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A DISTINCT GUT MICROBIAL ECOLOGY IS ASSOCIATED WITH ENHANCED CHEMOSENSITIVITY FOLLOWING NEUTROPHIL ATTENUATION IN PANCREATIC CANCER

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Background: Infiltration of innate immune cells, such as neutrophils, in the tumor microenvironment (TME) are associated with worse oncologic outcomes in pancreatic ductal adenocarcinoma (PDAC). Given recent evidence highlighting the complex intersection between chemosensitivity and the gut microbiome in solid tumors, we sought to investigate if the enhanced chemosensitivity observed with neutrophil attenuation in PDAC is associated with a distinct gut microbial ecology.

Methods: C57BL/6 mice were orthotopically injected with syngeneic KrasG12D/+;Trp53fl/+;Pdx-Cre(KPC) PDAC cells, and randomized into four treatment groups after 10d tumor growth (n=8-10/arm): vehicle-control, anti-Ly6G antibody treatment alone with neutrophil-attenuating but not depleting dosing (25 mg/dose) q3d, gemcitabine(100 mg/kg) and paclitaxel(10 mg/kg) qwk(G/P), and G/P+anti-Ly6G. Fecal samples from mice (n=3/group) were collected 10d after treatment and submitted for shotgun metagenomic sequencing.

Results: Bray-Curtis principal coordinate analysis of microbial β-diversity revealed significant differences in microbial composition with neutrophil attenuation and chemotherapy. Abundance of 37 species were differentially significant between G/P+anti-Ly6G and G/P-treated cohorts (p-adj<0.05). Seven Alistipes spp. (class Bacteroidia)—previously associated with chemoresistance in solid cancers—were significantly reduced in the gut microbiome of G/P+anti-Ly6G-treated mice. Bifidobacterium pseudolongum, previously associated with PDAC tumor progression, was the most significantly reduced bacterial species in the gut microbiome of G/P+anti-Ly6G-treated mice when compared with G/P alone-group.

Conclusion: Our data unearth potential crosstalk between a distinct but narrow gut microbial ecology and anti-tumor adaptive immunity in response to neutrophil attenuation that is associated with improved chemosensitivity in PDAC. Therapeutic manipulation of this microbial program may mitigate chemoresistance and improve outcomes in PDAC patients.

PANCREATIC SURGERY DURING COVID-19 PANDEMIC: MAJOR ACTIVITY DISRUPTION OF A THIRD-LEVEL REFERRAL CENTER IN 2020

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Introduction: The COVID-19 pandemic has severely limited the access to cancer surgery, but it is not known to what extent referral centers for pancreatic diseases were affected by its outbreak. The aim of this study is to describe the effect of COVID-19 pandemic on a third level referral center for pancreatic surgery in Italy.

Methods: The 2020 activity of The Pancreas Institute of the University of Verona was reviewed, comparing different phases of the COVID-19 pandemic outbreaks using the pre-COVID era as a control. Endpoints were the overall caseload of pancreatic resections; surgical waiting list; administration of preoperative therapy; major morbidity and mortality; residents’ training; number of inpatients beds; outpatient visits/procedures/diagnostics.

Results: In 2020 there was an overall significant reduction of pancreatic resections performed (394 vs. 506 in 2019), particularly during the first (March-May) and second (October-December) COVID-19 outbreaks, with an all-time-low of 16 resections/months in April (compared to 43 average resection/month in 2019). The rates of major morbidity (Clavien-Dindo ≥3) and mortality were similar to 2019 (12% vs 16%, P= 0.11 and 2% vs 3%, P= 0.29 respectively). During the first and second outbreaks resident’s training, inpatient beds, outpatient visits, diagnostics and procedures were severely impaired, while the waiting list for up-front cancer resections and the use of preoperative chemotherapy concomitantly raised.

Conclusion: The COVID-19 pandemic has severely disrupted the activity of a third level referral center for pancreatic surgery, affecting the access to cancer surgical procedures and raising concerns regarding the solidity of the current centralization model.