 isolates), a CIM test (two isolates), and on molecular diagnostic with the BDmax CPE panel (three isolates).

The performance of the Phoenix CPO Detect Test on the 135 strains with CPO suspicion exhibited no false negatives but 30 false positives, leading to a 77.8% accuracy (95%CI 68.8–84.5), 100%

 Table 1

 Phoenix CPO (carbapenemase-producing organism) Detect Test performance on a collection of 185 strains including 92 molecularly characterized CPOs and 93 non-CPOs

| Bacteria | Total | Carb pos | | Accuracy | Accuracy | | Sensitivity | | Specificity | |
|------------------|-------|----------|------|----------|-----------|------|-------------|------|-------------|------|
| | n | n % | | % | 95%CI | % | 95%CI | % | 95%CI | |
| Total | 185 | 92 | 49.7 | 92.4 | 87.6-95.8 | 97.8 | 92.4-99.7 | 87.1 | 78.6-93.2 | 0.85 |
| Enterobacterales | 157 | 69 | 43.9 | 91.7 | 86.3-95.5 | 98.6 | 92.2-100 | 86.4 | 77.4-92.8 | 0.84 |
| Non-fermentative | 27 | 23 | 85.2 | 96.3 | 81-99.9 | 95.7 | 78-99.9 | 100 | 39.8-100 | 0.95 |

Carb pos, carbapenemase positive; κ, kappa coefficient; 95%CI, 95% confidence interval.

Table 2Carbapenemase classification performance of the Phoenix CPO (carbapenemase-producing organism) Detect Test

| Bacteria | n | Classified | | Unclassified | | |
|------------------|----|------------|------|--------------|------|--|
| | | n | % | n | % | |
| Total | 90 | 74 | 82.2 | 16 | 17.8 | |
| Enterobacterales | 68 | 56 | 82.4 | 12 | 17.6 | |
| Non-fermentative | 22 | 18 | 81.8 | 4 | 18.2 | |

Classified, Phoenix-CPO-test-classified carbapenemases; Unclassified, Phoenix-CPO-test-unclassified carbapenemases.

sensitivity (95%CI 91.2—100) and 67.8% specificity (95%CI 57.3—77.1) (Table 4 and Supplementary material Table S9). It is noteworthy that 21 of the 30 false positives (70%) were observed with *Pseudomonas aeruginosa* isolates (Supplementary material Table S10). Interestingly, an overall sensitivity of 100% (95%CI 91.2—100) was observed.

The absence of carbapenemase in the Phoenix CPO Detect Test false-positive isolates were confirmed by negative tests, including Carba NP, CIM, MALDI-TOF and BDmax CPO tests.

The performance of the Phoenix CPO Detect Test on 160 routine strains with no CPO suspicion presented two false positives (1.25%) for an accuracy and specificity of 98.8% (95%CI 95.6—99.9) (Supplementary material Table S8).

Turnaround time, hands-on time and cost comparison

The turnaround time, hands-on time and cost were determined for 114 strains comparing routine laboratory procedures workflow with and without the implementation of the Phoenix CPO Detect Test (Fig. 1). The implementation of the Phoenix CPO Detect Test allowed a significant reduction of the turnaround time and hands-on time compared to the conventional analytical workflow, with an overall cost reduction of 45% representing a mean reduction per isolate of 20.6 CHF (18.4 EUR, 20.6 USD) (CHF 95%CI 16.5—24.8, EUR 95%CI 14.7—22.1, USD 95%CI 16.4—24.7) (Fig. 2).

Discussion

Main findings

With a high sensitivity, the Phoenix CPO Detect Test is reliable for the screening and detection of CPOs. The relatively low detection specificity indicates that additional methods are required to confirm positive detection by the CPO test.

However, the prospective study on routine isolates with no CPO suspicion showed a 98.8% specificity (95%CI 95.6—99.9), indicating that the number of confirmatory tests will be minimal in routine diagnostic laboratories with a low CPO suspicion prevalence. As with any other phenotypic test, the specificity of the Phoenix CPO Detect Test will strongly depend on the phenotype of the non-CPO, with an expected decreased specificity with highly challenging isolates combining ESBLs and/or AmpCs with porin loss [21].

The carbapenemase classification providing 94.6% accuracy (95% CI 86.7—98.5) is robust in reporting preliminary results before molecular characterization. Finally, the implementation of the Phoenix CPO Detect Test in routine practice allows a significant reduction in turnaround time, hands-on time and cost compared to the conventional approach (Fig. 2).

Strengths and weaknesses

The retrospective and prospective studies showed only two false negatives (1.48%) and 44 false positives (12.7%). The two falsenegative strains were positive with other phenotypic tests, excluding the possibility of an absence of expression and/or activity of these carbapenemases. However, low-level carbapenemase expression and/or growth impairment due to a carbapenemase-independent mechanism may have prevented their detection by the Phoenix CPO Detect Test.

Among the 90 detected carbapenemases, 70 were correctly classified, 16 were not classified and four were misclassified by the Phoenix CPO Detect Test (Supplementary material Table S6). Phenotypic detection and classification of strains carrying multiple carbapenemase types, ESBL, AmpC and potentially other uncharacterized carbapenemase resistance mechanisms is difficult due the coexistence of different resistance mechanisms that prevent phenotypic detection and classification by combinations of antibiotic and β -lactamase inhibitors. For instance, the failure to detect alternative carbapenemase classes or ESBL and AmpC with porin loss may lead to false-positive detection of class D OXA-48 types if, in addition, decreased susceptibility and/or natural resistance to carbapenems other than ertapenem and temocillin are observed. For instance, the natural resistance of P. aeruginosa to both ertapenem and temocillin may significantly interfere with the carbapenemase classification performance of the CPO Detect Test. Moreover, hyperproduction of AmpC cephalosporinase may be

 Table 3

 Performance of the Phoenix CPO (carbapenemase-producing organism) Detect Test for carbapenemase Ambler classification

| Class | Truth | Classified | Accuracy | Accuracy | | | Specificity | | |
|-------|-------|------------|----------|-----------|-------|-----------|-------------|-----------|--|
| | ${n}$ | n | % | 95%CI | % | 95%CI | % | 95%CI | |
| A | 9 | 10 | 98.7 | 92.7-100 | 100.0 | 66.4-100 | 98.5 | 91.8-100 | |
| В | 19 | 18 | 96.0 | 88.6-99.2 | 89.5 | 66.9-98.7 | 98.2 | 90.3-100 | |
| D | 46 | 46 | 94.6 | 86.7-98.5 | 95.7 | 85.2-99.5 | 92.9 | 76.5-99.1 | |

Class, Ambler classification; Truth, molecular characterization, 95%CI: 95% confidence interval.

 Table 4

 Performance of the Phoenix CPO (carbapenemase-producing organism) Detect Test for carbapenemase detection on 135 strains with CPO suspicion

| | • | • | - | | | | | | • | | | | |
|------------------|-------|----------|------|----------------------------|-------|----------|-------------|-------------|----------|-------------|-----------|------|--|
| Bacteria | Total | Carb pos | | Phoenix CPO Detect Test | | Accuracy | | Sensitivity | | Specificity | | κ | |
| | N° | N° | % | N° | N° FP | % | 95% CI | % | 95% CI | % | 95% CI | | |
| Total | 135 | 42 | 31.1 | 72 | 30 | 77.8 | 68.8-84.5 | 100 | 91.2-100 | 67.7 | 57.3-77.1 | 0.31 | |
| Enterobacterales | 85 | 29 | 34.1 | 38 | 9 | 89.4 | 80.9-95 | 100 | 88.1-100 | 84 | 71.7-92.4 | 0.53 | |
| Non fermentative | 50 | 13 | 26.0 | 34 | 21 | 58 | 43.2 - 71.8 | 100 | 75.3-100 | 43.2 | 27.1-60.5 | 0.13 | |

Carb pos: Carbapenemase positive (truth), Phoenix CPO Detect Test: N° of Phoenix CPO Detect Test CPO positive results, N° FP: Number of false positives, κ : Kappa coefficient, N° : Number of strains, κ : Percentage, 95% CI: 95% confidence interval.

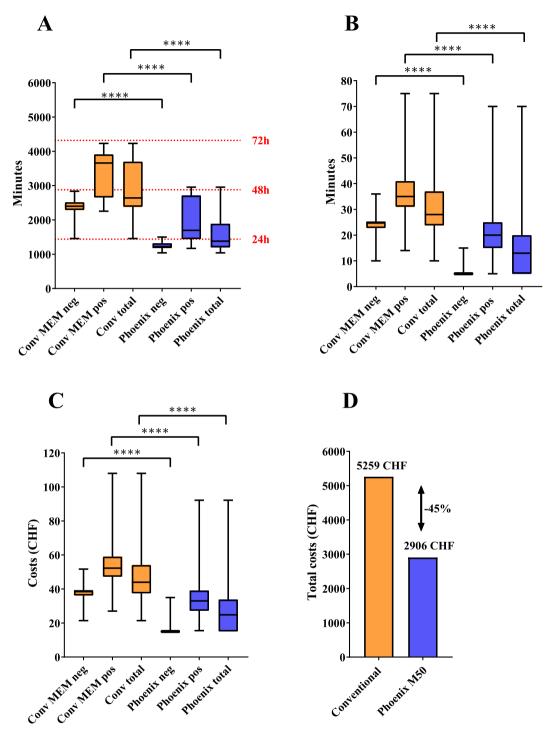


Fig. 2. (A) Turnaround time to confirm or exclude the presence of a carbapenemase-producing organism (CPO). By using the Phoenix CPO Detect Test, the turnaround time per test could be decreased by a mean 19.4 h (95%CI 13.9–24.9) for negative CPOs (p < 0.0001), a mean 21.5 h (95%CI 16.4–26.5) for positive CPOs (p < 0.0001) and a mean 21.3 h (95%CI 17.6–25) for combined negative and positive CPOs. (B) Hands-on time to perform all the phenotypic test required to confirm or exclude the presence of a CPO, including the initial AST tests (Vitek or Phoenix M50). By using the Phoenix CPO Detect Test, the hands-on time per test could be decreased by a mean 17 min (95%CI 12–22.1) for negative CPOs (p < 0.0001), a mean 15.3 min (95%CI 10.7–19.9) for positive CPOs (p < 0.0001) and a mean 16.8 min (95%CI 13.4–20.2) for combined negative and positive CPOs. (C) Hands-on time and cost of consumables to perform the phenotypic tests required to confirm or exclude the presence of a CPO. By using the Phoenix CPO Detect Test, the total cost was decreased by a mean 20.6 CHF (95%CI 14.4–26.8) (18.3 EUR: 95%CI 12.8–23.8, 20.5 USD: 95%CI 14.3–26.7) for negative CPOs (p < 0.0001), a mean 19.0 CHF (95%CI 13.4–24.7) (17.0 EUR: 95%CI 11.9–22, 19.0 USD: 95%CI 13.3–24.6) for positive CPOs (p < 0.0001) and a mean 20.6 CHF (95%CI 16.5–24.8) (18.4 EUR: 95%CI 14.7–22.1, 20.6 USD: 95%CI 16.4–24.7) for combined negative and positive CPOs (p < 0.0001). (D) Sum of the hands-on time and cost of consumables for 114 analysed strains with CPO suspicion. A cost saving of 45% was observed following the introduction of the Phoenix CPO Detect Test. The p values have been calculated using the Tukey's multiple comparison test (Graphpad Prism 7.0); $p \le 0.001$ (**), $p \le 0.001$ (***), $p \le 0.001$ (****).

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wrongly identified as a class A carbapenemase if a synergistic inhibition with cloxacillin is not documented.

The high sensitivity observed in this study (Tables 1 and 4) allowed direct reporting of CPO-negative strains without additional tests, significantly decreasing the turnaround time, hands-on time and cost. Despite a moderate specificity, a significant gain of turnaround time, hands-on time and costs compared to the conventional approach was also observed with positive Phoenix CPO Detect Tests. This results mainly from (a) Phoenix panels that, unlike the Vitek cards currently used in our laboratory, directly provide true carbapenem MICs that can be used as carbapenemase screening values, and (b) the replacement of MacConkey by blood agar purity plates allowing the execution of additional confirmation tests 24 h earlier (Fig. 1). In countries with a low CPO prevalence and poor positive predictive value (PPV), additional tests for carbapenemase detection and classification [1,22,23] are initiated only if the MIC values or disk diffusion inhibition zones are above the screening cut-off value [24] to reduce the hands-on time and cost of unnecessary phenotypic and molecular tests for CPO detection and classification.

Limitations

Because of a very low CPO prevalence, the prospective study was not performed on consecutive routine isolates but on 135 selected isolates with CPO suspicion representing an extreme diagnostic challenge and on 156 isolates with no CPO suspicion representing conventional isolates mostly encountered in countries with very low CPO prevalence. The results presented in the prospective study are thus biased by the selection criteria used to collect these two groups of isolates. The true performance of the Phoenix CPO Detect Test in a context of low and high CPO prevalence remains to be assessed by the implementation of this test in routine diagnostic laboratories.

It should be noted that the significant decrease in turnaround time, hands-on time and costs observed in this study with the Phoenix CPO Detect Test totally rely on comparison with the conventional laboratory workflow for CPO detection as implemented in our laboratory, which is especially adapted to countries with low CPO prevalence. The result may differ greatly with alternative analytical workflows setups, including direct molecular and phenotypic testing with rapid carbapenemase detection and classification assays [12,13]. The analytical workflow in countries with high CPO prevalence may include direct confirmatory phenotypic and molecular testing upon CPO suspicion following AST or from samples such as positive blood cultures to significantly reduce the turnaround time [18,20]. On the other hand, high-prevalence countries may also exhibit lower negative predictive value (NPV), thus requiring additional tests to exclude the presence of a CPO with a high probability.

Implications

The significantly decreased turnaround time observed with the Phoenix CPO Detect Test may have a positive impact on therapeutic and infection control decisions, including antibiotic de-escalation and escalation as well as costly patient isolation measures. Rapid detection and classification of CPOs is essential to avoid treatment failures with poor outcomes and to guide empirical antibiotic therapy as, for instance, class A CPOs can potentially be treated with ceftazidime/avibactam. The Phoenix CPO Detect Test panels also provide useful information for infection control surveillance since patients both at risk and not at risk are automatically screened for CPOs.

Conclusions

The Phoenix CPO Detect Test likely represents a new diagnostic tool with added value for the detection and management of CPO infection and colonization. The CPO test is reliable for the detection of CPOs with a high sensitivity, but the relatively low specificity requires the use of additional confirmatory methods. The carbapenemase classification accuracy is robust in providing preliminary results before molecular characterization. Finally, the implementation of the test in routine workflows allows a significant reduction in turnaround time, hands-on time and cost compared to the conventional approach. Overall, the implementation of the Phoenix CPO Detect Test may have a positive impact on laboratory workflows but also on therapeutic and infection control decisions.

Transparency declaration

A.C. and G.G. report grants from Becton Dickinson (USA) during the conduct of the study and outside the submitted work. A.T.C., T.P., C.B. and G.P. report grants from Becton Dickinson during the conduct of the study. Becton Dickinson also supported this study by funding reagents and the salary of one laboratory technician for 6 months.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2019.10.002.

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