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revision of the indicators based on gender differences.

More clinical studies focused on gender differences could lead towards a personalised medicine and more health appropriateness and effectiveness.

The FNOMCeO Committee for Health and Gender Medicine stresses its commitment to cooperate both with other national and local health institutions and with scientific societies in order to support a gender approach and develop a fair health system to improve children's, women's, men's and seniors' health.

Table 2. The aims of FNOMCeO Committee for Health and Gender Medicine

To plan post-graduate medical education
To inform citizens
To take part to the National and International Network for Gender Medicine
To cooperate with other Italian public institutions
To encourage clinical research

The 'Hospital Coordinating Group on Gender Health Promotion': at the IFO – Istituti Fisioterapici Ospitalieri – a center which uses gender as a health determinant

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The IFO Gender Health Coordination Group started its activity in 2018, when it was set up with a resolution as a result of a successful convergence of interests of some of the IFO's professionals and the Hospital's Strategic Board with the intention of launching, disseminating, expanding and above all stimulating research and knowledge in the field of gender differences in oncology and dermatology. Despite the exceptional evolution of medical research in recent decades, little attention has been paid so far to this aspect of medical science. An analysis of the literature shows that gender influences the pathophysiology, clinical signs, outcome and therapy of tumors and dermatological diseases. Therefore, this variable should be an important stratification factor and be considered in daily clinical practice and in all pre-clinical and clinical trials.

A better understanding of the existing differences could, in fact, direct therapeutic strategies towards increasingly personalized treatments and, therefore, towards more effective clinical management. In the field of oncology, over the last few decades, studies have proven to be biased in terms of gender, including in the field of research; suffice it to mention that in 1977 the Food and Drug Administration excluded women from phase I and II of clinical trials. The efficacy of chemotherapy differs in the two sexes/genders; however, the differences in the clinical characteristics of neoplasms, with the same histology and stage, are at times observed but not considered in daily clinical practice and guidelines. Relatively little is known about the gender differences in cancer therapy and their impact in the clinical management of the disease.

The low representation of women in clinical trials is certainly a crucial factor that has limited data collection to date. Moreover, due to the retrospective nature of these trials, there are many confusing factors (e.g., age, stage of disease, co-morbidity) that can influence the results to the point that the data emerging from the literature on gender differences is partial, fragmentary and at times contradictory. In general, it has been observed that some chemotherapy drugs have a better response rate in women than in men, without a significant increase in toxicity (e.g., cisplatin and irinotecan), while in other cases a higher toxicity in women is not associated with an increase in response (e.g., 5-fluorouracil). It has been observed that women develop cardiomyopathy and nephropathy less frequently than men, following treatment with anthracyclines, and that levels of reproductive hormones in women are inversely correlated with cardiac health; even the own anti-tumor activity exerted by anthracyclines seems to show a gender disparity. Studies conducted on murine models have shown a significantly greater reduction in tumor in male animals treated with anthracyclines than in females. The side effects of antineoplastic drugs are also strongly dependent on the peculiarities that the various tissues and organs have in the two sexes. For example, women have a higher incidence of oral mucositis, but lower rates of intestinal toxicity than men. Women are also more susceptible to nausea and vomiting, due to the lower activity of antiemetic drugs. While the molecular mechanisms underly-

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ing these differences are not yet or only partially known, the increase in toxicity often correlates with different pharmacokinetics.

Gender differences in pharmacokinetics and pharmacodynamics play a key role in both the efficacy and safety profile of drugs. The liver, the main organ responsible for drug metabolism, shows physiological differences between male and female. In particular, differences in liver transport, in the activity of drug detoxifying enzymes and in lipid metabolism have been described. Many detoxifying enzymes belonging to the cytochrome P450 (CYP) superfamily are expressed in the liver in a sex-dependent way and two of these, CYP3A4 and CYP2B6, which are responsible for the metabolism of more than 50% of the drugs, are more active in women than in men. For these reasons, women are particularly sensitive to drug-induced liver damage and are generally more susceptible to adverse reactions following treatment with anticancer drugs. Once again, hormonal levels play a key role in the gender differences observed in drug metabolism and excretion. The fact that drug metabolism in women is influenced by sex-specific factors such as menopause, pregnancy and menstruation also further complicate the issue. Although there are specific ethical considerations regarding the inclusion of women in clinical trials on drugs and their inclusion in clinical trials would entail an economic burden, the relationship between anticancer drug toxicity and hormonal influences is worth investigating.

Gender also seems to influence dermatological diseases in many ways, as for example in the case of allergic diseases, in particular contact dermatitis, especially in terms of quality of life and the subjective experience of one's own skin, which can, as a result, influence and modify the clinical and therapeutic approach. For example, the female population is more likely to be allergic to nickel and the black hair dye.

In HIV-related infections, gender differences can influence the risk of infection, disease progression and response to antiretroviral therapy. Women are more susceptible to HIV infection than men, partly because of anatomical, biological and social factors.

Other sexually transmitted infections and hormonal contraceptives, often used instead of 'barrier' contraceptives such as condoms, also play an important role. The possibility of transmitting the infection horizontally (heterosexually) and vertically places HIV-positive women at the center of complex problems that require specific management and greater support than that provided to male patients.

As a result of the above, our hospital has felt the need to develop and implement new gender strategies, with an integrated diagnostic and therapeutic approach, with a vision that takes into account, on the one hand, the offering of various networked care settings (outpatient, day service, hospitalization) and, on the other, all stages of the process ranging from prevention to diagnosis, treatment, and rehabilitation. The improvement of the quality and appropriateness of care are, in fact, objectives that can be achieved through a cross-cutting integration of medical specialties and professional skills that ensure that each patient is taken care of taking into account gender differences. Already in previous experiences, the IFO has been attentive to gender health issues, leading to the award of 'Pink Stamps' by Onda (National Observatory on Women's Health) Association.

For this reason, a Coordination group for the promotion of gender health has been set up to focus on the appropriateness of diagnosis and care in the oncological and dermatological field, using gender as a health determinant, and also tasked with contributing to pre-clinical and clinical research on this subject. With this objective in mind, the Group collaborates with many Italian and European centers and organizations committed to increasing awareness and knowledge of gender medicine through conferences, meetings with political and social decision-makers, participation in the growth of gender medicine in Europe and in the various regions of Italy, and ties with all institutions (University, Ministry of Health, Italian National Institute of Health) that deal with this dimension of medicine, for the aspects of clinical and care management and to develop dedicated approaches in translational and basic clinical research. In 2018, a national congress on the subject was held at the IFO, with the participation of a panel of experts. In addition to 'networking', its goal was the exchange of experiences and knowledge and the launch of important collaborations. It was followed by training events for IFO staff, aimed at disseminating and expanding gender issues.

As a result of these activities, the group has joined the Italian network of gender medicine, which includes the Center for Gender Specific Medicine of the Italian National Institute of Health, the Italian Health and Gender Group (GISeG), the Italian National Federation of the Orders of Doctors and Dentists (FNOMCeO), the Italian Federation of the Associations of Internist Hospital Managers (FADOI), the Italian Society of General Medicine and Primary Care (SIMG), the Italian Society of Rheumatology (SIR), the Italian National Association of Women Doctors (AIDM) and many scientific societies. Collaboration was also crucial in drafting a document for the application and dissemination of gender medicine, pursuant to article 3, paragraph 1, of Italian law 3/2018, prepared by the Ministry of Health, with the pre-

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cious support of the Center for Gender Specific Medicine of the Italian National Institute of Health and with the collaboration of a national technical and scientific panel of regional experts in gender medicine and the gender medicine representatives of the network of Scientific Institutes for Research, Hospitalization and Health Care (IRCCS), which the IFO was called to coordinate. This document aims to provide a coordinated and sustainable policy to spread gender medicine through dissemination, training and healthcare practices that take into account the differences arising from gender in research, prevention, diagnosis and care, in order to ensure the quality and appropriateness of services provided by the Italian National Health Service (NHS) in a uniform manner throughout the country. This document was followed by the Plan for the application and dissemination of gender medicine in Italy, formally approved on 13 June 2019 by the Italian Ministry of Health, who signed the implementing decree relating to Law 3/2018.

Lung and colorectal cancer in relation to gender: a focus on data from the National Health Observatory in Italian Regions

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The incidence, survival and mortality of tumors are the three key indicators that make it possible to assess, based on epidemiological studies, the severity of the disease and the effectiveness of the health system and to provide information about their behavior based on gender.

Worldwide, the incidence of cancer has changed greatly in recent decades in relation to demographic factors, in particular aging and the different exposure to risk factors such as smoking, unhealthy diet and hormonal status. These determinants have played a particular role in women, as a result of specific lifestyles and changes in the reproductive cycle.

Over the years, the fight against cancer has been fairly successful; in fact, the survival of many cancer patients, one of the most important indicators of the overall effectiveness of the health system, has significantly increased.

These results have been achieved through both increased secondary prevention and the development of new therapies. In addition, early diagnosis is crucial, as it significantly increases the chances of survival, reducing specific mortality, while therapies, both pharmacological and surgical, are decisive for the progress made in terms of prognosis.

This focus offers a key to interpreting the estimates of Italian data on incidence, survival and mortality in the 2005-2015 decade for two types of preventable tumors from a gender perspective: lung and colorectal cancer.

The analysis by macro-area of the country (North, Central, South and Islands) of the estimated annual percent change in the rate (standardized by age, European population, per 100,000 persons/year) of incidence and mortality and of the absolute percent difference of survival at 5 years after diagnosis has made it possible to identify four levels of progress (optimal, moderate, partial and inadequate).

The study has shown that there are differences in the progression of values in relation to gender.

Analyzing lung cancer over the 2005-2015 period (Table 1), it can be seen that, at national level, male gender was associated with optimal progress in terms of incidence (-2.7%), mortality (-3.2%) and survival (+5.7%), whereas female gender recorded an increase in incidence and mortality (+1.6% and +0.8%, respectively), although there was an increase in survival at 5 years from diagnosis (+5.6%). The incidence and mortality for men improved mainly in the North (-3.3% and -3.8%, respectively), while the increase in survival was greater in the South and Islands (+7.6%). As far as women are concerned, on the other hand, the worst data on incidence and mortality were found in Central Italy, with an increase of 2.5% and 1.7%, respectively, while the rather positive data on survival was recorded in the North (+8.6%).

The situation for colorectal cancer was different for each gender (Table 2). In this case, women showed a better progress, with a decrease at national level in both incidence (-0.4%) and mortality (-2.5%) and a significant increase in survival of 8.4%. Among men, mortality improved (-1.6%), incidence grew slightly (+0.5%), but above all, survival increased (+8.8%). By macro-area, the best progress among women was observed in the Central Regions with a decline in incidence (-0.5%) and mortality (-2.7%). As for survival, on