Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Brief report

Prevalence of thrombosis in patients with cancer and SARS-CoV-2 infection

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ABSTRACT

Background: Covid-19 infection and cancer are associated with an increased risk of thrombotic events. The aim of our study is to analyze the cumulative incidence of thrombosis in oncological patients with Covid-19 and detect differences with the non-cancer Covid-19 population.
Methods: We retrospectively reviewed 1127 medical records of all admitted patients to ward of the Hospital Universitario Infanta Leonor (Madrid, Spain), including 86 patients with active cancer between March 5th, 2020 to May 3rd, 2020. We analyzed cumulative incidence of thrombosis and risk factors associated to the cancer patient's cohort.
Results: We diagnosed 10 thrombotic events in 8 oncological patients with a cumulative incidence of 9.3%. A statistically significant association was found regarding thrombosis and history of obesity ($p = 0.009$). No differences related to cumulative incidence of thrombosis between both groups were detected (9.8% vs 5.80%) in our hospital ($p = 0.25$).
Conclusion: No significant differences were observed in the cumulative incidence of thrombosis in the two study groups. The thrombotic effect of Covid-19 is not as evident in cancer patients and does not seem to be added to its prothrombotic activity.

Prevalencia de trombosis en pacientes con cáncer e infección por SARS-CoV-2

Palabras clave:
COVID-19
Cáncer
Trombosis
Incidencia acumulada
Factores de riesgo

RESUMEN

Antecedentes: La infección por COVID-19 y el cáncer se asocian a mayor riesgo de eventos trombóticos. El objetivo de nuestro estudio es analizar la incidencia acumulada de trombosis en pacientes oncológicos con COVID-19 y detectar diferencias con la población sin cáncer y COVID-19.
Métodos: Revisamos retrospectivamente 1.127 historias clínicas de los pacientes ingresados en del Hospital Infanta Leonor (Madrid, España), incluyendo 86 pacientes con cáncer activo entre el 5 de marzo y el 3 de mayo de 2020. Se analizó la incidencia acumulada de trombosis y los factores de riesgo asociados a la cohorte de pacientes con cáncer.
Resultados: Diagnosticamos 10 eventos trombóticos en 8 pacientes oncológicos, con una incidencia acumulada del 9,3%. Se encontró una asociación estadísticamente significativa entre trombosis y obesidad (p = 0,009). No se detectaron diferencias relacionadas con la incidencia acumulada de trombosis entre ambos grupos (9,8%vs. 5,80%, p = 0,25).

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Conclusión: No se observaron diferencias significativas en la incidencia acumulada de trombosis en los 2 grupos de estudio. El efecto trombótico de la COVID-19 no es tan evidente en los pacientes con cáncer y no parece sumarse a su actividad protrombótica.

Background

Since the start of the pandemic in December 2019, millions of cases of SARS-CoV-2 infection have been detected worldwide.[1] Patients diagnosed with cancer are susceptible to severe infections by this virus, with higher mortality than other groups of patients.[2,3]

There are multiple evidences of the association with the appearance of thrombotic events in a high percentage of general Covid-19 patient.[4–6] Oncological patients have an increased risk of thrombosis associated with the tumor disease (cancer associated thrombosis) and with oncological treatment,[7] so it seems reasonable to think that patients with cancer and Covid-19 infection have a higher risk of thrombosis with respect to the general population.

The aim of our study is to analyze the cumulative incidence of thrombotic events in patients with cancer and Covid-19 infection comparing with the general Covid-19 patients and risk factors for thrombosis in both groups.

Methods

Study design

Single cohort, longitudinal study of patients with Covid-19 admitted to the general ward of the Hospital Universitario Infanta Leonor (Madrid, Spain) between March 5th, 2020 to May 3rd, 2020. We retrospectively reviewed 1127 medical records until data cut off, including 86 patients with active cancer. We define active cancer as that diagnosed in the five years prior to inclusion in the study. We analyzed cumulative incidence of thrombosis in cancer patients and Covid-19 infection and its difference between this cohort and the non-cancer patients. We also study the thrombosis risk factors associated in the cancer patient's cohort.

Covid-19 diagnosis was made based on WHO criteria and/or confirmed by RT-PCR of nasopharyngeal specimens. Severe Covid-19 infection was defined as presence of bilateral pneumonia with CURB-65 scale score ≥ 2/Fi$O_2 \geq 35\%$ or admission to an Intensive Care Unit (ICU).Thrombosis diagnosis was made after performing additional image tests when clinically mandatory. We followed our centre's protocol recommendations, treating all patients with low-molecular-weight heparin at prophylactic or intermediate doses according to D Dimer levels (< or >1000 μg/dl).

Approval was obtained from the reference local ethics committee (COVID-CANCER HUIL STUDY, ref. 213/20 and COVID-19@Vallecas, ref. 027-20). All procedures were performed in accordance with the Declaration of Helsinki. Study data were collected and managed using REDCap (Research Electronic Data Capture) that is a secure, web-based software platform designed to support data capture for research studies.[8]

Statistical analysis

Descriptive analyses are reported as relative frequencies for discrete variables. Continuous variables are reported as mean ± standard deviation (SD) or median and interquartile range (IQR) for normal and not normally distributed variables, respectively. To determine differences on thrombosis incidence between cancer patients and general population, Fisher's Exact Test was performed. On the other hand, to determine the relationship between clinical and demographic risk factors with thrombosis development, Chi square Test, univariate logistic regression and multivariate logistic regression were performed. Statistical analyses were carried out with STATA SE version 14.1 (StataCorp, CollegeStation, TX, USA). A p value <0.05 was considered statistically significant.

Results

A total of 1127 Covid-19 patients were admitted to our institution until data cut off. Eighty-six of these patients were oncological patients at Medical Oncology Department in Hospital Universitario Infanta Leonor in Madrid (Spain). We compared the incidence of thrombosis between the two groups and risk factors.

Thrombotic incidence in general patients and differences with cancer patients

In general population, a total of 70 thrombotic events were diagnosed in 61 patients (5.8%) of the total 1041 Covid-19 patients without cancer. In this group, 43 patients (62%) suffered venous thrombotic events, 6 (9%) were diagnosed with both venous and arterial complications (concurrently in most cases), 18 (26%) had only arterial events, and 2 patients suffered microvascular ischemic lesions.

We detected no differences related cumulative incidence of thrombosis between cancer patients and general patients: 9.8% (8 of 86 total cancer patients) in cancer patients versus 5.8% (61 of 1041 total patients) in general patients in our hospital ($p = 0.25$).

We compared comorbidities between the two groups. We found a statistically significant relationship with a history of chronic kidney disease (1/69 general thrombosis patients versus 2/8 oncological thrombosis patients, $p = 0.02$). No statistically significant relationship was found with the rest of the comorbidities (Table 1).

Regarding ICU admissions: thirteen patients (19%) of general population were admitted to the ICU during hospitalization. However, none of the cancer patients were admitted to the intensive care unit.

Cancer patients

We included 86 cancer patients whose median age was 70 years old with higher prevalence of males ($n = 55$, 63.9%), and most patients metastatic disease ($n = 33$, 38.3%). Most frequent primary sites of cancer were: lung, colorectal and prostate (26.7%, 22.1%, 17.4% respectively).

In this cohort, we diagnosed 10 thrombotic events in 8 of the total 86 patients with a cumulative incidence of 9.3%. Five patients suffered pulmonary embolism, 1 patient deep vein thrombosis, 2 patients acute coronary syndrome and 2 patients an ischemic stroke.

Thrombosis risk factors in cancer patients and demographic characteristics

Among the classical thrombosis risk factors we have found a statistically significant association with obesity (37% thrombosis patients versus 7.6% without thrombosis, $p = 0.009$). Atrend toward

Table 1
Difference in comorbidities between general patients with thrombosis and oncological patients with thrombosis.

Characteristics	General thrombosis patients $N = 69$	Oncological thrombosis patients $N = 8$	p value
Acute coronary syndrome	2 (2.8%)	0	1
Arterial hypertension	36 (52.2%)	4 (50%)	1
Chronic obstructive pulmonary disease	20 (28.9%)	4 (50%)	0.24
Chronic kidney disease	1 (1%)	2 (25%)	0.02
Obesity	19 (27.5%)	3 (37.5%)	0.68
Diabetes mellitus	13 (18.8%)	1 (12.5%)	1
Dyslipidemia	19 (27.5%)	3 (37.5%)	0.68
Smoking	12 (17.3%)	3 (37.5%)	0.19
Previous thrombosis	2 (2.8%)	2 (25%)	0.07

Table 2
Difference in demographic characteristics between patients with and without thrombosis in cancer patients.

Characteristics	Thrombosis patients $N = 8$	Non thrombosis patients $N = 78$	P value
Type of cancer			
Lung	1 (4.3%)	22 (95.6%)	0.409
Colorectal	3 (15.7%)	16 (84.2%)	
Prostate	2 (13.3%)	13 (86.6%)	
Metastatic disease	3 (37.5%)	30 (38.4%)	0.958
Previous chemotherapy	2 (25%)	22 (28.2%)	0.847
Heart disease	1 (12.5%)	20 (25.6%)	0.410
Acute coronary syndrome	0	6 (7.6%)	0.416
Arterial hypertension	4 (50%)	46 (58.9%)	0.624
Chronic obstructive pulmonary disease	4 (50%)	23 (29.4%)	0.234
Chronic kidney disease	2 (25%)	6 (7.6%)	0.108
Obesity	3 (37.5%)	6 (7.6%)	0.009
Diabetes mellitus	1 (12.5%)	16 (20.5%)	0.588
Dyslipemia	3 (37.5%)	22 (28.2%)	0.581
Smoking	3 (37.5%)	24 (30.7%)	0.750

Table 3
Comparative analytical characteristics in cancer patients with and without thrombosis.

Analytical characteristics	Thrombosis $N = 8$	Non thrombosis $N = 78$	p value
Hemoglobin (Mean, g/dl)	12.03	12.06	0.9779
Lymphocytes (Mean /L)	1400	800	0.0135
Platelets (Median, $\times 10^3$)	259	219	0.2329
D-Dimer (Median, μg/dl)	1410	845	0.5427
LDH (Median, U/L)	235	236	0.8888
Fibrinogen (Median, mg/dl)	387	501	0.11
Partial thromboplastin time activated (s)	25.5	26.6	0.57
CPR (Median, mg/L)	42.5	67.1	0.82

significance was detected regarding a previous history of chronic kidney disease (25% thrombosis group versus 7.6% without thrombosis $p = 0.108$).

On the other hand, no statistically significant differences were found on the remaining risk factors (Table 2).

Analytical characteristics in cancer patients

In the cancer patients cohort, we detected a statistically significant difference between the number of lymphocytes (1400 in patients with thrombosis versus 800×10^3 μL/L in patients without thrombosis, $p = 0.0135$). Nevertheless, no statistically significance differences were found in all other parameters (Table 3).

Discussion

Several studies have confirmed that Covid-19 induces hyperinflammation leading to pro-coagulant states and thus, increases the incidence of thrombosis.[9] We also know that the risk of thrombosis is increased in patients with cancer intrinsically, therefore, the aim of our study was to assess the prevalence of thrombosis in the general population compared to cancer's patients.

In our study, we found a high percentage of in-hospital thrombosis in all patients. This higher incidence of thrombosis was detected despite the fact that these patients received prophylactic and intermediate doses of treatment with low molecular weight heparin, with an incidence of 5.8% in patients without cancer versus 9.8% in patients with cancer, but without showing statistically significant differences between both subgroups ($p = 0.25$).

There are few reports so far describing the incidence of thrombosis in patients with Covid-19 and cancer. In the work developed by Patell et al., a unicentric cohort study with a number of patients considerably lower than our work, they found during the first 28 days after Covid-19 diagnosis a cumulative incidence of thrombosis of 18.2% in general patients and 14.2% in oncological patients. These incidences are higher than ours, probably because of the long follow-up period, and because it also includes hematological patients and patients requiring admission to the ICU that are excluded in our study.[10]

In the study by Patell et al., no risk factors of thrombosis in this population profile were evaluated. We detected that oncological patients with obesity history or lymphocytes above 1400 μL/L had a greater risk of thrombosis.

It is worth noting the limitations of our study, which is retrospective and unicentric, so we could be underestimating the incidence of thrombosis. Furthermore, we do not know whether the two groups are completely homogeneous, so it is difficult to conclude whether cancer is associated with higher rates of thrombosis in Covid19 patients.

Finally, as a conclusion, we could define that the thrombotic effect of Covid-19 is not so evident in cancer patients and does not appear to add to the prothrombotic activity of cancer. In our study, we did not observe significant differences in the incidence of thrombosis in the two study groups. A classic factor of thrombosis such as obesity is the most outstanding one as a predictor of the development of thrombotic events in our patients.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Author contributions

B.O. contributed to the conception and design of the study, data acquisition, statistical analysis, interpretation of the data and writing of the manuscript. J.R. contributed to the conception and design of the study, interpretation of the data and writing of the manuscript. N.M.R., M.F.V. and P.R.contributed to data acquisition and statistical analysis. C.P and G.S.M contributed to the conception and design of the study, interpretation of the data and writing of the manuscript. A.M.M., M.P.P., A.L.A. contributed to the acquisition of the data. M.A.L. contributed to the conception and design of the study, interpretation of the data and writing of the manuscript. All authors reviewed and approved the final version of the manuscript.

Conflict of interest

The authors declare no conflict of interest for the present work.

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Appendix A.

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