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Brief Report

Evaluating the impact of the multiplex respiratory virus panel polymerase chain reaction test on the clinical management of suspected respiratory viral infections in adult patients in a hospital setting

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A retrospective cohort design was used to study the impact of a multiplex respiratory virus panel polymerase chain reaction test in 186 adult patients with suspected influenza-like illness. Decisions regarding continuation of empirical antiviral therapy appear to be impacted by the test. However, the impact on reducing antibiotic use remains unclear.

Respiratory tract infections are very common and manifest themselves through a wide range of symptoms.[1,2] It is often difficult to distinguish between viral and bacterial etiologies on clinical grounds alone; however, rapid and accurate etiologic identification is important to guide patient management and hence reduce morbidity and mortality and implement appropriate infection control practices.[3-5] Targeted therapy is expected to decrease the risk of emergence of drug-resistant bacterial strains and of nosocomial infections, such as *Clostridium difficile*.[6] In the context of limited health care resources, there is interest in assessing the impact of respiratory virus diagnostic testing on antimicrobial therapy.

Nucleic acid amplification testing is now considered the gold standard for respiratory virus testing.[7] An in-house multiplex reverse transcription polymerase chain reaction (MRVP) that simultaneously detects and identifies 12 respiratory virus targets (influenza A, influenza B, parainfluenza 1-2-3, adenovirus, rhinovirus, enterovirus, coronavirus (types 229E and OC43), respiratory syncytial virus, and human metapneumovirus) and has an excellent turnaround time of ≤24 hours has been used since 2009 at the McGill University Health Centre. The objective of our study was to evaluate the impact of the MRVP test on the use of antiviral and antimicrobial therapy among adult patients in a hospital setting (either emergency room or inpatients) with suspected influenza-like illness.

MATERIALS AND METHODS

Study design and setting

The study was designed as a retrospective cohort study conducted among adult patients in the emergency department and inpatients during the peak of the 2013-2014 influenza season. Similar to many hospital centers in Canada, the McGill University Health Centre emergency room includes a holding area for internal medicine patients, including sick patients under observation and admitted patients waiting for a bed. Length of stay in these patients can average ≥24 hours. Polymerase chain reaction testing is indicated for patients likely to be admitted or at risk for complications.

MRVP test: Description of test and validation studies

The MRVP test is carried out using automated specimen extraction (NucliSENS Extractor; bioMérieux, Marcy-l'Étoile, France) and simultaneous amplification of 11 respiratory viruses on a LightCycler 480 (Roche Applied Systems, Penzberg, Upper Bavaria, Germany). The assay was validated in 2008 and field tested in 2009[8,9] (see Supplementary Appendix S1 for details).

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Data collection

Between January 1 and March 1, 2014, 93 adult patients with suspected influenza-like illness and who tested positive by MRVP (positive for influenza or other respiratory virus) were enrolled (exposed group). For efficiency, of 564 patients (either emergency department patients or inpatients) who had a negative MRVP test during the study period, an equal number of patients (n = 93) were randomly selected within a 1-week time frame of the exposed group.

Clinical data, including demographic characteristics, comorbidities (present or absent), patient location at the time of MRVP testing, prescription of antibiotics and antivirals, and chest radiograph results, were collected from the medical charts. Use of antibiotics considered potentially prescribed for respiratory bacterial infection (namely ceftriaxone, doxycycline, azithromycin, piperacillin-tazobactam, and fluoroquinolones [moxifloxacin]) was recorded.

Statistical analyses

Patients were classified according to their MRVP results into 1 of the following 3 groups: influenza positive, noninfluenza positive, and negative to all viruses. We compared clinical characteristics of patients in the 3 groups by calculating the difference in means (for continuous characteristics) or difference in proportions (for categorical characteristics) together with a 95% confidence interval. We evaluated whether the MRVP test result was associated with the changes in management in antiviral and antibiotic treatment (see the definition in Supplementary Appendix S1), after stratifying by patient location. We also evaluated the association between MRVP and the decision to admit patients from the emergency room setting. All analyses were performed using IBM SPSS 20 for Windows (IBM, Armonk, NY).

Table 1
Distribution of demographic and clinical characteristics by the MRVP test results

Characteristic	Positive influenza (n = 61)	Positive noninfluenza (n = 32)	Negative (n = 93)
Age, median (minimum-maximum)	60 (18-93)	68 (31-91)	71 (25-103)
Sex, female	34 (55.1)	17 (53.1)	44 (47.3)
Location			
Emergency room	44 (72.1)	22 (68.8)	31 (33.3)
Ward	17 (27.9)	10 (31.2)	62 (66.7)
Source of infection			
Community acquired	51 (83.6)	24 (75.0)	N/A
Nosocomial	10 (16.4)	8 (25.0)	N/A
Comorbidity	50 (82.0)	30 (93.8)	92 (98.9)
Suspected pneumonia*	13 (21.3)	7 (21.9)	17 (18.3)
Fever†	18 (29.5)	14 (43.8)	7 (7.5)
Cough†	24 (39.3)	16 (50)	10 (10.7)
Rhinorrhea†	3 (2)	0 (0)	4 (4.3)
Shortness of breath†	7 (11.5)	3 (9.4)	12 (12.9)
Diarrhea†	1 (2)	0 (0)	0 (0)
Chest pain†	3 (5)	0 (0)	4 (4.3)

NOTE. Values are n (%) or as otherwise indicated.
MRVP, multiplex reverse transcription polymerase chain reaction; *N/A*, not applicable.
*Chest radiograph results were missing for 9, 2, and 8 patients in the positive influenza, positive noninfluenza and negative categories, respectively.
†Results were missing for 8 patients among the influenza-negative category.

RESULTS

Of 186 selected patients, half were men (Table 1). On average, patients in the positive influenza group were younger than the negative influenza group (difference in mean, -11 years; 95% confidence interval, -20 to 1) and the positive noninfluenza group (difference in mean, -7 years; 95% confidence interval, -17 to 5). Patients in the 2 test positive groups were more likely to present with fever and cough than those who tested negative. The percentage of patients with a comorbidity was very high in all 3 groups. The percentage of patients suspected to have pneumonia based on chest radiography results was similar in all 3 groups.

Seventy percent of the patients with positive results and one-third of patients with negative results were only treated in the emergency room, whereas the rest were hospitalized at the time of testing. Polymerase chain reaction test results were available on the same day for 80 (43%) of the patients and on the next day for the remaining patients. Results were available for all patients in our study prior to their discharge from hospital.

Among hospitalized patients, 7 of 17 (41.2%) patients positive for influenza were empirically treated with oseltamivir antiviral prior to test result, and all of them continued the treatment given the MRVP test result (Table 2). After a negative MRVP result, empirical oseltamivir antiviral treatment was discontinued in two-thirds (10/15) of the hospitalized patients. Empirical oseltamivir antiviral treatment was also discontinued in all hospitalized patients with a positive noninfluenza result.

The proportions of empirical antibiotic treatment in hospitalized patients were 66.1% in patients with negative MRVP test, 70.0% in patients with positive noninfluenza, and 70.6% in patients with positive influenza. Empirical antibiotic treatment was continued in 85.4% of hospitalized patients with negative MRVP test. Empirical antibiotic treatment was discontinued in only one-quarter (ie, 3/12) of MRVP-positive hospitalized patients. When further stratifying hospitalized MRVP-positive patients according to whether they had suspected pneumonia, we found that 5 of 6 patients with suspected pneumonia continued empirical antibiotics compared with

Table 2
Distribution of clinical management before and after the MRVP test in patients in the ward

		Antiviral treatment			Antibiotic treatment		
			Postresult treatment			Postresult treatment	
Test results	n	Empirically treated*	Continued†	Discontinued†	Empirically treated*	Continued†	Discontinued†
Hospitalized patients							
Negative	62	15 (24.2)	5 (33.3)	10 (66.7)	41 (66.1)	35 (85.4)	6 (14.6)
Positive noninfluenza	10	4 (40.0)	0 (0)	4 (100)	7 (70.0)	5 (71.4)	2 (28.6)
Positive influenza	17	7 (41.2)	7 (100)	0 (0)	12 (70.6)	9 (75.0)	3 (25.0)
Patients diagnosed in the emergency room							
Negative	31	8 (25.8)	1 (12.5)	7 (87.5)	22 (70.9)	17 (77.2)	5 (22.7)
Positive noninfluenza	22	7 (31.8)	2 (28.6)	5 (71.4)	11 (50.0)	7 (63.6)	4 (36.4)
Positive influenza	44	16 (36.4)	14 (87.5)	2 (12.5)	19 (43.2)	13 (68.4)	6 (31.6)

NOTE. Values are n (%) or as otherwise indicated.
MRVP, multiplex reverse transcription polymerase chain reaction.
*Proportion within the test result group.
†Proportion within the empirically treated group.

4 of 6 patients with no suspected pneumonia. The high prevalence of comorbidity did not permit a stratified analysis.

Most influenza-positive patients, who were not treated empirically, were highly likely to be initiated after the test results: 80% (8/10) among hospitalized patients and 85% (6/7) among emergency room patients scheduled to be admitted. Among patients with a negative MRVP test who were not empirically treated, antibiotic treatment was initiated in only 1 patient in each setting: 1 in 21 (5%) hospitalized patients and 1 in 9 (11%) emergency room patients.

Among patients tested in the emergency room, 20.6% (7/34) of MRVP-positive patients were admitted compared with 78.9% (15/19) of MRVP-negative patients.

DISCUSSION

Our findings show that the antiviral management was generally appropriate during influenza season. After the MRVP result, all admitted patients with positive influenza continued empirical oseltamivir antiviral treatment. A high proportion of patients with negative results and all patients with noninfluenza positive result discontinued the treatment. Antiviral was initiated in most admitted patients with positive influenza who were not empirically treated.

Impact of the MRVP test on antibiotic management was less evident. Seventy percent of patients in the ward who turned out to have positive influenza were empirically treated with antibiotics, and only a quarter of them discontinued the treatment given the MRVP result. The suspicion of a concomitant presence of a secondary bacterial infection is the most likely explanation for the continuation of antibiotic in these cases. However, the small sample size of this study precluded our ability to study this hypothesis in greater depth. Moreover, the introduction, use, and interpretation of this MRVP test is relatively new to our institution, and clinical practice may have not changed yet. Nonetheless, a MRVP-positive result in the emergency room setting appears to be associated with discharge from the hospital.

Our nonrandomized study design has the drawback that the differences in MRVP-positive and MRVP-negative patients may be attributable to the difference in distribution of important confounding factors (eg, age, comorbidity). We could not further analyze the role of comorbidity on the continuous use of antibiotics or antivirals because almost all of the treated patients had a comorbidity. In future studies, a finer definition of comorbidity and suspicion of a bacterial respiratory infection would be needed to investigate the reasons for continuation of antibiotic use. Another limitation of this work is that we were not able to measure the impact of the MRVP test on infection control because of the lack of individual-level data on initiation of these measures.

We conclude that the MRVP test could potentially positively impact the clinical management of respiratory viral infections in adult patients. However, the impact on reducing antibiotic use remains unclear. Our findings support the concept that viral respiratory tract infections are a common cause of inappropriate antibiotic usage and should be targeted for education and antibiotic stewardship programs.

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APPENDIX. SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at doi:10.1016/j.ajic.2016.04.221.

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