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The burden of non-influenza respiratory viruses in adult patients admitted for influenza-like illness: A three-year prospective multicentric study

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Background: Non-influenza respiratory viruses (NIRV) are associated with a substantial proportion of influenza-like illness (ILI), but their epidemiology and outcome are poorly characterized. We aimed to determine the characteristics and the risk factors for NIRV among adults admitted for ILI during influenza seasons in France.

Material/methods: We performed a *post-hoc* analysis of patients enrolled in FLUVAC, a prospective observational study of adult patients admitted for ILI in 6 French university hospitals during 3 consecutive influenza seasons (2012-2015). All patients were screened for 7 NIRV (picornavirus, respiratory syncytial virus, coronavirus, human metapneumovirus, adenovirus, bocavirus, parainfluenza virus), and for influenza by polymerase chain reaction on nasopharyngeal samples. We compared patients with NIRV, to patients with influenza, and to patients with negative samples.

Results: Among the 1452 patients enrolled in FLUVAC, we excluded 31 patients coinfected with NIRV and influenza. Of the 1421 patients analyzed (Table), influenza was detected in 535 (38%), and NIRV in 215 (15%). Main NIRV were picornavirus (27%), respiratory syncytial virus (24%), coronavirus (22%), human metapneumovirus (18%), adenovirus (5%), and bocavirus (4%). In-hospital mortality was 5% for NIRV, 4% for influenza, and 5% in patients with negative samples. As compared to patients with influenza, patients with NIRV were older (median, 73 years *vs.* 68, p=0.026), more likely to have chronic respiratory diseases (53% *vs.* 45%, p=0.034), solid cancer (14% *vs.* 9%, p=0.029), and to be on immunomodulatory drugs (21% *vs.* 14%, p=0.028), but less likely to be diabetic (18% *vs.*

25%, p=0.038). As compared to patients with negative samples, patients with NIRV were more likely to have chronic respiratory diseases (53% *vs.* 44%, p=0.024), and to be on immunomodulatory drugs (21% *vs.* 15%, p=0.041), but less likely to be diabetic (18% *vs.* 27%, p=0.011). On multivariate analysis, only chronic respiratory diseases (OR 1.5 [1.1-2.0], p=0.008), and diabetes (OR 0.5 [0.4-0.8], p=0.01) remained associated with NIRV detection.

Conclusions: NIRV are common in adult patients admitted for ILI during influenza seasons, more likely to be identified in patients with chronic respiratory diseases and less likely in patients with diabetes. Outcomes are similar in patients with NIRV, influenza, or negative samples.

	Influenza virus (n=535)	Non-influenza respiratory virus (n=215)	Negative samples (n=671)
Median age, years (IQR)	68 (53-81)	73 (60-83)	70 (54-83)
Male (%)	269 (50%)	116 (54%)	380 (57%)
Chronic respiratory Diseases (%)	237 (45%)	114 (53%)	296 (44%)
Diabetes (%)	135 (25%)	39 (18%)	179 (27%)
Solid Cancer (%)	48 (9%)	31 (14%)	84 (13%)
Immunomodulatory drugs (%)	75 (14%)	44 (21%)	98 (15%)
ICU admission (%)	26 (10%)	16 (11%)	39 (9%)
≥ 1 complication (%)	248 (47%)	94 (44%)	266 (40%)
Pneumonia (%)	152 (29%)	68 (32%)	160 (24%)
Mortality (%)	23 (4%)	11 (5%)	32 (5%)