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

François Bénézit,

Rennes University Hospital, France

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Disclosure : none

Background : need for an epidemiologic update

- Prevalent infection
- About 200 million viral pneumonia every year
- PCR are available in most labs
- New respiratory viruses :
  - Human metapneumovirus (2001)
  - Bocavirus (2005)
- New or under development drugs :
  - Pavilizumab and Respiratory Syncytial Virus (RSV) prevention (2009)
  - Presatovir , fusion inhibitor of RSV , ongoing phase II study

Ruuskanen, Lancet 2011

Methods

- Post-hoc analysis (FLUVAC study)
- Prospective
- Multicenter, six French University Hospital
  (Cochin, Bichat, Pontchaillou, Limoges, Montpellier, E. Herriot)
- 2012-2015, three winter seasons
- **ILI, Influenza-like Illness :**
  - **Sudden onset**
  - **With ≥ 1 systemic symptom : fever, malaise, headache, myalgia**
  - **And ≥ 1 respiratory symptom : cough, sore throat, shortness of breath**
- Standardisation of the parameters collected by research assistants
- Patient consents and approval by ethical comitee

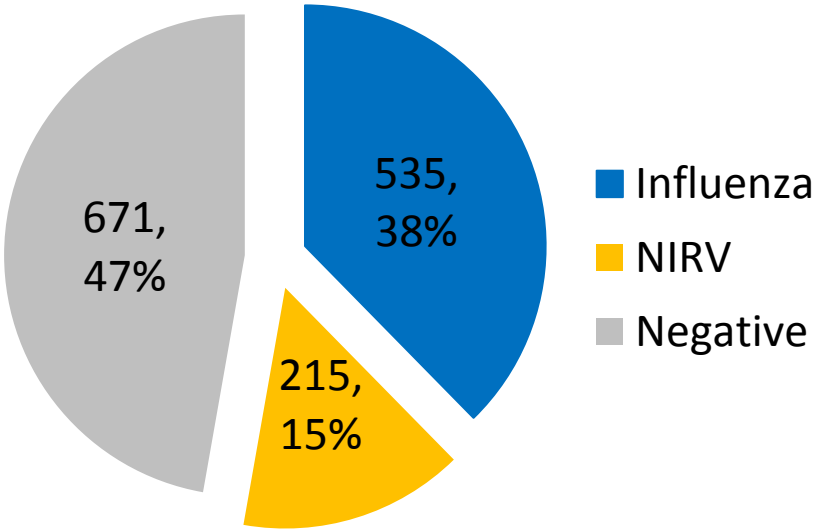
Virologic analyses

- **Nasopharyngeal swab**
- Or bronchoalveolar lavage/ tracheal aspirate
- All PCR done in an unique center, in Lyon
- Home-made RT-PCR for influenza
- **Respiratory MultiWell System r-gene®** for the non-influenza respiratory viruses :
  - Adenovirus
  - Bocavirus
  - Coronavirus 229E
  - Human metapneumovirus
  - Parainfluenza virus 1-4
  - Picornavirus
  - Respiratory syncytial virus (RSV)

  ] = NIRV

Results : virologic results

- 1452 patients
- 781 (54%) had at least one virus
- 31 patients excluded (detection influenza+NIRV)
- 7 patients had > 1 NIRV



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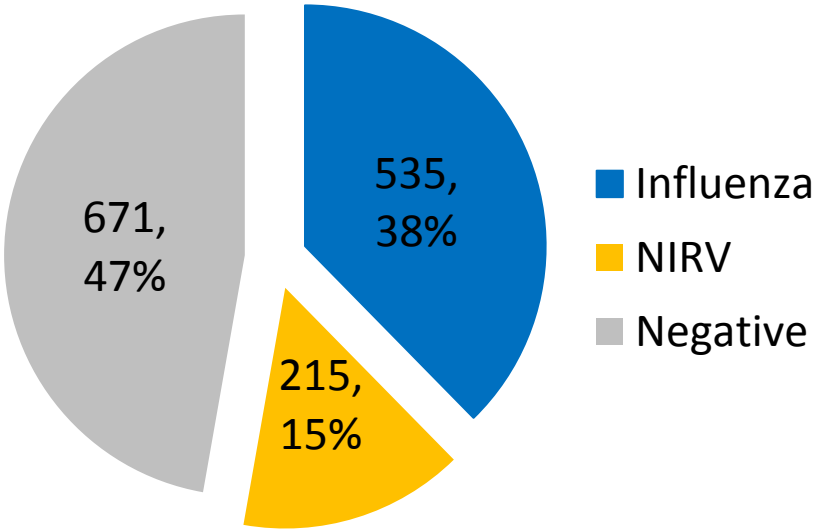

Picornavirus	61	30%
RSV	53	26%
Coronavirus 229E	48	24%
Metapneumovirus	40	20%
Adenovirus	12	6%
Bocavirus	8	4%
Parainfluenza virus	0	0%

Clinical Results

	NIRV
Baseline Characteristics	
Men	116 (54%)
Median age, years (IQR)	**73 (60-83)**
Age >= 65 years	141 (65,6%)
Median BMI, kg/m2 (IQR)	24,5 (21-28)
Chronic diseases	**174 (81%)**
Chronic respiratory disease	**114 (53%)**
Chronic heart disease	90 (42%)
Asplenia	4 (2%)
Cirrhosis	2 (1%)
Malignant Blood disease	10 (5%)
Cancer	31 (14%)
Immunodeficiency	21 (10%)
Diabetes	39 (18%)
Chronic treatment	
Immunomodulatory treatment	**44 (21%)**
Antidiabetics	33 (15%)
Pregnancy	4 (27%)
Current smokers	52 (24%)
Influenza vaccination for the current season	**100 (47%)**
ICU admission	16 (11%)
Hospitalisation in the 12 previous months	**100 (46%)**
Mean number of hospitalization in the past 12 months (SD)	3,1 (5,0)
Clinical presentation	
Median time from symptom onset to hospitalisation, days (IQR)	3,0 (2-4)
Fever (>=38°C)	169 (79%)
Weakness/Malaise	55 (26%)
Headache	47 (22%)
Myalgia	44 (21%)
Cough	167 (78%)
Dyspnea	160 (74%)
Sudden symptom onset	67 (49%)
Outcomes	
Complications	
At least one complication	**94 (44%)**
Pneumonia	68 (32%)
Respiratory failure	47 (22%)
ARDS	20 (9%)
Cardiac failure	30 (14%)
Median length of stay, days (IQR)	8 (5-17)
Mortality	**11 (5%)**

NIRV versus Influenza

Multivariate analysis :

- **Chronic respiratory diseases OR 1.4 IC95% [1.1-2.0] (p=0,04)**
- **Immunomodulatory drugs OR 1.5 IC95% [1.1-2.3] (p=0,04)**
- Diabetes OR 0.6 IC95% [0.4-0.9] (p=0,007)

No difference for complication (44% *vs* 47%, p=0.5)

No difference for mortality (5% *vs* 4%, p=0,69)

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NIRV versus negative samples

Multivariate analysis:

- **Chronic respiratory diseases OR 1,2 IC95% [1.1-2.0] (p=0,008)**
- Diabetes OR 0.5 IC95% [0.4-0.8] (p=0.01)

No difference for complication (44% *vs* 40%, p=0.28)

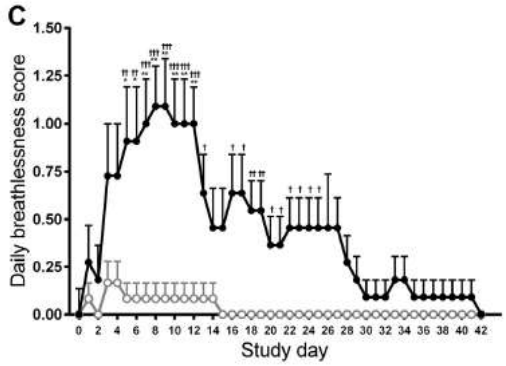
No difference for mortality (5% *vs* 5%, p=0,85)

Discussion

- Age usually associated with an increased risk

  Ruuskanen, Lancet 2011; Falsey, NEJM 2005

- Chronic respiratory disease, a known risk factor



Gunawardana, Antiviral Res 2014

- Negative association with diabetes?

Shah 2003

Muller 2005

- Quality of control group. Negative sample = bacterial infection?

Take Home Message

Non-influenza respiratory viruses

- Quite prevalent disease : 15% of Influenza-like Illness requiring hospitalization
- 44% developped at least one complication
- Mortality of 5%, like influenza
- Association with chronic respiratory diseases

- Need to investigate diabetes and viral susceptibility
- Our study need to be continued, to assess each virus specificity