UNIVERSITÀ DEGLI STUDI DI MILANO

Covid-19 nelle RSA

Una prima valutazione di che cosa è accaduto e azioni di miglioramento

5 marzo, 2021

Cardiac involvement in elderly With Sars-Cov-2 infection

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Cardiac involvement in elderly
With Sars-Cov-2 infection

AS PRELIMINARY REMARK ON WHAT HAPPENED, BUT MOSTLY IN WHICH CONDITIONS,
BY WHO LIVED FIRST WAVE IN HOSPITAL AND SECOND IN LONG-TERM HOUSES

1. at beginning of pandemia there were not guidelines on management of this new disease

2. guests of long-term houses were very often affected by some comorbidities, that negatively influenced the disease

3. long-term houses were/are not equipped to manage «acute patients», lack of equipped laboratory and full imaging departement

4. this last aspects made difficult move guests to most equipped hospitals (last generation TC/NMR), in order to contain contagion

THESE WERE THE CONDITIONS IN WHICH LONG-TERM HOUSES CARRIED ON PANDEMIA

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As well as respiratory system, heart is a Coronavirus possible target

A recent retrospective study revealed (1):

- among 113 deceased patients, 77% showed an acute myocardial injury VS 161 survivors
- myocardial injury was definited by high sensitive Troponin-I (hsTnl) elevation
- mean hsTln value was 40.8 pg/ml in deceased patients
- 3.3 pg/ml in the control group

This means that patients with acute myocardial injury showed, an increased death probability VS patients without heart injury

INDEPENDENTLY by cardiovascular comorbidities

(1) Chen T et al. *Clinical charateristics of 113 deceased patients with Coronavirus disease.* BMJ 2020; 368:m1091

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Another study (2) analyzed 416 medical records Wuhan's Universitary Hospital

- 19.7% showed myocardial injury > high levels of hsTnl, evalued at entrance
- following 20 days 51.2% of patients deceased VS il 4.5% of patients with normal hsTnl
- patients with acute myocardial injury, had a mortality rate after 20 days sharply elevated

INDEPENDENTLY

by pre-existing cardiovascular comorbidities

(2) Shi S et al. *Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan*. JAMA Cardiol 2020 mar 25

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A further study (3) demonstrated:

- 187 pt. among which 27.8% had acute myocardial injury with increased T-troponin (TnT)

- After one month mortality was:
  - 59.6% in pt. with elevated TnT
  - VS 8.9% in pt. with normal values of TnT

- Among elevated TnT group, were also observed:
  - increased NT pro-BNP values
  - increased PCR values

(3) Guo T et al. *Cardiovascular implications of fatal outcomes of patients with COVID-19* JAMA Cardiol. 2020 Mar 27

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Pathophysiological hypotesis of troponin involvement (4) :

- instability of pre-existing atherosclerotic plaques
  - known in many others viral/inflammatory syndromes
    - «cytokine storm» and clinical features of type1 acute myocardial infarction (AMI)

- increased O2 supply by myocytes ruled by infection/inflammation inadequate offer and clinical features of type2 AMI

- potentials exacerbation of cardiac failure (infection/inflammation)

- adrenergic hyperactivation (by ARDS) and psychic stress causes left ventricular failure (Tako- Tsubo Syndrome)

- autopsy findings recorded wide microcirculation thrombosis

(4) Bonow RO et al. *Association of COVID-19 with myocardial injury and mortality.* JAMA Cardiol. 2020 Mar 27

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- Cheked high myocardial injury incidence and prognostic impact, is fundamental that in high cardiovascular disease incidence areas adopt it:

    1. perform instrumental examinations to better define myocardial injury, in hospitalized pt. and also in healed

        - for example: hsTnl or TnT evaluation as prognostic indicator at the admission and periodically during hospitalization

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Anyway this TnT raise is an aspect, in most cases, of

NOT ISCHEMIC INJURY

Then one of potential situations responsible of myocardial injury is:

SARS-COV-2 myocarditis

That can be explained through two mechanisms:

1. direct damage mediated by virus/ACE2 interaction expressed by myocardiocyte
2. indirect damage due to «cytokine storm»

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1. ACE2 is the door through which virus penetrate into cells

   - affinity is about ten times higher regard «predecessors»

   - enzyme is situated on:
     - pulmonary epithelium
     - heart
     - bowel
     - kidney
     - Blood vessel
       - (5) it was recently observed that in soluble form could intercept circulating virus and prevent/mitigate cell binding

(5) Ciaglia E et al. *COVID-19 Infection and Circulating ACE2 Levels: Protective Role in Women and Children*. Front. Pediatr., 23 April 2020

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2. extra-pulmonary phase (cytokine storm)

    - quickly leads to ARDS and shock
    - elevated markers:
        - PCR, IL-2, IL-6, GCSF, TNF-alfa, D-dimer, troponin, NT pro-BNP

- In addition to laboratory tests, the gold-standard to perform myocarditys non-invasive diagnosis is NMR
    - not always easily executable:
        - patient movement impossibility (contagion spread)
        - long-term homes not equipped of complete imaging wards

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A Wuhan's researcher group, recently observed (6):

- 26 pt. (mean age 38, 10 male), healed by SARS-COV-2 and subjected to NMR for cardiac symptoms recurrence (palpitations and/or chest pain)
  - 58% (15) showed pathological findings
  - in particular 54% (14) had an edema pattern
  - 31% (8) subepicardic and intramyocardial fibrosis pattern , with right ventricular function reduced

Based on this data is reasonable to presume, that myocarditis can be a rather frequent phenomenon and that diagnosis is underestimated for reasons already said

Is then possible hypothesize that, where executable, timing NMR in healed pz, would help to identify those patients at cardiac event higher risk

(6) Huang L et al. *Cardiac involvement in patients recovered from Covid-19 identified using NMR imaging*. JACC Cardiovasc. Imaging 2020 Nov, 13:2330-2339

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Last but not least:

ARRHYTHMIAS

Lazzerini et al. (7) suggests that Sars-Cov-2 infection, is often associated to an higher risk of arrythmics events with significant impact on mortality associated to infection

- palpitations are often the first symptoms
- arrythmias (tachycardia/ventricular fibrillation), more frequent after ARDS, in severe patients
- related to heart injury (high troponin), but only 50%
- in the remaining 50% which mechanisms are involved?

(7) Lazzerini PE et al. *Covid-19 arrhythmic risk and inflammation: mind the gap.* Circulation 2020; https:/doi.org/10.1161/CIRCULATIONAHA.120.047293

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The focus has shifted on pharmacological treatments role in Covid-19 management

- Some of these drugs can have effects on QT interval elongation
  - chloroquine and hydroxychloroquine, lopinavir, ritonavir
  - macrolodes, fluoroquinolones

IN PARTICULAR:

- Considering that these products are administered in more severe events and often in elderly people, there are many cardiovascular comorbidities (coronary artery disease, heart failure, arrythmias, hypertension, diabetes), that already causes QT elongation, situation is further complicated

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Furthermore, elevated systemic inflammation level associated to Covid-19, can act as pro-arrythmic factor (Long QT Syndrome, Torsades de pointes)

- the mechanism is due to cytokines electphysiological effects on myocardium
  - direct way: sympathetic hyperactivation
  - Indirect way: increased drugs bioavailability due to IL-6 inhibition on p450 cytochrome

Hypoxia and electrolytic abnormalities are very often in acute phase and could ease the onset of arrythmias

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- Based on these observations, the suggest is that to reduce inflammatory status in Covid-19 patients, could be crucial not only to avoid pulmonary involvement but also cardiac complications

- Actually are not well known arrythmic risks in patients with less severe disease and in post-acute phase

- Long-term risk stratification in arrythmic patients, is primary about their correct management, mostly in presence of left ventricular failure.

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Most people who have COVID-19, recover completely within a few weeks. But some people, even those who had mild versions of the disease, continue to experience symptoms after their initial recovery.

This condition has been called post-COVID-19 syndrome or "long COVID-19.

Older people and people with many serious medical conditions, are the most likely to experience lingering COVID-19 symptoms for weeks to months after infection. The most common signs and symptoms that linger over time include:

- Fatigue
- Shortness of breath
- Cough
- Joint pain
- Chest pain

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Other long-term signs and symptoms may include:

- Muscle pain or headache
- Fast or pounding heartbeat
- Loss of smell or taste
- Memory, concentration or sleep problems
- Rash or hair loss

Heart damage caused by COVID-19

The heart damage may increase the risk of long-term health problems:

- Imaging tests taken months after recovery from COVID-19 have shown lasting damage to the heart muscle, even in people who experienced only mild COVID-19 symptoms. This may increase the risk of heart failure or other heart complications in the future.

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TELEMEDICINE ROLE

It is obvious that in next future, telemedicine will play a basic role in patients management

In this context to have indicators which can improve clinical management, appears not only important, but in my opinion could contribute to avoid complications, that often in elderly have poor prognosis.

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THANK YOU