Different approaches to the analysis of causes of death during the COVID-19 epidemic

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Abstract. – **OBJECTIVE:** The aim of the study is to assess the impact of the COVID-19 pandemic on causes of mortality through multiple methodological approaches.

MATERIALS AND METHODS: The causes of mortality in the Veneto region (Italy) during the first epidemic wave, March-April 2020, were compared with the corresponding months of the previous two years. Both the underlying cause of death (UCOD), and all diseases reported in the death certificate (multiple causes of death) were investigated; a further analysis was carried out through a simulation where the UCOD was selected after substituting ICD-10 codes for COVID with unspecified pneumonia.

RESULTS: Overall 10,222 deaths were registered in March-April 2020, corresponding to a 24% increase compared to the previous two years. COVID-19 was mentioned in 1,444 certificates, and selected as the UCOD in 1,207 deaths. Based on the UCOD, the increases in mortality were observed for COVID and related respiratory conditions, diabetes mellitus, hypertensive heart diseases, cerebrovascular diseases, and ill-defined causes. Multiple causes of death and the simulation analysis demonstrated further increases in mortality related to dementia/Alzheimer and chronic lower respiratory diseases.

CONCLUSIONS: This first report demonstrates an increase of several causes of death during the pandemic, underlying the need of a continuous surveillance of mortality records through different analytic strategies.

Key Words:
COVID-19, Mortality, Multiple causes of death.

Introduction

About 125 million cases and 2.7 million deaths due to coronavirus 2019 disease (COVID-19) were registered worldwide as of March 25, 2021, with Italy being one of the most affected countries[1]. Age, male gender, and comorbidities are predictors of mortality in people affected by COVID-19[2]. Nonetheless, only sparse data are available on causes of death during the pandemic. A small number of studies investigated comorbidities reported in death certificates of decedents from COVID-19[3] compared to non-COVID deaths[4] or assessed excess mortality during the pandemic from COVID-19 and from all other causes combined[5]. To date, the few population-based data on mortality from multiple disease categories during the pandemic are limited to the underlying cause of death (UCOD)[6].

The Veneto Region (Northeastern Italy, 4.9 million inhabitants) was one of the Italian regions hit hardest by the early phase of the COVID-19 pandemic in March-April 2020[7]. Aim of the study is to assess the impact of such first epidemic wave on main causes of death by means of multiple methodological approaches.

Materials and Methods

Copy of death certificates of each resident in the Veneto region is routinely transmitted to the Regional Epidemiology Department for coding of the causes of death according to the International Classification of Diseases, 10th Edition (ICD-10). Standard mortality statistics are based on rules set by the World Health Organization (WHO) which identify the UCOD from all the conditions reported in the certificate. The UCOD generally corresponds to the underlying cause stated by the certifying physician but could also be another disease reported in the death certificate, or a derived condi-

tion. Until 2017 such rules have been applied in Veneto by means of the Automated Classification of Medical Entities (ACME), a computer program developed by the US National Center for Health Statistics to standardize assignment of the underlying cause[8]. Starting from 2018, selection of the UCOD has been performed by means of the IRIS software, currently adopted in most European countries[9].

The distribution of the main causes of death in March-April 2020 was compared with the corresponding months of the previous two years. Both the underlying cause of death (UCOD), and all diseases reported on the death certificate (multiple causes of death) were investigated. To further assess which chronic conditions, in conjunction with COVID-19, had a greater role in mortality, a sensitivity analysis was carried out through a simulation where the UCOD was selected by the IRIS software after substituting ICD-10 codes for COVID (U07.1, U07.2) with unspecified pneumonia (J18.9). Therefore, excess deaths by cause during the epidemic wave with respect to the reference period were assessed by three approaches: analysis of the UCOD, analysis of multiple causes of death, and the simulation analysis.

Results

Overall 10,222 deaths were registered in March-April 2020, corresponding to a 24% increase in total mortality during the epidemic wave compared to the previous two years, and to approximately 2,000 excess deaths (950 in March and 1,050 in April). COVID-19 was mentioned in 1,444 death certificates (503 in March and 941 in April), and selected as the UCOD in 1,207 deaths (Table I). COVID-19 deaths were also analyzed together with conditions most likely to be reported in patients with undiagnosed infection (flu, pneumonia, adult respiratory distress syndrome, interstitial pneumonia, respiratory failure). Based on the UCOD, increases in mortality were observed, as well as for COVID and related respiratory conditions, for diabetes, hypertensive heart diseases, cerebrovascular diseases, and ill-defined causes (including senility and unspecified causes).

Multiple causes of death analyses demonstrated further increases in mortality associated to dementia/Alzheimer, chronic lower respiratory diseases, other circulatory diseases including ischemic heart diseases and atrial fibrillation, and,

Table I. Distribution of causes of death registered in March-April 2020 among residents in the Veneto region (Italy) compared to the corresponding period in 2018-2019: underlying cause of death (UCOD), multiple causes of death (MCOD), and UCOD selected in a simulation after substituting COVID-19 reported in the certificate with unspecified pneumonia.

Cause of death (ICD-10 codes)	UCOD, n	Δ 2020 vs. 2018-19	MCOD*, n	Δ 2020 vs. 2018-19	UCOD, n simulation	Δ 2020 vs. 2018-19
All deaths	10222	24%	-	-	-	-
COVID-19 (U07.1, U07.2)	1207	-	1444	-	-	-
Flu, Pneumonia (J09-J189)	281	13%	-	-	844	240%
Selected respiratory diseases (J80, J849, J96x)	122	135%	-	-	210	304%
COVID-19 + Flu, pneumonia + selected respiratory diseases	1610	437%	-	-	1054	251%
Neoplasms (C00-D48)	2293	0%	2862	7%	2391	4%
Diabetes mellitus (E10-E14)	296	25%	1377	36%	309	30%
Dementia, Alzheimer (F01-F03, G30)	657	7%	1387	34%	788	29%
Circulatory diseases (I00-I99)	3087	10%	-	-	3211	15%
Hypertensive diseases (I10-I15)	597	32%	1535	41%	607	34%
Ischemic heart diseases (I20-I25)	846	4%	1388	17%	862	6%
Atrial fibrillation (I48)	144	4%	1035	26%	147	6%
Cerebrovascular diseases (I60-I69)	726	21%	1118	27%	806	35%
Chronic lower respiratory diseases (J40-J47)	261	4%	577	25%	328	31%
Chronic liver diseases (K70, K73, K74)	85	-9%	221	-2%	93	0%
Symptoms, signs, unspecified (R00-R99)	361	158%	-	-	361	158%
Injury/poisoning (S00-T98)	235	-24%	-	-	235	-24%

*MCOD reported only for COVID and underlying chronic diseases.

to a lesser extent, neoplasms. Large increases in mortality from dementia/Alzheimer and chronic lower respiratory diseases were confirmed also by the simulation analysis. The only disease category with a sharp decline in mortality was represented by injury/poisoning.

Since the IRIS software was adopted in Veneto in 2018, the period 2018-2019 was set as reference to better assure comparability of UCOD selection; however, the main results did not change if the period 2015-2019 (including years with selection of the UCOD performed through the ACME software) was taken as reference (data not shown).

Discussion

Overall excess deaths registered in the Veneto region exceeded those with any mention of CO-VID-19 in death certificates, especially in March at the beginning of the epidemic wave, when underreporting of COVID-19 was more probable[5,6]. COVID-related deaths were possibly classified as other respiratory disorders, ill-defined conditions, or other diseases. On the other hand, when COVID-19 was mentioned in part I of the death certificate (where the causal chain of events leading to death was reported), it was usually selected as the UCOD. In fact, according to rules established by the WHO, a death due to COVID should be counted independently of pre-existing conditions triggering a sever course of the disease, e.g., cancer[10]. As a consequence, the role of severe chronic diseases, where COVID-19 might have represented a terminal complication leading to death, might be underestimated by standard tabulation of mortality data limited to the UCOD. Therefore, to fully investigate the role of such underlying conditions, further analytical approaches were adopted: multiple causes of death analyses; a simulation substituting, before the selection of the underlying cause, COVID codes with pneumonia, a common acute complication of chronic diseases which, according to international rules, is not generally selected as the UCOD. By this latter approach, approximately one third of deaths classified in the COVID-related category (COVID-19, flu, pneumonia, adult respiratory distress syndrome, interstitial pneumonia, respiratory failure) were re-assigned to other disease categories. By the above multiple approaches, COVID-19 was therefore demonstrated to have increased also the mortality from several degenerative chronic disorders, inclu-

ding diabetes, hypertensive heart diseases, cerebrovascular diseases, dementia/Alzheimer, and chronic lower respiratory diseases.

By contrast, the reduction in mortality from traumatic causes is likely a side effect of restrictions enforced during the epidemic, leading to a reduction of road traffic accidents and possibly other injuries. In fact, a decline in mortality from traffic accidents resulting from quarantine measures has already been reported in the Suzhou region of China[11].

Conclusions

Briefly, this first report on several causes of death increasing during the pandemic underlines the need of a continuous surveillance of mortality records through different analytic strategies.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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