COVID-19 epidemic strongly affected cancer research in Italy: a survey of the Italian Cancer Society (SIC)

(Article begins on next page)

19 April 2024

TITLE:

COVID-19 epidemic strongly affected cancer research in Italy: a survey of the Italian Cancer Society (SIC)

Fabrizio Bianchi[1], Elisa Dama[1], Federica Di Nicolantonio[2,3], Gustavo Baldassarre, Ilaria Guerriero, Erica Torchiaro, Antonino Bruno, Giovanni Blandino, Paola Allavena, Paola Chiarugi, Gabriella Sozzi, Maurizio D'Incalci, Nicola Normanno.

[1] Unit of Cancer Biomarkers, Fondazione IRCCS Casa Sollievo della Sofferenza, 71013 San Giovanni Rotondo (FG), Italy

[2] Department of Oncology, University of Torino, Candiolo, Italy.

[3] Candiolo Cancer Institute, FPO - IRCCS, Candiolo, Italy.

Antonino Bruno: Laboratory of Immunology, Unit of Molecular Pathology, Immunology and Biochemistry, IRCCS MultiMedica, 20139, Milan, Italy

Highlights

• The SIC conducted a survey on the effect of COVID-19 lockdown on cancer research laboratories in Italy.

• The impact of the lockdown on research activities was high, with complete or partial shutdown of >80% of the laboratories.

• Response to the pandemic was fragmented with different strategies adopted without a clearly defined contingency plan.

• An adequate organization of research centers is urgently needed to ensure laboratory activities in a safe environment.

ABSTRACT

Background

Italy was among the first countries hit by the pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The application of strict lockdown measures disproportionately affected both cancer patient care as well as basic and translational cancer research.

Materials and methods

The Italian Cancer Society (SIC) conducted a survey on the effect of lockdown on laboratories involved in cancer research in Italy. The survey was completed by 570 researchers at different stages of their career, working in cancer centers, research institutes and universities from 19 Italian regions.

Results

During the lockdown period, the impact of the COVID-19 pandemic emergency on face-to-face research activities was high, with a complete (47.7%) or partial (36.1%) shutdown of the laboratories. In the post-lockdown period, research activities were resumed in most of the respondents' institutions (80.4%), though with some restrictions (77.2%). COVID-19 testing was offered to research personnel only in ~50% of research institutions. Overall, the response to the pandemic was fragmented as in many cases institutions adopted different strategies often aimed at limiting possible infections without a clearly defined contingency plan. Nevertheless, research was able to provide the first answers and possible ways out of the pandemic, also with the contribution of many cancer researchers that sacrificed their research programs to help overcome the pandemic by offering their knowledge and technologies.

Conclusions

Given the current persistence of an emergency situation in many European countries, a more adequate organization of research centers will be urgent and necessary to ensure the continuity of laboratory activities in a safe environment.

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has resulted in an ongoing pandemic that, has affected more than 115 millions of people and caused over 2,5 million deaths worldwide (https://coronavirus.jhu.edu/map.html, accessed March 5, 2021).

Italy was among the first countries hit by this pandemic and its rapid evolution in Northern Italy led to the application of strict lock down measures that profoundly affected all activities and

disproportionately affected both cancer patient care as well as cancer research. This effect became then evident not only in Italy but worldwide, as recently reviewed by Painter and colleagues (1).

Cancer patients that demonstrated a particularly adverse outcome upon SARS-CoV-2 infection (1–3). The pandemic also negatively impacted cancer care with about 90% of cancer centers experiencing a reduction in their ability to provide services worldwide (4) and in the possibility to perform cancer screening programs, especially in racial and ethnic minorities (5,6).

Also, the SARS-CoV-2 pandemic had a relevant impact on clinical research in oncology, with a reduction of 74% of patients enrolled in clinical trials in May 2020, compared with the same period in 2019 (7). This drop in patients' recruitment has been related on one side to decreased ability of clinical, support and preclinical units in providing nonessential activities and on the other to the reallocation of resources to more impellent services and trials (7). For instance, between January and June 2020, more than 1200 SARS-CoV-2-related clinical trials have been registered in only 9 countries (7).

Last but not least, the SARS-CoV-2 pandemic profoundly affected basic, translational and clinical cancer research. A cut in cancer research funding, due pandemic, has been anticipated worldwide (1,8,9) and many researchers reported reduction or complete shutdown in their laboratory activities with possible profound consequences on years of previous activities in building models, collect samples and support the clinical activities not only in Italy (https://www.nature.com/articles/d41586-020-00826-7 https://www.airc.it/fiducia), but also worldwide (10,11).

Yet, although there is the clear perception that preclinical cancer research has been strongly affected by the current pandemic, we still do not have any systematic report on how the pandemic impacted at national and/or international level on the activities of cancer research laboratories and how the cancer research community lived during the months of more severe lockdown.

To fill this gap, here, we show the results generated by a survey conducted by the Italian Cancer Society (SIC) on the effect of lockdown on laboratories involved in cancer research in Italy. The survey was completed by 570 researchers at different stage of their career, working in cancer centers, research Institutes and universities from 19 Italian regions. We then discuss what the Italian cancer community has learnt from this experience and what we propose should be next steps to face the new challenges raised by the SARS-CoV-2 pandemic.

RESULTS

Italian cancer researchers were invited to respond an on-line questionnaire aimed at verifying the impact of COVID-19 pandemic and the consequent lock down to their activity (see methods). The

response rate to this survey was high with a total of 570 researchers participating (Figure 1). Participants were 44 years old on average, with 68.4% female and 28.8% male (Table 1). Over two-hundreds survey respondents were group leaders, professors, and directors of research institutions (Table 1). Cancer centers and universities were the prominent affiliations among survey respondents (81%; Table 1). Overall, research institutions were located in northern (58.4%), central (18.9%), and southern (20.7%) Italy (Table 1). During the lockdown period, namely Phase 1 from 9th March to 4th May 2020, the impact of COVID-19 pandemic emergency on face-to-face research activities was high (70.7%; high Top-3 boxes; Table 2) with a complete (47.7%) or partial (36.1%) shutdown of the laboratories (Table 2). Geographical distribution of area of work was significantly associated with research activities interruption (p<0.01; chi-square test), with a prevalence in northern of Italy (60-75%; Table 4). This result could be interpreted in light of a higher number of COVID19 infections in northern Italy as well as of more severe restrictions to both access research centers and individual mobility.

The use of remote-working modality was the choice to continue research activities (85.3%; neutral and high Top-3 boxes; Table 2). This allowed keeping a regular communication among laboratory members (97.2% of agreement, Table 2) and maintaining research collaborations with other research facilities (52.6% of agreement; Table 2). Remarkably, survey respondents positively evaluated remote-working modality used in combination with face-to-face meetings in a future post-pandemic situation (Table S1). On the other hand, the COVID-19 emergency had a negative impact on the interaction between researchers and clinicians as expected, with 69.1% of ceased activities in Phase 1 (Table 2).

Importantly, a sizable fraction of researchers was involved in COVID-19 research activities/diagnostics (31.9%; Table 2) with, as expected, a high percentage of group leaders/professors/directors (41.9%, p=0.0031; Table 4) contributing to COVID-19 research protocols drafting and research infrastructures reorganization. Lastly, salary remain overall unchanged (94.6% of agreement; Table 2).

In the post-lockdown period i.e., Phase II, research activities were resumed in most of the respondents' institutions (80.4%; table 3) though with some restrictions for new internal guidelines (77.2%; Table 3), to primarily ensure safety in workplace and productivity. Workplace space reorganization and work shifts modification happened quite frequently in 60.5% and 82.5% of instances (Table 3). Furthermore, COVID-19 testing was offered to research personnel in ~50% of research institutions (Table 3). Group leaders, professors and directors of research department/institute were also frequently involved in drafting internal guidelines for resume research activities (p<0.0001; Table 4).

Finally, we developed a "lockdown-score" (see methods) to assess the overall impact of COVID-19 emergency on research during the Phase 1, considering the geographical distribution of research centres as well as the career level of interviewed researchers. Cancer research in southern Italy seemed to be slightly less impacted by COVID19 (p=0.0566; Table S2), while the impact on "junior group leaders" appeared to be significantly high (p=0.0419; Table S2).

METHODS

In May 2020, the Italian Cancer Society (Società Italiana di Cancerologia, SIC) launched a survey to assess the impact of COVID-19 pandemic on cancer research conducted in Italy. To deploy the questionnaire rapidly and perceive a very fast data-collection, a web-based modality was chosen. Google Forms platform was the choice to implement the survey, and responses were automatically stored in a database built with Excel (Microsoft).

The survey was proposed to scientists involved in cancer research in universities, cancer centers and research institutes. Responses were collected between the 5th and the 27th of May, with 93% of responses registered in the first 10 days (Figure 1).

Twenty-nine questions were asked, including rating scale (from 0 to 10), multiple-choice, closed-ended and open-ended questions. Questions covered characteristics of responders, as well as modality of research activity during the first two phases (Phase 1 and 2) of the COVID-19 pandemic, that in Italy were distinguished by over two months of total lockdown all around Italy (Phase 1, from March 9th), and a gradual easing of lockdown from May 4th to May 18th (Phase 2). Rating scale responses (from 0 to 10) were recoded into 3-level variables, combining the bottom 3-boxes (from 0 to 2) as low, the middle rates (from 3 to 7) as neutral, and the top 3-boxes (from 8 to 10) as high. Manual content analysis was performed on multiple-choice and open-ended questions, and responses were categorized into 3 levels (no/partially/yes or increased/unchanged/decreased, as appropriate). Eleven questions related to the lockdown phase were further summarized by means of a "lockdown score", representing the sum over the 11 responses, after having assigned the lowest (bottom 3-boxes/no/increased), middle (neutral/partially/unchanged) and the highest (top 3-boxes/yes/decreased) categories to 0, 0.5 and 1 values, respectively. The sum was then divided by 11 to normalize the lockdown score into range 0-1. High score represents a high impact on research activities during the lockdown phase.

Responses were described as frequencies and percentages, or median and first/third quartiles for categorical and continuous variables, respectively. Chi-square test was used to assess association between variables. Kruskal-Wallis test was used to compare continuous distributions. P-values less than 0.05 were considered statistically significant.

Discussion

This survey for the first time provides a quantitative estimation of the impact of COVID-19 on cancer research in Italy during and immediately after the lockdown in spring 2020. The results of this survey are very impressive, as they clearly demonstrate that the emergency linked to COVID-19 has effectively interrupted the activities of numerous laboratories engaged in the fight against cancer for many months.

As expected, the impact on research activities was most evident in the Northern Italian regions, given the larger spread of the epidemic in this part of the country in the first quarter of 2020. The consequences of this activity limitation are difficult to estimate, but we can safely say that the reduction in the activities of laboratories involved in cancer research will result in a delay in those fundamental discoveries for developing new technologies to fight cancer. In 2020, precision oncology reached several important milestones. A number of highly active new targeted therapies become available for diseases that are extremely difficult to treat (12). The pandemic unfortunately jeopardized the development of new drugs as well as the identification and validation of innovative biomarkers for diagnosis anticipation and prognosis prediction. This will negatively impact cancer patients' prognosis in a short coming.

Importantly, our survey revealed also that the response to the pandemic was fragmented, as in many cases institutions adopted different strategies often aimed at limiting possible infections without a clearly defined contingency plan. It is worth noting, that such unorganized response to emergency was expected because our country was not at all prepared for this challenge, as demonstrated by the high number of deaths that we still continue to record. During the first phase of the pandemic, Italian healthcare workers did not have access to adequate PPE (personal protective equipment), such as face masks that were difficult to find. Therefore, in order to avoid massive infection of healthcare workers, clinical center directors decided to shut down research laboratories, rather than trying to develop contingency plans and protocols to allow to work safely. This evidence is confirmed also by the fact that some research laboratories in northern Italy had not resumed activities even after the lockdown. Even more surprisingly, no defined measures, such as swabbing research workers, were adopted when the laboratories reopened, thus underlying the absence in many instances of COVID-19 work safely protocols for resuming research activities.

COVID-19 lockdown has affected all research laboratories, but the observation that junior group leaders have been affected by this difficult period more than others, highlights how this situation of uncertainty can negatively impact particularly on younger researchers at the beginning of their academic career.

The pandemic has now lasted for more than a year and is continuing to negatively impact on cancer research. Activities resumed in almost all the institutions, but the problems related to the reorganization of spaces, the preparation of risk plans, the monitoring of the spread of the epidemic in the research community, were only partially addressed. This unprecedented situation has, however, forced us to perceive and develop new ways of working and communicating, to alternate work in the laboratory with remote working, perhaps to plan laboratory activities better. However, it is undeniable that the progress of research is based on the continuous idea exchange among collaborators, among researchers of different backgrounds and on constant mentoring between lab heads and trainees. The limitation of these activities will certainly affect above all the training and personal growth of the youngest researchers.

Among the effects of the pandemic, there is fear of a considerable decrease in funding for research in general and for cancer research in particular. Yet, if there is one thing we should have learned from the pandemic, it is precisely the relevance of research: research was able to provide the first answers and possible ways out of this situation, also with the contribution of many cancer researchers that sacrificed their research programs to help overcoming the pandemic offering their knowledge and technologies. Finally, a more adequate organization of research centers will be urgent and necessary to assure the continuity of laboratory activities in a safety environment.

References

1. Bakouny Z, Hawley JE, Choueiri TK, Peters S, Rini BI, Warner JL, et al. COVID-19 and Cancer: Current Challenges and Perspectives. Cancer Cell. 2020;38:629–46.
2. Garassino MC, Whisenant JG, Huang L-C, Trama A, Torri V, Agustoni F, et al. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol. 2020;21:914–22.
3. Passamonti F, Cattaneo C, Arcaini L, Bruna R, Cavo M, Merli F, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. Lancet Haematol. 2020;7:e737–45.

4.   Jazieh AR, Akbulut H, Curigliano G, Rogado A, Alsharm AA, Razis ED, et al. Impact of the COVID-19 Pandemic on Cancer Care: A Global Collaborative Study. JCO Glob Oncol. 2020;6:1428–38.

5.   Gathani T, Clayton G, MacInnes E, Horgan K. The COVID-19 pandemic and impact on breast cancer diagnoses: what happened in England in the first half of 2020. Br J Cancer. 2020;

6.   Carethers JM, Sengupta R, Blakey R, Ribas A, D'Souza G. Disparities in Cancer Prevention in the COVID-19 Era. Cancer Prev Res Phila Pa. 2020;13:893–6.

7.   Bailey C, Black JRM, Swanton C. Cancer Research: The Lessons to Learn from COVID-19. Cancer Discov. 2020;10:1263–6.

8.   Burki TK. Cuts in cancer research funding due to COVID-19. Lancet Oncol. 2020;

9.   COVID-19 Hits Cancer Research Funding. Cancer Discov. 2020;10:756.

10.   Zon L, Gomes AP, Cance WG, Ribas A, Tuveson D, Postel-Vinay S, et al. Impact of COVID-19 Pandemic on Cancer Research. Cancer Cell. 2020;38:591–3.

11.   Colbert LE, Kouzy R, Abi Jaoude J, Ludmir EB, Taniguchi CM. Cancer Research after COVID-19: Where Do We Go from Here? Cancer Cell. 2020;37:637–8.

12.   William C. Hahn, et al. An expanded universe of cancer targets. Cell. 2021;184:1142-1155.

Table 1. Characteristics of responders. N=570.

	N	%
Gender		
Male	164	28.8
Female	390	68.4
NA	16	2.8
Age [years]		
20-25	8	1.4
26-30	76	13.3
31-35	90	15.8
36-40	89	15.6
41-50	114	20.0
> 50	185	32.5
NA	8	1.4
Educational level		
Phd	363	63.7
Phd fellow	49	8.6
No Phd	142	24.9
NA	16	2.8
Main Country of work		
Italy	562	98.6
Not-Italy	4	0.7
NA	4	0.7
Italian geographical area of work		
Northern Italy	333	58.4
Central Italy	108	18.9
Southern Italy	118	20.7
NA	11	1.9
Role		
Director/Group Leader/Professor	215	37.7
Junior Group Leader	15	2.6
Researcher	190	33.3
Student	58	10.2
Technician/administrative/consultant	41	7.2
NA	51	8.9
Time spent on computer activities		
Low	12	2.1
Neutral	327	57.4
High	229	40.2
NA	2	0.4
Research fields (multiple options)		
Basic research	301	39.3
Translational research	395	51.6
Pre-clinical/Clinical research	59	7.7
Public Health	1	0.1
Bioinformatics	3	0.4
Epidemiology	2	0.3
Biomedical research	1	0.1
NA	3	0.4
Research institute		
University	195	34.2
Cancer center	267	46.8
University and cancer center	27	4.7
Other	77	13.5
NA	4	0.7

percentages could not add up to 100% due to rounding

Table 2. Research activities during lockdown phase. N=570.

	N (%)			
	Low	**Neutral**	**High**	**NA**
Impact on research activities	37 (6.5%)	210 (36.8%)	323 (56.7%)	0
Impact on face-to-face research activities	44 (7.7%)	110 (19.3%)	403 (70.7%)	13 (2.3%)
Use of remote working	82 (14.4%)	171 (30.0%)	315 (55.3%)	2 (0.4%)
	No	**Partially**	**Yes**	**NA**
Laboratory research activities shutdown	90 (15.8%)	206 (36.1%)	272 (47.7%)	2 (0.4%)
Research group internal communication ceased (no mail/no virtual meeting/no phone call)	554 (97.2%)	-	13 (2.3%)	3 (0.5%)
Collaboration with other facilities ceased	300 (52.6%)	-	78 (13.7%)	192 (33.7%) [a]
Collaboration with clinicians ceased	171 (30.0%)	-	394 (69.1%)	5 (0.9%)
Involvement in COVID-19 research protocols	386 (67.7%)	-	182 (31.9%)	2 (0.4%)
Involvement in COVID-19 research activities/diagnosis	403 (70.7%)	-	165 (28.9%)	2 (0.4%)
	Increased	**Unchanged**	**Decreased**	**NA**
Number of worked hours per week	153 (26.8%)	205 (36.0%)	207 (36.3%)	5 (0.9%)
Salary variation	9 (1.6%)	539 (94.6%)	12 (2.1%)	10 (1.8%)

percentages could not add up to 100% due to rounding;

[a] *including 189 responders not using facilities for their research*

Table 3. Research activities during phase 2. N=570.

	N (%)			
	No	**Partially**	**Yes**	**NA**
Laboratory research activities resumed	111 (19.5%)	-	458 (80.4%)	1 (0.2%)
Internal guidelines for research activities during phase 2 provided	103 (18.1%)	-	440 (77.2%)	27 (4.7%)
Involvement in the drafting of internal guidelines for research activities during phase 2	485 (85.1%)	-	81 (14.2%)	4 (0.7%)
Workplace space reorganization during phase 2	149 (26.1%)	-	345 (60.5%)	76 (13.3%)
Work shifts modified during phase 2	22 (3.9%)	3 (0.5%)	470 (82.5%)	75 (13.2%)
DPI provided by research institute	33 (5.8%)	4 (0.7%)	486 (85.3%)	47 (8.2%)
COVID-19 testing during phase 2	163 (28.6%)	8 (1.4%)	277 (48.6%)	122 (21.4%)
Collaboration with facilities	13 (2.3%)	154 (27.0%)	244 (42.8%)	159 (27.9%)

percentages could not add up to 100% due to rounding

Table 4. Distribution of research activities during lockdown phase and phase 2, according to Italian geographical area of work and role of responders. Distributions for significant association (chi-square test) are reported.

	Italian geographical			Role				
	Northern	Central	Southern	Director/Group	Junior Group Leader	Researcher	Student	Technician/
Laboratory research activities shutdown		p=0.0003						
Low	6.9	4.6	6.8					
Neutral	33.3	30.6	54.2					
Top	59.8	64.8	39.0					
Impact on face-to-face research activities		p=0.0029				p=0.0434		
Low	9.2	2.8	8.9	7.1	0.0	5.5	14.3	10.0
Neutral	15.6	23.4	30.1	24.5	13.3	20.8	5.4	20.0
Top	75.2	73.8	61.1	68.4	86.7	73.8	80.4	70.0
Use of smart working		p=0.0121				p <0.0001		
Low	13.3	7.4	22.0	16.4	13.3	6.3	15.8	43.9
Neutral	27.8	36.1	30.5	32.2	26.7	30.0	26.3	19.5
Top	58.9	56.5	47.5	51.4	60.0	63.7	57.9	36.6
Involvement in COVID-19		p=0.0284				p=0.0031		
No	71.2	68.5	57.8	58.1	86.7	71.4	79.3	68.3
Yes	28.8	31.5	42.2	41.9	13.3	28.6	20.7	31.7
Involvement in COVID-19						p <0.0001		
No				56.3	80.0	81.6	89.7	58.5
Yes				43.7	20.0	18.4	10.3	41.5
Number of worked hours per week						p <0.0001		
Increased				35.1	33.3	23.3	15.5	29.0
Unchanged				36.5	33.3	40.2	20.7	47.4
Decreased				28.5	33.3	36.5	63.8	23.7
Salary variation		p=0.0053						
Increased	1.2	0.0	4.4					
Unchanged	97.3	94.4	94.8					
Decreased	1.5	5.6	0.9					
Laboratory research activities resumed		p=0.0457						
No	18.3	14.8	27.1					
Yes	81.7	85.2	72.9					
Involvement in the drafting of internal guidelines		p=0.0141				p<0.0001		
No	82.8	93.4	89.0	75.7	93.3	91.1	91.1	92.7
Yes	17.2	6.6	11.0	24.3	6.7	9.0	8.9	7.3

Figure legend

Figure 1. Survey response rate between the 5th and the 27th of May. Black dots represent the number of responders per day. Red squares represent the cumulative number of responders per day.