

PERSPECTIVES IN HEALTH AND MEDICINE

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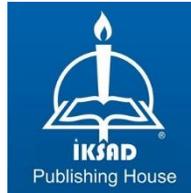
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CONTENTS

PREFACE

Ömer Tolga GÜLER, Elif AVŞAROĞLU ERCAN.....1

CHAPTER 1

A VERSATILE PERSPECTIVE TO THE SIGNIFICANCE IMPOSED TO HYMEN IN TURKEY

Gokcen ERDOGAN.....3

CHAPTER 2

PALLIATIVE CARE FOR PATIENTS WITH GYNECOLOGICAL CANCER

*Esra KARATAŞ OKYAY
Yunus Emre KARATAŞ*.....23

CHAPTER 3

BORON AND CANCER TREATMENT

*Nurhayat ATASOY,
Ufuk MERCAN YÜCEL*.....55

CHAPTER 4

PRIMARY THYROID LYMPHOMA

Aziz OCAKOĞLU.....67

CHAPTER 5

CASTLEMAN DISEASE; LYMPHOPROLIFERATIVE DISORDER

Nevin SAKOGLU.....83

CHAPTER 6

NONMICROSURGICAL EAR REPLANTATIONS

Bilgen Can.....99

CHAPTER 7

DETECTION AND IMAGING OF CORONA VIRUSES UNDER THE ELECTRON MICROSCOPE

Serap Mutlu ÖZÇELİK OTÇU

Ayfer Şanlı AKTAŞ.....109

CHAPTER 8

POSITIVE AND NEGATIVE EFFECTS OF USING CHEST COMPUTED TOMOGRAPHY IN COVID-19

Sibel KARACA.....127

FOREWORD

In the age of information, medical evidences have been accumulating in a dramatic rate. This book provides a glimpse to this desert of evidence and is for specialists in surgical and medical sciences interested in up-to-date information in each topic.

We hope that this book will stand as a source of information and inspiration for those who touch lives of their patients.

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CHAPTER 1

A VERSATILE PERSPECTIVE TO THE SIGNIFICANCE IMPOSED TO HYMEN IN TURKEY

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INTRODUCTION

In addition to biological, physiological and psychological differences between men and women, there are also cultural differences determined by social discourse. Individuals do not acquire roles related to their genders, they are born into ready-made roles (Gillario et al. 2017) The hymen, which is a different body part of a woman from a physical and biological point of view, is expressed as “membrane of virginity” in Turkish society and is seen as a representation of the conduct of society's concepts such as morality, honor and virginity, rather than a health function. This structure, which is expected to rupture and visibly bleed with the first sexual intercourse, is also expected to be preserved until marriage (Partoune et al. 2020; Rahman 2018).

This protectionism is requested from the woman not on her own behalf, but on behalf of the whole society. In cases where it is determined or assumed that she is not protected, the woman pays for this with impurity, dishonor, and sometimes with her life. Sometimes, young girls whose maidenhood is suspected are forced to undergo a virginity examination against their will. At this stage, the ethical and legal responsibility of the physician is to refuse this examination and to raise awareness of the woman and her relatives (Olson and Moreno 2017). It is noteworthy that in societies that impose these sanctions on women, there is generally a supportive and tolerant attitude towards men's sexual experience (Erdogan 2021). This emerging gender inequality causes psychological, socio-cultural, legal, ethical and

religious problems, reveals the lack of knowledge and education, and necessitates the search for solutions.

1. Medical Aspect

Biologically, in newborns with female characteristics, the membrane that surrounds the ostium vagina is called hymen, and is thought to protect it from diseases that may arise from external effects until puberty. This membrane usually has a central opening, although structurally it varies from person to person. Through this opening, menstrual blood flows out. Sometimes this structure can be imperforated, that is, completely closed. When the bloody tissue that cannot be thrown out with the first menstruation (menarche) creates intense pressure and pain, it is noticed and intervened under the control of a physician. This medical intervention mentioned is hymenectomy, that is, the opening of the hymen with a surgical procedure. The hymen can sometimes be torn during the first sexual intercourse and some bleeding may occur. In some women, this membrane tissue has never been formed congenitally, and therefore, bleeding and tearing is not observed during the first intercourse. Even if the membrane tissue is present, sometimes bleeding may not be seen in the first intercourse. With the elastic structure of the membrane and the convenience provided by vaginal fluids, sexual intercourse takes place without damage. Also, even if there is bleeding, it does not always indicate bleeding from the membrane, and sometimes there may be bleeding caused by damage to the external genitalia. Hymen can also tear during masturbation, sometimes due to a neglected

aspect of sexual education (Olson and Moreno 2017; Leye et al. 2018).

2. Ethical Aspect

Requests for hymen examination may come to the physician in different ways. These may be hymen control or repair.

Considering the function of the hymen in the body, it is assumed that it protects the genital area against infections that may come from the outside, so hymen examination has no place in determining general health problems. Hymen examination can only be performed in the examination of forensic cases with sexual assault notification. However, in some cultures, as a result of wrong and incomplete beliefs, hymen is assigned the function of determining the first intercourse. These cultures tend to oppose women experiencing sex with a sexual partner if they are not married. As a result, when there are doubts about a woman's virginity, they consider it normal to have a hymen examination. When a physician is consulted in such a situation, the physician's stance is not to perform the examination and to inform the patient and their relatives by using her/his professional knowledge. In addition, in genital examinations, ethically, it is appropriate not to report hymen-related information. Requesting a woman to have a hymen examination by someone else is a practice that violates the woman's rights on her own body, and requesting a self-examination or repair by herself also means that the woman submits to expectations or pressures of society on gender roles. When a physician refuses this examination, knowing that refusing to do a

hymen examination is a professional right, she/he stands before this social pressure (Cook and Dickens 2009).

3. Sociocultural Aspect

Information dating back to the first years of history shows that the first people gave special importance to women in the face of the miracle of birth, admired and blessed them. The dominance of the matriarchal structure at that time, with the transition to monotheistic religions, left its place to the patriarchal structure dominated by male dominance. (Mishori et al. 2019)

The differences between men and women are physiological, biological, psychological and also cultural. The whole of the value judgments developed by the society on the genders expresses the gender culture. While culture expects people to fulfill certain roles, it determines, defines, shapes, controls, predicts, limits, directs these roles separately according to genders and transfers these evaluations between generations. It cannot be expected that human beings, who are social beings, continue their lives insensitive to these values. It is known that in different cultures throughout history, women have been exposed to gender discrimination and are disadvantaged in this discrimination. One of the areas of social pressure applied to women is the area of sexuality. The situation in Turkey is similar to that in the world. Sexual myths passed down between generations are the most obvious indicators of this (Erdogan 2021). Sexual myths are unrealistic expectations and misconceptions that individuals believe to be true about sexual matters, but have no scientific proof of reality, are

often exaggerated, stereotyped, and limit the ability to live sexually in a healthy and free manner. These myths differ between cultures and individuals, and are passed on from generation to generation. In the study conducted by Aygin et al., with a sample consisting of university students and women, in which their views on sexual myths were evaluated, 82.2% of the participants stated that they did not find premarital sexual intercourse normal and 58.6% stated that the person to marry should be a virgin. It was also revealed that those aged 19 and under were more likely to approve of sexual myths. (Aygin et al. 2017). In a study conducted by Torun et al. with all male participants in Ümraniye district of Istanbul, the prevalence of believing in sexual myths was determined as 45%, 34.1% of 57 participants agreed with the myth that "it is immoral for a woman to initiate sex", 37.1% of 62 participants stated that they agreed with the myth that 'if a woman refuses sexual intercourse, her husband has the right to beat her'. In addition, in the study conducted by CETAD with 1500 participants nationwide and evaluating sexual myths, it was emphasized that the percentage of men believing in sexual myths is high. Besides, the first sexual information age of the participants was 12.59, and the first sexual information source was identified as friends by 68.9% (Torun et al. 2011). In a study conducted with the participation of midwifery students in Turkey and evaluating the views on premarital sexual experience, 82.9% of 150 participants said that virginity is important for women, while 11.6% of 21 participants stated that it is appropriate for men to experience sexuality before marriage.

In Turkey, the perception of gender begins to be instilled in children at a very early age. Even unveiling a girl's skirt while playing is condemned, and from the age of play, girls are encouraged to equate their genitals and sexuality with shame (Tomas et al. 2015).

Every culture creates its own norms on sexual matters. Over time, a connection has been formed between sexuality norms and marriage and family, by and by the issue of 'premarital sexual experience' has come to the fore. In most Western cultures, the expectation of virginity in marriage has almost disappeared, premarital sexual experience has been experienced at equal rates between men and women, and premarital sex has become more acceptable. However, towards the eastern sphere, it is seen that there are restrictions on premarital sexual experience especially for women in Turkey and other Muslim countries. In fact, studies have pointed out that men are supported and tolerated in this regard, experience sexuality at an earlier age than women, and women are supervised hereof and negative attitudes are displayed in response to these experiences. At this point, the concept of purity appears before women. While the concept of purity carries the meanings of truth, honesty and virtue for both genders around the world, it refers to the sexual purity of women in Turkey. Again, the same concept gives tolerance to men and imposes an expectation of virginity on women. It makes the dominance of the family and the man a watchperson over the sexuality of women (Erdogan 2021; Ventriglio and Bhugra 2019).

In patriarchal societies, the concept of purity is associated with virginity and the hymen is considered the only measurable indicator of purity. Virginity is used to describe female sexuality rather than male sexuality, and the virtuous woman is empowered to protect her sexual purity, while the virtuous man is empowered to protect the sexual purity of her female relatives. Thus, in Turkish culture, it is proclaimed that women should not have experienced sexuality and sexual intercourse until marriage, and when a man marries someone whose hymen is not intact, he assumes that he has been "contaminated" before. Thus, the presence or absence of the hymen, which is the only and greatest proof of virginity, causes women to be classified as discourse, and girls are described as 'girl' until they lose their virginity, and 'woman' after losing their virginity or having their first sexual experience after marriage (Huda and Kamal 2020). A discourse is the production of all interest, knowledge, reality, objects and metaphors about the world; in short all perceptions, ways of speaking and social practices. According to discourse psychology, although gender is an internal essence that creates people's psychological behaviors, it has become a practice produced as it is repeated by the society in the discursive field and gender roles are constructed as a result of these transferred discourses. Accordingly, people are not born with male or female roles, but into socially prepared roles. The discursive approach to gender considers being a woman not as a cause but as a result of practices such as sensuality, motherhood, care, ironing and cooking. The general conclusion of discourse studies on gender is that there is a link between gender and

discourse, that gender is socially constructed and gender roles are revealed through social interaction, and that these discourses are both a source and a limiter. In his study evaluating what it means to be a woman in Turkey, Elci examines the answers he receives from women through discourse analysis and finds that the discourse practices that prepare the ground for gender inequality also secretly prevail in the language of women, that the discourses that construct being a woman are produced by social institutions such as marriage and family. It has been revealed that women also talk about being a woman through these practices, and these practices are reproduced and strengthened as they are spoken (Elci 2011).

In a study conducted by Okyay in 2007 with university students, 42.5% of the students defended the idea that women should remain virgin until marriage, and in another study, 32% of the students matched virginity and honour in their statements (Okyay 2007). In a study that was applied to a sample of non-students in Diyarbakır, 32.9% of the participants expressed the concept of honor as woman, mother, sister, family, and 12% expressed dishonor as woman cheating on her husband and 10% as losing her virginity (Sir 2006). According to the results of a study conducted in Turkey by the United Nations, Population Fund and Science Association in 2006, it was revealed that the greatest dishonor was perceived as having sexual intercourse before marriage by a young girl or woman. In Turkey, which is a developing country where the majority of the population is Muslim, the fact that the violation of the concept of honor is tolerated for men and perceived as a reason for murder for women reveals the

reality of gender discrimination in Turkey. According to the global gender gap report of the World Economic Fund in 2013, Turkey ranked 120th among 136 countries in terms of gender equality (Gursoy and Ozkan Arslan 2014).

4. Legal Aspect

Almost all of the documents on human rights are based on the idea of 'all human beings are free; are born equal in dignity and rights'. These rights are the values that come with being human, are indispensable and inalienable, and are above all moral, political, public and social concerns. All national and international conventions, regardless of race, religion, language, color, gender, political and all other views, national or social origin, property, birth etc., states that every state should respect and guarantee the rights of the people living in its own country and under its sovereignty, and it prohibits discrimination. As one of the countries party to these conventions, Turkey is deemed to have accepted some obligations and includes some regulations in its domestic law. Women's rights in Turkey emerged in the 19th century in parallel with the developments in the world. However, the historical process clearly reveals that women are exposed to discrimination. Legally, discrimination is defined as "to treat people differently because of prejudice and hostility". Gender-based discrimination, on the other hand, can be defined as the fact that individuals with equal qualifications are treated differently based on their gender only. Although practices based on gender discrimination are tried to be prevented by legal regulations, they continue to exist openly and

covertly in practice (Kostiuchenko et al. 2020). Because discourse construction is excluded from legal regulations and this discourse constitutes the source of violence and exploitation that women are exposed to. It is possible to see sexuality as the basis of gender differentiation. Because, like gender sexuality is also produced by the social discourse developed by the institutions of patriarchy. This gender division gives rise to two contrasting definitions of sexuality, defined as female sexuality suppressed by the patriarchal structure and male sexuality provoked. From the perspective of Turkey, the most typical indicators of this are virginity checks and honor killings (Yıldız 2009; Şimşek 2011).

In Turkey, the situation before the penal code amendment in 2004 was a reflection of the society's view of sexuality and sexual crimes were among the crimes against public morals and the family, under the title of crimes against society. People's control of their bodies was treated as a problem of society, not of their personal space (Gil-Llario et al. 2017).

The most destructive results of honor culture and traditional moral structure in Turkey are violence and murders against women in the name of honor. Considering the 2000-2005 evaluation results of the Human Rights Presidency of the Republic of Turkey, 1091 cases of morals and honor were recorded, of which 322 are honor killings (Gursoy and Ozkan Arslan 2014).

Combining the concepts of honor and chastity, and efforts to try to control them over the female body lead to medical control of women

under the name of virginity or marriage examination and to interfere with their bodies without their consent. This situation, which causes psycho-social problems in women, is also illegal from a legal point of view. Pursuant to Article 17/2 of the Constitution, "a person's bodily integrity cannot be touched except for medical obligations and the cases written in the law". In accordance with Article 20/1, everyone has the right to demand respect for his private and family life. The expression "the privacy of private and family life is inviolable" clearly states that hymen examination cannot be performed except in legal and compulsory situations (Constitution of the Republic of Turkey, 1999). Accordingly, the hymen examination, which is requested and applied except for the mandatory conditions specified, is an indicator of violence against women and violation of rights (Dikmen et al. 2017).

5. Religious Aspect

The two great powers that keep sexuality under control are society and religion (Kellog et al. 2014). Religion is a belief system that responds to people's need for belonging, directs them about what behaviors to do, when and to what extent, and sets rules about what is appropriate and what is not. The expression of religiosity is used to indicate people's religious actions, commitment and belief. Since religiosity is a cultural element, differences are observed between different individuals of the same culture and experiences between cultures (Kıyılıoğlu 2014). Many studies examining the relationship between religiosity and risky sexual behavior have dealt with early sexual

experience, sexual polygamy, sexual experience before marriage, i.e. the variables of virginity, as risky sexual behavior. One of the longitudinal studies on adolescents revealed that religiosity affects sexuality, but sexuality does not affect religiosity. It was concluded that young people aged 15-16 continued to be virgin after 2 years. In a similar study conducted with adolescents, it was concluded that religiosity delayed the age of onset of sexuality for girls, and some of the boys were affected by this situation. In a study conducted in the USA, it was revealed that the conservative view of sexuality is that the first sexual experience should be at later ages or after marriage/engagement. A study of male students in Ghana found that Muslims and traditionalists displayed less risky behavior. A study conducted with METU and Uludağ University students in Turkey revealed that students with religious and traditional attitudes did not approve of premarital sex (Kıyılıoğlu 2014).

Since Adam and Eve, who are at the beginning of the creation myths, it is believed that man is superior to woman and Eve is a born sinner. The understanding that divides men and women hierarchically and legitimizes the superiority of men over women and their control over the female body has developed under the influence of monotheistic religions. The culture of honour and purity includes Muslim countries such as Turkey and Arab countries as well as Christian countries such as Greece, Spain, Italy and Brazil. Because, like Islam, Christianity and Judaism support traditional gender roles, the superiority of men over women, and the matching of women's sexual behaviors with the concept of honour. Christianity considers sexual pleasure as a bodily

sin and emerges as a religion that spreads the idea that sexual acts are cursed and sinful. These issues, which are also included in the holy books, result in the hierarchical interpretation of the books and gender inequality. The expressions in the Quran, the holy book of Muslims, are interpreted as the man is defined as the protector of the woman and the woman as the obedient to the man. Islam considers the extra-marital affair between men and women as adultery and considers it a sin. In countries governed by Islamic rules or sharia rules, men and women who commit adultery are given severe punishments (Aksoy and Vefikuluçay Yılmaz 2019).

CONCLUSION

Gender discrimination, which is a subject that draws attention easily when we look at the history of humanity, has continued its existence until today with an approach that puts women in the second place in Turkey, as in many countries of the world, even though it emphasized the sanctity of women due to their fertility feature before monotheistic religions.

Official consultants and non-governmental organizations, who attended the conference held in San Francisco in 1945 after the Second World War, with participants representing more than eighty percent of the world's population and where the universal declaration of human rights was discussed, believed that the world order planned to be established after the war would be within the framework of equality and respect for human rights. The focus of non-governmental organizations was to ensure equality and non-discrimination, as well

as human rights and religious rights. Although human rights are the basic rights that human beings bring with their existence, women have not been able to benefit from these rights equally in the historical scene. According to the existing perceptive, while the man is considered as the creator of civilization and culture, the woman is considered as the product of nature and the subordination of women is emphasized. Women, on the other hand, have become aware of this unnatural and social distinction over time and have provided the birth of the concept of women's human rights. In other words, the rights mentioned in women's rights are actually the same as human rights. (Kaypak and Kahraman 2016).

It is noteworthy that what creates the distinction between men and women stems from the patriarchal discourse and secretly takes its place in the language of women, so that a gender culture far from equality is formed and transmitted through generations.

One of the controllers of this gender culture is religion. The interpretation of monotheistic religions and belief systems by people with a hierarchical approach shows women under the protection and control of men and puts them in the background. As a result of these approaches and perspectives, the control of society and especially of men over women has extended from many fields such as economy, politics and professional career to personal aspects and even sexuality.

The most obvious example of the reflections of these interventions on life is the sacrifice of women, who are on the axis that the concept of honour is specific to the sexual purity of women, who take away the

control of the woman over her own body, who do not or are thought to not comply with the control of the hymen and social expectations, in honour killings.

The biggest of the strengths that can stand in the way of these practices, ranging from not benefiting equally from women's human rights, to the deprivation of their right to live is the education appropriate for their age and developmental period, and as well, the legal regulations that enable women to benefit from human rights also including social discourse and that women's discourse in daily speech practices, and ensuring that women's discourse is handled with an egalitarian approach in daily speech practices with legal obligations. Thus, through the discourses in the myths passed down from generation to generation, women will come to the place they deserve in the coming years.

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CHAPTER 2

PALLIATIVE CARE FOR PATIENTS WITH GYNECOLOGICAL CANCER

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INTRODUCTION

The period of time until the death of the sick individual, which is called the terminal period is a short time, medical interventions are inconclusive, and the life functions are terminated. During this period, clinical changes such as fatigue, loss of strength, decrease in food intake, dysfunction, difficulty in breathing and decrease in consciousness level occur in these patient. In the terminal period, the primary wishes of the patient are to reduce the pain, to increase the quality of life as much as possible, and to be independent from family members in self-care (Karan & Akin, 2012). During this period, all social, psychological and physiological needs of the patient should be met as much as possible (Kousoulou et al., 2019). The patient may want to spend this period in his/her social environment (with family members) or in palliative care centers without being a burden to the family (Yun et al., 2018). In the context of palliative care, the good death process of patients with terminal diagnosis should be supported by health professionals (Çavdar, 2011).

THE CONCEPT AND DEVELOPMENT OF PALLIATIVE CARE

Although medical care focuses on the philosophy of curing diseases and prolonging life, another important function is to alleviate suffering and improve quality of life. At this point, palliative care; while aiming to alleviate the suffering of people with advanced disease and their families, it also focuses on increasing the quality of life of the patient. In palliative care, where social support and medical treatment are

carried out in a coordinated manner, the services offered to the patient are carried out simultaneously (Morrison & Meier, 2004).

The World Health Organization (WHO) has defined palliative care as “the prevention and relief of any physical, psychological, social or spiritual suffering experienced by adults and children with life-limiting health problems”. As can be understood from the definition of WHO, palliative care is necessary in many life-limiting health problems. For example, cardiovascular diseases, cancer, chronic respiratory diseases, AIDS, diabetes, kidney failure, chronic liver disease, rheumatoid arthritis, neurological disease, dementia, congenital anomalies and drug-resistant tuberculosis are some of the diseases that require palliative care (Organization, 2016).

Palliative care services are examined under 3 main headings. These are hospital-based, home-based and community-based palliative care. In hospital-based palliative care, the services required to improve pain and other symptoms are given to the patient by healthcare professionals in patient services, while in home-based palliative care, palliative care is provided to the patient in the home environment. In community-based palliative care, patients are provided with psychosocial and moral support and necessary training for palliative care (Uslu & Terzioğlu, 2015). While palliative care service is provided by health professionals such as doctors, nurses, therapists, dietitians, social workers, psychologists, volunteers and non-governmental organizations can also be counted in the team providing palliative care services (Sepúlveda et al., 2002).

Palliative care, which is rapidly developing today, was first put into service by establishing a palliative care unit in France in 1842. Clark et al. (2020) has gathered the development status of palliative care services for 198 countries in the world in 4 main groups. In the first group, countries that do not have hospice care services and activities, in the second group, countries where there are policies for the development of palliative care services although there is no palliative care service yet, in the third group, the countries where palliative care services are provided with local and regional supports, and finally, the health system in the fourth group, countries with integrated palliative care services. Clark et al. reported that, while there is no known palliative care service in the regions where 3.1% of the world population lives, the palliative care service, which is at the forefront of integration into the health systems in the regions where 27.6% of the world population lives, and 14.2% of the world population. Palliative care services are available in the regions where they live, which are at an advanced stage of integration into the health system (Clark et al., 2020).

Group	Countries
Group I	Cape Verde, Central African Republic, Chad, Comoros, Congo (Republic), Guinea-Bissau, Lesotho, Mali, Seychelles, South Sudan, Antigua & Barbuda, Cuba, Dominica , Grenada , Guyana, Saint Lucia, St Kitts & Nevis , St. Vincent and the Grenadines, Suriname, Djibouti, Iraq, Somalia, Somalia, Syria, Yemen, Andorra, Kosovo, Monaco, Montenegro, San Marino, Turkmenistan, Vatican City, Bhutan, Maldives, North Korea, Timor l'Este, Brunei, Kiribati, Laos , Marshall Islands, Micronesia, Nauru, Palau, Solomon Islands, Tonga,

	Tuvalu , Vanuatu
Group II	Angola, Burkina Faso, Burundi, Equatorial Guinea, Eritrea, Gabon, Liberia, Sao Tome e Principe, Bahamas, Haiti, United Arab Emirates, Uzbekistan, Samoa
Group IIIa	Algeria, Benin, Botswana, Cameroon, Congo (DR), Ethiopia, Ghana, Guinea, Madagascar, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, Tanzania, Togo, Bolivia, Dominican Republic, Ecuador , Guatemala, Honduras, Jamaica, Nicaragua, Paraguay, Peru, Trinidad & Tobago, Venezuela, Afghanistan, Bahrain, Egypt, Iran, Kuwait, Lebanon, Libya, Morocco, Pakistan, Palestine, Sudan, Tunisia, Armenia, Azerbaijan, Bosnia and Herzegovina, Croatia, Estonia, Greece, Kyrgyzstan, Moldova, Tajikistan, Turkey, Bangladesh, India, Indonesia, Myanmar, Nepal, Sri Lanka, Cambodia, Fiji, Malaysia, Papua New Guinea, Philippines, Vietnam
Group IIIb	Gambia, Kenya, Zambia, Belize, Brazil, Colombia, El Salvador, Panama, Jordan, Oman, Qatar, Saudi Arabia, Albania, Belarus, Bulgaria, Cyprus, Finland, Luxembourg, Macedonia, Malta, Serbia, Slovenia
Group IV4a	Ivory Coast, South Africa, Uganda, Zimbabwe, Argentina, Chile, Mexico, Uruguay, Austria, Czech Republic, Georgia, Hungary, Kazakhstan, Latvia, Russia, Slovakia, Switzerland, Ukraine, Thailand, China, Singapore
Group IVb	Malawi, Swaziland, Barbados, Canada, Costa Rica, USA, Belgium, Denmark, France, Germany, Iceland, Ireland, Israel, Italy, Liechtenstein, Lithuania, Mongolia, Netherlands, Norway, Poland, Portugal, Romania, Spain, Sweden , UK, Australia, Japan, New Zealand, South Korea, Taiwan

Although there is evidence that palliative care services were provided in the past in Turkey, the scope of these services is not clear. As a matter of fact, the planning and implementation of palliative care in Turkey was initiated in 2010 with the PALYA-TÜRK project (Dinçer, 2019). In the 2013-2018 Turkey Cancer Control Plan, the reason for the delay in the planning and implementation of palliative care services in Turkey was explained as that there was no need for palliative care services due to the traditional Turkish family structure, but the need increased due to changing demographic characteristics (Halk & Kurumu, 2016).

According to the directive published by the Ministry of Health, palliative care services in Turkey are carried out by inpatient health facilities, family medicine and home health service units. Palliative care centers offer services such as examination, analysis, treatment, medical care, rehabilitation, psychosocial support, psychosocial assessment, pain management (opioid use), and nutritional support (Bakanlığı, 2015). Currently, palliative care services are provided with more than 4300 beds in more than 300 centers in Turkey. These centers, which meet the minimum physical and equipment standards, provide services on a 24-hour basis.

SYMPTOMS IN PALLIATIVE CARE PATIENTS AND SYMPTOM MANAGEMENT

Patients treated in a palliative care clinic have more than one symptom of varying severity. The most common symptoms are; pain, anxiety, dry mouth, sore mouth, nausea, fainting, skin changes, depression,

dyspnea (shortness of breath), anxiety, weakness, difficulty in movement, constipation, bad taste, reflux and insomnia (Borasio, 2011; Uysal et al., 2015).

Most of the patients admitted to the palliative care clinic state that they experience pain. The main purpose of palliative care is essentially to manage pain. In this respect, pain management begins with the assessment of pain and continues with its treatment. Medication is administered by healthcare professionals according to the severity of pain felt by the patient. These drugs are classified as nonopioid, opioid, adjuvant and choanalgesic (Kabalak et al., 2013). In palliative care pain treatment, complementary and integrative therapy methods such as dance therapy, yoga, massage therapy, acupuncture, music therapy are used as well as modern medicine and drug therapy methods (Yıldırım et al., 2019). This wide variety of methods used for pain management; It has been reported in studies that patients hospitalized in the palliative care clinic significantly reduced the severity of their pain in the following days of hospitalization (Uysal et al., 2015).

The negative situation, pain and uncertainty of the future of the patients compel the patient emotionally. This situation triggers the anxiety syndrome in the patient. Complementary and integrative treatment methods such as moral support, non-pharmacological techniques, music therapy and drug therapy are used for the management of anxiety syndrome in palliative care (Kolva et al., 2011).

Dehydration that occurs during the palliative care period when oral food intake is insufficient causes dry mouth in palliative care patients. The patient with dry mouth may have difficulty in swallowing and speaking. The symptom of dry mouth is prevented by moistening the patient's oral mucosa and giving the patient frequent oral water (Nguyen & Weinreb, 2002).

Nausea and vomiting in patients with malnutrition negatively affect the physiological and psychological state of the person. Nausea and vomiting also cause loss of appetite in the patient. Loss of appetite, especially due to nausea and vomiting; causes a decrease in fluid and nutritional supplementation and results in constipation. In palliative care, pharmacological and non-pharmacological treatment methods are applied in the treatment of nausea, vomiting and malnutrition. It has been reported by scientific studies that decreased appetite, malnutrition and other related symptoms with palliative care support (Harding et al., 2011).

Dyspnea (shortness of breath) is one of the symptoms that make the patients admitted to the palliative care clinic feel death (Kabalak et al., 2013). The incidence of dyspnea is particularly high in cancer patients. It has been proven by scientific studies that there is a regression in the symptom of dyspnea as a result of diagnostic treatments in palliative care patients (Modonesi et al., 2005)

Another very common symptom in the terminal period is weakness and constant fatigue in the patient. Most of the time, the cause of unknown fatigue is explained as a decrease in appetite and poor well-

being (Cheung et al., 2009). Low-dose drugs, exercise, psychological support are the methods used in palliative care for the management of this symptom (Kabalak et al., 2013).

ONCOLOGICAL TREATMENTS IN PALLIATIVE CARE

Cancer is a group of diseases that invade the body by spreading to other organs with the uncontrolled growth and proliferation of abnormal cells in the body. According to the data of the WHO International Agency for Research on Cancer, cancer is the cause of 10 million deaths in 2020. Lung, prostate, stomach and liver are the most common cancer types in men, while breast, colorectal and cervix are the most common cancers among women (Organization, 2021a). The primary aim of cancer treatment, which negatively affects both the diagnosed individual and their relatives' quality of life, is to cure the patient. However, relief of pain and other complaints of patients who do not have a cure is possible with palliative care services. It is known that some cancer patients improve their quality of life and prolong their survival thanks to palliative care services (Bakitas et al., 2015; Ferrell et al., 2017). In this regard, palliative care treatment options are important in oncological patients. Palliative care treatment options; Palliative Chemotherapy, Palliative Radiotherapy and Palliative Surgery are examined as sub-titles (Aydoğan & Uygun, 2011).

Palliative chemotherapy, radiotherapy and surgery; prolongs life expectancy in many types of cancer. It has also been reported by various studies that it contributes significantly to the patient's quality

of life. However, in terminally ill patients for whom sufficient data is not available, these treatment options may lead to unnecessary costs and adversely affect the quality of life of the person in the final phase. In this regard, palliative chemotherapy, radiotherapy and surgery; It is carried out in cases where the expected benefit outweighs the possible risk by evaluating the cancer type and its unique characteristics such as its stage (Aydoğan & Uygun, 2011). While all treatment options to be applied in palliative care are shared with the patient and their relatives, the patient's choice is reasonably protected.

CANCER

Cancer is a chronic disease that adversely affects human health and has serious effects. Although there are many developments in medicine and the treatment of many diseases is easily done, the treatment of cancer cannot be done in general. Cancer, which is used as a general term for a large group of diseases that can affect any part of the body; It is defined as “bad tumors that occur with the irregular division and proliferation of cells in an organ or tissue, which can cause serious disorders and even death if left untreated” (Aslan & Özen, 2019). One of the most important features of cancer is the rapid growth of abnormal cells and spread to other organs (Organization, 2021a). Cancer is a disease that requires a long-term struggle both financially and morally, as well as causing many health problems (Aslan & Özen, 2019). The incidence and mortality of cancer is increasing rapidly worldwide. According to WHO estimates; there were approximately 19.3 new cases and 10 million cancer deaths

worldwide in 2020. It has also been reported that 50.6 million cancer patients (5-year prevalence) live worldwide (Organization, 2021b). It is estimated that the world population will reach 8.3 billion in 2030 and the population will age significantly. Aging is also important in terms of cancer risk. In addition, the incidence of cancer is increasing regardless of population and aging. It is estimated that approximately 26.4 million cancer cases and 17 million cancer-related deaths will occur in 2030 (Saygılı & Çelik, 2020). It is predicted that there will be approximately 28.4 million new cancer cases worldwide in 2040, which corresponds to a 47% increase in the number of approximately 19.3 million cases in 2020. According to the report of Turkey Cancer Statistics; in 2020, a total of 233 thousand people were diagnosed with cancer, of which 101,018 were women. The most common cancer occurring worldwide is female breast cancer. This is followed by lung cancer, colorectal cancer, prostate cancer and stomach cancer, respectively. Cancers that cause the most loss of life are lung cancer, colorectal cancer, liver cancer, stomach cancer and female breast cancer, respectively. The top 5 most common cancer types in our country in 2020 are lung cancer, breast cancer, colorectal (large intestine) cancer, prostate cancer and thyroid cancer. The top 5 most common cancer types in women are breast cancer, thyroid cancer, colorectal cancer, lung cancer and uterine cancer (Organization, 2021b).

Cancer is a disease that negatively affects the person and his family, and has both physical and emotional effects. After the diagnosis of cancer, the person may experience a crisis situation. On the one hand,

he enters a serious treatment process; on the other hand, he tries to adapt to the disease. The treatment phase is planned according to the type of cancer disease and this treatment consists of methods such as surgery, radiotherapy and chemotherapy (Şahin et al., 2020). One out of every 5 people in the world is diagnosed with cancer during their lifetime, and 1 out of every 8 men and 1 out of every 11 women die from cancer (Organization, 2021b). Patients in the terminal/palliative period have three conditions: pain, loneliness and isolation. Patients in this period are provided with relief from more pain and other symptoms. Mentally and physically as a whole, the patient should be supported to spend the remaining time as high as possible (Bag, 2014).

GYNECOLOGICAL CANCERS

Gynecological cancer is any cancer that starts in the female reproductive organs. Although they are often discussed as a group, each gynecological cancer is different. Each has different signs, symptoms, and risk factors. Gynecological cancers are one of the most important causes of mortality and morbidity in women (Ferlay et al., 2015). The mean incidence in gynecological cancers is 22.7 per 100,000. 13.7% of cancers seen in women are gynecological cancers and constitute an important part of cancer-related deaths (Gultekin et al., 2017). According to the International Agency for Research on Cancer, the most common gynecological cancer in women in the world is cervical cancer, while endometrial cancer is second and ovarian cancer is third. In addition, when evaluated in terms of

mortality, deaths due to cervical cancer are in the first place, and ovarian cancer is in the second place due to the non-specific symptoms (Bulut et al., 2020). In our country, gynecological cancers are among the top 10 cancers seen in women. Gynecological cancers can negatively affect the physical integrity of women, as well as their self, personality and social integrity, sexual identity and reproductive health/ability (Rahou et al., 2016). It has been stated that anxiety, anxiety, depression, hopelessness and loneliness levels increase, self-esteem decreases, and family and social support weaken in women in gynecological cancers (Reb & Cope, 2019). For these reasons, women with gynecological cancer need more support and information than their psychosocial, spiritual, physical and functional needs (Bulut et al., 2020).

Endometrial Cancer

Endometrial cancer is a type of cancer that occurs when cells in the endometrium grow out of control. The most common cancer among gynecological cancers in the world and in Turkey is endometrial cancer. There are two types of uterine cancers: uterine sarcoma and endometrial cancer. In Turkey, according to the data of the Cancer Department, endometrial cancer is among the top 4 most common cancers in women (breast, thyroid, colorectal and uterine corpus cancers, respectively) and its incidence is 5.5% (Müdürlüğü, 2021).

There are a number of risk factors that cause endometrial cancers. About 25% of women with endometrial cancer are nulliparous. It is thought that the high progesterone level that occurs during pregnancy

protects against endometrial cancer and this protection does not occur in nulliparous women. Nulliparous have high estrogen exposure due to anovulation. Therefore, endometrial cancer is more common in nulliparous patients. The higher the parity, the lower the cancer risk (Ronnett et al., 2002). The risk of endometrial cancer is increased in women with both early menarche and late menopause due to high estrogen levels and an excess of anovulatory cycles throughout life. Obesity is a major risk factor for endometrial cancer. Adipose tissue can be a source for estrogen formation (Yu et al., 2010). Cancer risk is also increased in those with Polycystic Ovary Syndrome. This is due to its association with chronic anovulation and obesity. An increased risk of cancer was found to be 3.1 in those with chronic anovulatory cycles. In addition, it has been stated that having a family history of endometrium and diabetes increase the susceptibility to the disease (Kommos et al., 2018).

The most prominent symptom of endometrial cancer is vaginal bleeding. Since there is no sensitive and cost-effective screening method for the early diagnosis of endometrial cancer, there is no routine screening method. Standard diagnostic evaluation of this cancer is made by physical examination, USG, endometrial biopsy, dilatation and curettage. In order to evaluate the condition of the pelvis and abdomen and to examine the lymph nodes, tests such as hystero-graphy, hysteroscopy, MRI and CT are also performed. One of the cancer screening markers, CA125 is frequently checked. In endometrial cancer; surgery, radiotherapy, chemotherapy, hormonal therapy and targeted therapy methods are used (Amant et al., 2018).

Ovarian (Over) Cancer

The ovary, which produces eggs and is located on both sides of the uterus, is the primary source of estrogen and progesterone hormones that protect the health of the female reproductive system in premenopausal women (Colvin & Abdullatif, 2013). Ovarian cancer is one of the third most common gynecological cancers after cervical and uterine cancer (Momenimovahed et al., 2019). Due to the lack of specific symptoms and the lack of appropriate screening methods, it is recognized at a late stage and is the gynecological cancer with the highest mortality. According to the 2020 report of World Cancer Statistics, 313,959 women have been diagnosed with ovarian cancer worldwide and 207 252 women have died due to ovarian cancer (Organization, 2021b). In the 2020 report of Turkey Cancer Statistics, 4,059 women were diagnosed with ovarian cancer in Turkey and 2,730 women died due to ovarian cancer (Özdoğan, 2021). Many risk factors such as positive family history, advanced age, early menarche, late menopause, nulliparity, fertility drugs, endometriosis, obesity, environmental factors, smoking and alcohol use play a role in the development of ovarian cancer (Berek & Hacker, 2010). Many findings have been obtained that factors such as pregnancy, breastfeeding and the use of birth control pills prevent the formation of ovarian cancer (Whiteman et al., 2003). Ovarian cancer is very insidious and the patient is usually in stage III or IV at the time of diagnosis. Patients usually apply to the health institution with complaints of abdominal and back pain, menstrual irregularity, dyspepsia and constipation. As the disease progresses; Abdominal

distention, acid accumulation, increased intra-abdominal pressure, and respiratory distress are observed, while abnormal vaginal bleeding is rare (Berek & Hacker, 2010). To make a diagnosis; detailed history, physical examination, pelvic examination and some tumor markers (Berek & Hacker, 2010; Kehoe et al., 2015).

Cervical Cancer

The part that is approximately 2 cm long in the lower 1/3 of the uterus is called the cervix. The cervix is the narrow neck of the uterus that opens to the vagina and also acts as an important barrier to help prevent infections from reaching the uterus (Taşyürek, 2017). Cervical cancer is the 4th most common cancer worldwide, after lung, breast and colorectal cancers (Ferlay et al., 2015). It ranks 3rd among gynecological cancers in our country (Müdürlüğü, 2021). It is reported that the most important cause of cervical cancer is human papilloma virus (HPV). It is a genital HPV DNA tumor virus with a high infection potential and generally infects the mucosal epithelium of the cervix and causes hyperproliferation in the cells with the appearance of warts (Organization, 2021a). It has been reported that some factors are effective in the formation of cervical cancer. Specific type HPV infection, sexually transmitted diseases, Human Immunodeficiency Virus (HIV) infection, polygamy, early sexual intercourse age, smoking, early and long-term use of oral contraceptives, vitamin C-restricted diet, advanced age, low education level and risk factors such as socio-economic status are a few of them (Işık et al., 2016; Taşkın, 2020). Women often have complaints such as menstrual irregularities,

coitus and postmenopausal abnormal vaginal bleeding, foul-smelling vaginal discharge and increased discharge, low back and groin pain, back pain, dyspareunia, fatigue, weight loss, bloody stools and swelling in the legs. There are specific and sensitive screening methods for cervical cancer. These are Pap-Smear test, HPV-DNA test, naked eye observation of the cervix, endocervical curettage, colposcopy and cervical biopsy (Bhatla et al., 2018). The PapSmear test is the basic screening test used to screen for cervical cancer. In Turkey, according to national cancer screening standards, Pap-smear test is performed on women between the ages of 30-65 at Cancer Early Screening and Education Centers (Müdürlüğü, 2021).

Vaginal Cancer

The vagina is a tube-shaped female reproductive organ, also known as the birth canal that extends from the cervix to the vulva. Vaginal cancer is the least common cancer among gynecological cancers and its incidence increases with age. Incidence and mortality rates have decreased by about 1% per year since the 1990s (Oncology, 2021; Society, 2015). According to the 2020 report of the World Cancer Statistics, 17,908 women worldwide were diagnosed with vaginal cancer and 7,995 women died due to vaginal cancer (Organization, 2021b). In the 2020 report of Turkey Cancer Statistics, 111 women were diagnosed with vaginal cancer in Turkey and 36 women died due to vaginal cancer (Özdoğan, 2021). Vaginal cancers are usually seen before the age of 70. As in other gynecological cancers, in the formation of vaginal cancer; there are many risk factors such as being

between the ages of 50-70, smoking-alcohol use, low socio-economic level, sexually transmitted infections, family history of cancer, exposure to intrauterine DES, chronic vaginal irritation and pelvic radiation, and use of intravaginal pessaries. The most important symptom of vaginal cancer; irregular and painless vaginal bleeding, increased amount of vaginal discharge and postcoital bleeding (Adams & Cuello, 2018).

Vulvar Cancer

Vulva is a structure that includes the mons pubis, labia major and minor, clitoris, vestibule, bartholin's glands, minor vestibular glands, skene glands, urethral and vaginal openings. These structures make up the outer vulva, and vulvar cancer can develop in any of these structures. Inner vulva can be divided into superficial and deep urogenital triangle compartments. Vulvar cancer is as rare as vaginal cancer. According to the 2020 report of World Cancer Statistics, 45,240 women worldwide were diagnosed with vulvar cancer and 17,427 women died due to vulvar cancer (Organization, 2021b). In the 2020 report of Turkey Cancer Statistics, 286 women were diagnosed with vulvar cancer in Turkey and 93 women died due to vulvar cancer (Özdoğan, 2021). Vulvar cancer; It is more common in places where the incidence of cervical cancer and HPV-HIV is high. There is no specific etiological factor for vulvar cancers. Cervical and vaginal cancer risk factors are valid for vulvar cancer (Rogers & Cuello, 2018). The most important cause of this cancer is HPV type 16. Therefore, HPV vaccine is of great importance in the prevention of

vulvar cancer. There is no specific screening method for vulvar cancer. However, self-examination of the vulva is very important to detect cancer-related lichen sclerosis and ulcers. Women with vulvar cancer often complain of itching, burning, or the presence of a lesion. Other symptoms of vulvar cancer; labia skin discoloration, rash, warts or thickening of the skin, tenderness or swelling, groin pain during urination or sexual intercourse, and vaginal bleeding (Kang et al., 2017).

Treating cancer is only one aspect of any cancer treatment plan. Palliative care is an urgent and humanitarian need worldwide for cancer patients. This need is especially greater among patients with advanced disease and less chance of cure. Comprehensive cancer treatment cannot be achieved without supportive and palliative care (Saygılı & Çelik, 2020).

PALLIATIVE CARE IN GYNECOLOGICAL CANCERS

Gynecological cancers constitute the majority of cancers seen especially in developing countries and can be a significant cause of mortality and morbidity. Treatments in gynecological cancers may be inadequate, and the quality of life of women and their families may be adversely affected due to symptoms (Terzioglu & Uslu Sahan, 2016). In the treatment of gynecological cancer, the goals of care may evolve from treatment and symptom control to maintaining quality of life. Therefore, interest in palliative care in gynecological cancers is increasing. The American Society of Clinical Oncology recommends integrating palliative care into standard care with treatment

immediately after cancer diagnosis (Seven et al., 2016). In palliative care, the quality of life of patients and their families is improved by reducing adversities through early diagnosis, evaluation and treatment of problems (Organization, 2002, 2021a). Thanks to palliative care, it is seen that women remain active during the period between diagnosis and death, their pain and discomfort are reduced, and they experience a comfortable death process. Palliative care improves quality of life, positively affects mood, reduces symptoms, and increases satisfaction and survival. It also reduces the stress of the people accompanying the patient and increases their satisfaction (Terzioglu & Uslu Sahan, 2016).

The aim of the care given in the advanced stages of the disease in patients with gynecological cancer is to increase the quality of life rather than prolonging the life span. In these patients, palliative care has an important place in reducing pain, preventing nausea-vomiting and experiencing symptoms such as fatigue at a minimum level (Anderson, 1994). Providing patients with early palliative care can reduce hospitalization rates and interventions. After being diagnosed with cancer, patients may experience both physical and psychological problems such as pain, nausea, fatigue, loss of appetite, sexual dysfunction, depression and anxiety, all of which require effective care and treatment. Palliative care provided by multidisciplinary teams can reduce these symptoms (Seven et al., 2016). As with most incurable cancers, pain is a major problem. Eighty percent of patients with gynecological cancer experience moderate-to-severe pain during

the illness (Karlin, 2018). Therefore, it is necessary to use various analgesics. It can also be used to reduce pain in psychosocial and complementary and alternative interventions, in addition to pharmacological therapy (Paley et al., 2015). Intestinal obstruction and fistulas are common problems arising from gynecological cancer. Surgery may be considered in these patients. Patients undergoing chemotherapy are at risk for the development of constipation. The health professional should evaluate the patient's normal bowel habits and plan non-pharmacological applications. If non-pharmacological applications do not provide benefit, laxatives should be applied (Uslu, 2013). Nausea and vomiting are common side effects throughout the course of the disease. Most cancer patients may experience nausea and/or vomiting during curative treatment or palliative cancer care (Wood et al., 2007). The aim of the management of nausea and vomiting is to prevent the occurrence of nausea and vomiting. Cancer patients experience nausea and vomiting for different reasons, and antiemetic use may be necessary regardless of the cause. However, antiemetic should be evidence-based and supported by non-pharmacological interventions (Uslu, 2013). Non-pharmacological interventions such as relaxation and distraction measures and cognitive behavioral therapy may be effective if dyspnea is present. If these techniques do not reduce shortness of breath, pharmacological interventions may be undertaken (Karlin et al., 2018). Ascites is seen in gynecological oncology, especially in patients with ovarian cancer. Paracentesis is frequently applied to these patients. Paracentesis is a simple procedure performed in the patient bed or with ultrasound

guidance (White & Carolan-Rees, 2012). Anxiety and depression are seen in a quarter of patients treated for gynecological cancer (Stafford et al., 2013). In the presence of anxiety or depression, patients should be referred to psychiatry and support group services. In areas where these resources are lacking, palliative care teams can help manage these psychosocial symptoms (Karlin et al., 2018).

EFFECT OF PALLIATIVE CARE ON GYNECOLOGICAL CANCERS

The aim of gynecological cancer treatment is to maximize survival rates by minimizing the negative effects of the disease. Studies in the literature show that palliative care, which is considered an integral part of cancer treatment, improves the quality of life in cancer patients (Terzioglu & Uslu Sahan, 2016). In a study conducted to determine the effect of palliative care on the quality of life of patients with advanced cancer, it was found that palliative care reduced the symptoms of the disease, had a positive effect on the quality of life and the course of the disease (Brinkman-Stoppelenburg et al., 2020). In another study, it was found that the average quality of life scores of patients who received palliative care from the time of cancer diagnosis were higher than those who received standard oncology treatment (Bakitas et al., 2009). A review of 100 studies to determine the effect of early palliative care on cancer patients found that early palliative care improved the health status of cancer patients (Hui et al., 2014). In another study conducted to determine the effect of palliative care on the satisfaction of cancer patients, it can be said that palliative care is

effective in the satisfaction of cancer patients and causes an increase in the satisfaction level of cancer patients. Therefore, it has been determined that palliative care can be used to help improve the patient's condition (Mehdinezhad et al., 2016). In addition, it was stated that cancer patients who received palliative care had a longer life expectancy and these patients were exposed to less chemotherapy (Terzioglu & Uslu Sahan, 2016). Palliative care is effective in symptom control, especially in advanced stages of gynecological cancers (Rezk et al., 2011). In a study conducted to determine the effect of palliative care on patient outcomes and interventions in terminally ill gynecological cancer patients, it was reported that patients receiving palliative care treatment had better symptom control, received less chemotherapy in the last stage of their lives, and prolonged survival (Keyser et al., 2010).

CONCLUSION

As a result, palliative care is very important for gynecological cancer patients. Palliative care can reduce the symptoms of gynecological cancer patients and their families during the disease and increase their quality of life. In addition, palliative care applied allows the person to experience a comfortable death process. Therefore, once a person is diagnosed with gynecological cancer, palliative care should be integrated into the standard of care.

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CHAPTER 3

BORON AND CANCER TREATMENT

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1. INTRODUCTION

Boron (B), atomic number 5, atomic weight 10.81g, density 2.84g / cm³, and melting point 2300 °C are semiconductors between metal and nonmetal. Boron is a micronutrient element in living nutrition. Boron is mostly in the form of boric acid in tissues and body fluids. 98.4% of the amount of boron in human blood is boric acid, and 1.6% is borate anion. Boron is an essential element for human and animal health. Although boron has toxic effects at high concentrations, it has a wide variety of physiological effects on biological systems at low concentrations, and there are many studies related to this (Ulusık et al., 2018). The World Health Organization has rearranged the safe and sufficient boron value for healthy people from its former value of 1 mg/day to 1-13 mg/day (Şimşek et al.,2003).

The American Toxic Substances and Diseases Association (ATSDR) has established a minimum risk level of 0.01 mg/kg/day for orally ingested boron in humans (Agency for toxicological substances and diseases registry,1992). It has also been found that boron has very beneficial effects on the human body. It has been determined that boron plays a role in regulating body minerals such as calcium and vitamin D and protects the bone structure by preventing calcium and magnesium's decrease. It also contributes to the improvement of learning, talent and school skills of minors; It is known that boron is taken in tablet form to develop sports performance and athletic structure (Uygan and Çetin, 2004).

No matter how it enters the body, 90-95% of it is immediately excreted with urea without accumulating in the body. In other words, it is not kept in the body. It only accumulates somewhat in bones, nails, hair, and organs such as the liver and spleen. Approximately 1-10 mg of boron intake per day will be appropriate and safe. In some literature, it is emphasized that 3 mg boron's daily information will be sufficient. Boron tablets in the market have been prepared in 3 or 6 mg doses. The most common forms of boron uptake into metabolism are sodium borate, boron citrate, boron aspartate and boron glycinate.

Boron oxide and boric acid are also the most common boron compounds, especially boric acid, which evaporates from the oceans and mixes into the air, descends into the soil with rain and snow, and disperses groundwater. Studies to determine the carcinogenic effect of boron on animals have shown that boric acid and borax are not genotoxic (Dieter, 1994). It has been proven that contact with boron compounds does not cause cancer, does not change genes, and does not cause chromosomal irregularity even at high concentrations. It is known that boron and boron compounds have antioxidant effects. Boron element increases the amount of reduced glutathione in the body's cells, thus reducing oxidative stress. Again, in some sources, it is stated that it increases glutathione and reduces the oxidative damage that may occur in the body (Uçkun, 2013).

It is a pathological condition that occurs due to a disorder in the mechanisms regulating cell growth and division (cell cycle). Malignant tumours show metastasis feature by spreading to tissues after origina-

ting. Some abnormalities in the DNA sequence cause all cancers. 10-15% of cancers are inherited, that is, inherited by genes from the parents, and the remaining 85-90% are shaped by exposure to mutagens in living cells, slight progressive changes in cell DNA, and errors in replication. Is considered. Sometimes one of these mutations causes the cell in which it is located to grow and the formation of a cancer clone derived from this cell.

Cancer is multifactorial, and many factors, from bacteria to viruses, radiation to inheritance, environmental factors, dietary habits and chemicals, are blamed in cancer formation. Today, boron is used quite frequently in the health field. Boron and its compounds are used in medicines and ointments used in many treatment areas such as wound therapy, burn treatment, rheumatoid treatment, solutions we use for lens cleaning, eye drops, etc. (EFSA J 2004).

2.MATERIAL AND METHOD

In the experiments, half of the boron taken orally appeared in the urine after 24 hours and the other half within four days. Even after 23 days, large amounts of boron compounds were found in the urine. The body's boron level can be measured by performing a blood or urine test. Today, there are many methods used for the Determination of boron; atomic absorption spectrometry (AAS), Inductively coupled plasma-atomic emission spectrometry (ICP-AES), Inductively coupled plasma-mass spectrometry (ICP-MS) are some of them. Briefly, boron has been determined in various samples by volumetric, spectroscopic,

chromatographic, nuclear reaction-based analytical methods and electroanalytical methods (ATSDR., 1992).

3. DISCUSSION

Boron is an essential element for living things and was used for medical treatment thousands of years ago (Abu Ali et al., 2005). The boron neutron capture therapy (BNCT) method, which has come to the fore, especially recently, has been a ray of hope for cancer treatment. This method, which has been tried in many cancer treatments, has been a treatment mainly used in the treatment of brain cancer and is known as a method in which the damage of healthy cells is at the lowest level in addition to the destruction of cancerous cells (Onrat & Konuk, 2004; Yiğitbaşıoğlu, 2004).

It has also been observed that boric acid prevents cancerous prostate cells growth and the proliferation of cancerous cells. It has also been observed that boron taken into the body with diet is inversely proportional to lung and cervical cancers (Meacham, 2009).

In some experiments in animals and humans, boron has been shown to positively affect the central nervous system and be a bioactive element associated with a reduced risk for some types of cancer (Nielsen, 2008).

In cases where the antioxidant capacity is insufficient to respond to this situation with the increase of free radical production, the resulting stress causes direct damage to proteins, DNA and lipids in the cell. Oxidative stress is a state of instability between the production of free

radicals in tissues and organs and the body's ability to counteract its harmful effects through neutralization by antioxidants (Süleyman et al., 2018) It is an imbalance between oxidants (reactive oxygen and nitrogen species) and antioxidants that tend towards the oxidative state (Li et al., 2019) and the increase of free reactive oxygen radicals, which are called SOR when hemostatic processes fail, are caused by the disruption of oxidative balance due to antioxidant insufficiency. It is the type of damage that causes molecules to be damaged or cells to die (Atalay, 2018). Free reactive oxygen radicals are produced excessively to maintain standard tissue integration and functions. These overproduced free oxygen radicals are endogenous glutathione (GSH), glutathione peroxidase (GPO), glutathione reductase (GRx), glutathione s transferase (GST), superoxide dismutase (SOD), catalase (CAT) and other antioxidants (A, C, E). vitamins) are detoxified by defence systems. In the physiological conditions of the body, the oxidant-antioxidant balance is in favour of the antioxidants. Still, if the antioxidants cannot detoxify the oxidants, this balance is disrupted and shifts in favour of the oxidant. When the balance is disturbed, tissues undergo oxidative stress, become damaged and cause many disease conditions. (Süleyman et al., 2018). These diseases are many diseases such as DNA, carbohydrates, proteins, neurodegenerative diseases, cardiovascular diseases, chronic obstructive pulmonary disease, namely COPD and cancer (Li et al., 2019).

In treating brain tumours with neutron capture, 20 g of borax is given to patients. In terms of its chronic effect on humans, it has been determined that 3 g boric acid or 5 g borax per day has no effect, and 5-

10 g borax only increases protein metabolism and the amount of nitrogen in the urine. When the dose of 4-5 g per day was repeated, anorexia and disease were observed, but there was no incapacity to work (Kalafatoğlu et al., 1997).

The boron neutron capture therapy (BNCT) method, which has come to the fore, especially recently, has been a ray of hope for cancer treatment. This method, which has been tried in many cancer treatments, has been a treatment mainly used in the treatment of brain cancer and is known as a method in which the damage of healthy cells is at the lowest level in addition to the destruction of cancerous cells (Onrat and Konuk, 2004). Cancer Treatment BNCT method: In this type of cancer treatment, neutron bombardment is performed by administering p-boronophenylalanine, the drug form of boron, to the tumour tissue.



He and Li stay in the body for a concise time while emitting energy over a wide area. With total kinetic energy of 2.3-2.8 MeV, these emitted particles scatter in a radius of 10 µm, which is about cell size. Thus, only cancerous cells are destroyed, and other healthy cells are not damaged (Svantesson, 2002).

It has been observed that environmental factors are influential in prostate cancer rather than genetic factors. Nutrition is one of the most critical environmental factors. Low dose boron intake with diet reduces the risk of prostate cancer. High doses of boron intake have the opposite effect (Cui et al., 2003).

In the research on "Effects of Boron Minerals on Human Health" conducted by Ankara University Faculty of Medicine, when the findings obtained from people living on or near mineral deposits and people who are still working in boron factories and quarries or retired from these workplaces are examined, boron has It is concluded that there is no effect. Within the scope of the research project titled "Effects of Boron and Its Compounds on Human Health and the Environment", it was investigated whether the primary and secondary sexual power and reproductive abilities of people exposed to boron are affected children's health during and after pregnancy. As a result of the research, it was observed that 10-12 ppm boron intake per day did not affect primary and secondary sexual performance. It has been determined that exposure to boron and boron compounds does not pose any danger for the inhabitants of boron regions and employees of boron production (Şimşek et al., 2003).

As a result of the studies carried out, it is seen that boron is an essential mineral. However, like any substance that has a toxic effect, excess boron, of course, has a poisonous effect.

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CHAPTER 4

PRIMARY THYROID LYMPHOMA

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INTRODUCTION

Primary thyroid lymphoma (PTL) is seen in 5% of thyroid cancers (Bostancı,2017) (Wang,2015) (Derringer,2000)(Widder,2004). It constitutes between 1% and 7% of extranodal lymphomas (Bostancı,2017) (Wang,2015) (Derringer,2000) (Widder,2004). The annual incidence is around 2 in 1 million. It is mostly seen in women (8/1). It is seen in men at a young age, and in women in their 70s. Most of them develop on the basis of Hashimoto's thyroiditis (Buyukasik,2011) (Jayaprakash,2014) (Ahmed,2012). The thyroiditis of Hashimoto rises the development risk of PTL from 40 to 80 times (Derringer,2000). In thyroid gland, B cell type of NHL is the most common type. Classification of PTL such as diffuse large B-cell lymphoma (DLBCL) (50%), mucosa-associated lymphoid tissue lymphoma (10-23%), small lymphocytic lymphoma, and T-cell lymphoma (Walsh,2013) (Nam,2012) (Graff-Baker,2009) (Matsuzuka,1993). The risk of developing PTL in patients diagnosed with thyroiditis is lower than patients with Hashimoto disease. The success rate of PTL treatment is affected by the stage and histological form of the tumor. The lymphoma classification published by the WHO in 2008 categorizes lymphomas according to the dominant cell form. Those are B, T, Natural Killer and Hodgkin's lymphoma (Jaffe,2009).

Rarely, Hashimoto's thyroiditis can develop into lymphoma. The rate of lymphoma development in patients with thyroiditis is around 0.5%(Holm,1985) (Watanabe,2011). MALT lymphoma usually

develops on the basis of Hashimoto's thyroiditis (Mizokami,2016). In 60-90% of cases diagnosed with PTL, thyroiditis is present in the background (Watanabe,2011) (Thieblemont,2002) (Pedersen,1996). The reason for the development of lymphoma is estimated to be that chronic antigen stimulation triggers malignant transformation in autoimmune disorders (Kossev,1999).

Pathology: On cytological examination, a single type of wide extraordinary lymphoid cells with reduced or no colloid secretion are observed in DLBCL(Sangalli,2011). Nuclear abnormalities including micronucleoli or segmentation can be observed. Fine needle aspiration biopsy of patients with MALT lymphoma increases the number of medium-sized lymphoid cells and reactive lymphoid follicles (Rawal,2007). Small lymphocytes, Hürthle cells and increased interstitial connective tissue are seen in lymphomas developing on the basis of Hashimoto's thyroiditis (Maitra,2010). Antigens in the tissue are detected by using antibodies in immunohistochemical examination. Thus, it improves the accuracy of cytology in the diagnosis of lymphoma. Against B cell CD19 and CD20 antigens, the antibodies can be seen in DLBCL cases. For the DLBCL and MALT lymphoma disease, CD10 antigen is not observed. In the majority of DLBCL patients, Bcl-6 is seen as positive. Approximately 50% of Bcl-6 positive patients are also observed positive for Bcl-2 (Niitsu,2007). In the plasma cell structure, staining with the IgM heavy chain is an evidence supporting MALT lymphoma (Rawal,2007).

Clinic: The clinical course is more aggressive in patients with DLBCL than in patients with MALT and follicular lymphoma. Generally, such patients usually apply to the clinic with the complaint of a rapidly growing painless neck mass. There may be compression symptoms arising from this mass (Earnest,2006). This complaint is reported in more than 70% of DLBCL patients (Thieblemont,2002). Difficulty in breathing and swallowing are seen in 30% of patients (Watanabe,2011). Sometimes MALT lymphoma may transform into DLBCL form (Graff-Baker,2009). In that case, it progresses with a more aggressive clinical picture. Although hypothyroidism is identified in approximately 30% of the patients, they are usually euthyroid at the diagnosis stage (Watanabe,2011) (Sarinah,2010). Antithyroid antibodies; antithyroidperoxydase and antithyroglobulin are the most reliable serological markers in cases with Hashimoto disease. Additional B-symptoms in case of systemic spread of lymphoma; high fever, weight loss of more than 10%, and night sweats can be seen (Alzouebi,2012).

Diagnosis: Ultrasonography is the first diagnostic method used in diagnosis (Haugen,2016). Only half of the patients can be diagnosed with PTL based on ultrasound findings (Widder,2004). According to ultrasound findings, patients with PTL are classified as nodular, diffuse, or mixed (Ota,2006). Patients with PTL have increased posterior echogenicity, and those with the nodular type have sharp margins. The positive predictive value of ultrasound imaging was found to be 64.9% in the nodular type, 63.2% in the mixed type, and

33.7% in the diffuse type (Ota,2006). However, the specificity of ultrasound among diagnostic methods is low as 32.6% (Ota,2006).

Fine needle aspiration biopsy (FNAB): The next step in diagnosis is biopsy. The reported accuracy of FNAB is between 40-100%(Young,1998) (Jeffers,1998). FNAB is not a definitive method on its own. The sensitivity rate of FNAB is >90%, while its negative predictive value is 96% (Cheng,2012). False negative rates may increase in FNAB owing to the tissue similarity with thyroiditis and the possibility of both pathologies being seen in the same gland. In MALT lymphoma, the cell structure is often heterogeneous and similar to Hashimoto's thyroiditis. Recognition of DLBCL is less effortless owing to its large atypical cell structure (Stein,2013). Existence of lymphoglandular structures supports the diagnosis (Gupta,2005). When FNAB is combined with immunohistochemical examination, its diagnostic value increases. FNAB was combined with immunohistochemical examination in 17 patients with PTL. DLBCL was diagnosed with FNAB in 6 of 7 patients (85.7%) (Sangalli,2011). Contrarily, only 40% of the patients with MALT lymphoma could be accurately recognized. Even though the 30% of patients did not have Hashimoto's thyroiditis, they were diagnosed as if they had. Diagnosis of DLBCL is easier due to the increased concentration of big non-typical cells. Differentiating MALT lymphoma from thyroiditis can be difficult owing to its heterogeneous nature. Although surgical biopsy is used less frequently today, it is still required in cases where low-grade MALT lymphoma cannot be distinguished from thyroiditis. In a study by Sangalli et al., open surgical biopsy was performed for

accurate recognition in 6 of 10 patients with MALT lymphoma (Sangalli,2011). Postoperative histopathological examination and immunohistochemistry are considered as gold standard in the recognition of PTL.

Staging is performed afterwards. For the staging process, the Ann Arbor system is used.

Table I	Ann Arbor Staging of PTL
Stage	Disease in any region except thyroid gland
IE	Involvement of disease in only single extralymphatic organ or site
IIE	Lymph nodes involvement on the same side of the diaphragm
IIIE	Lymph nodes on either part of the diaphragm
IVE	Systemic involvement

The majority of patients are diagnosed in Stage IE (30-66%) or Stage IIE (25-66%) (Derringer,2000) (Watanabe,2011) (Sarinah,2010). Stage IIIE and Stage IVE are seen between 2-7%. Detailed radiological examination should be performed to find the stage of presentation of the illness for determining the response to treatment and prognosis. Imaging of the body with computed tomography is the primary method for staging. CT is more remarkable than ultrasound in assessing the extension of the disease locally (Takashima,1989). In recent years;PET-CT is more commonly used in diagnosis and response to treatment in regional and metastatic disease.

Treatment: Surgery and radiotherapy were thought to be the standard treatment modalities until it was discovered that thyroid lymphoma is

sensitive to chemotherapy and radiotherapy (RT). Today, surgical treatment has a limited role (Blair,1985). During the treatment plan, the stage and histological type of the disease should be known.

Vigliotti et al. found that the response to RT alone or combined radiotherapy-chemotherapy was equal in stage IE and IIE localized patients without mediastinal involvement (Viglotti,1986). It was observed that survival rates in this type of treatment protocol were better according to chemotherapy or surgery alone. Tsang et al. observed that RT alone gave excellent results in localized MALT lymphomas (Tsang,2003). In the 5 years posttreatment follow-up process, 100% complete response rate to treatment was observed without recurrence. In low-grade localized MALT lymphomas, RT alone is successful in treatment. Pyke et al. did not observe any diversity in remission proportions or disease-free survival in cases with localized disease who underwent RT + surgery versus RT alone(Pyke,1992). On the other hand, they found that complete remission was achieved in two patients with Stage IE PTL undergoing surgical intervention. Thyroidectomy is an effective treatment method in patients with stage IE MALT lymphoma, but it has no extra advantage over RT alone (Zelenetz,2006).

The treatment protocol in patients with DLBCL should include chemotherapy and radiotherapy because of the more aggressive and recurrent tendency (Viglotti,1986). The chemotherapy protocol contains cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP), and lately added Rituximab (R) (R-CHOP), known as anti-

CD20 monoclonal antibody. While the chance of survival for 8 years is 100% in patients who received 6 cycles of CHOP +RT, the survival rate is around 75% in cases in which chemotherapy + RT taken 2 times. In cases that chemotherapy was not applied, the mortality rate was around 35%. In the study of Doria et al. including 211 patients at Stage IE and IIE PTL, they found that the combined treatment protocol applied reduced the rates of distant metastasis and recurrence by 7.7%(Doria,1994). Disease-free survival time of 5 and 10 years was 76% in patients who underwent surgery + RT, 50% in those who received chemotherapy alone, and 91% in those who received combined therapy. Recurrence was seen in 3 of 4 patients who were treated only with surgery.

In a study, which included 401 patients with Stage I and II NHL and diverse histological subgroups, only CHOP or CHOP+RT treatment protocol was applied to the patients randomly. While the survival rate without disease was 77% in the patients who underwent CHOP+RT treatment protocol, this rate was calculated as 64% in the other group. Rituximab (R) has recently been added to the chemotherapy protocol of lymphoma treatment. 6 cycles of R-CHOP protocol was applied to 1222 patients with nodal DLBCL (Pfreundschuh,2008). This treatment protocol was found to significantly increase disease-free survival. Surgical treatment is applied to relieve compression symptoms and protect the airway in diffuse or aggressive cases.

The prognosis in PTL is related to the dissemination of the illness and the phase of the neoplasm. 5-year survival rates according to the stage

of the disease; is 86, 81 and 64% in Stage I, Stage II and Stage III/IV, respectively. According to the histological type of the disease, the 5-year survival rate is 75% in patients with DLBCL, 96% in MALT lymphoma, 87% in follicular lymphoma, 86% in small lymphocytic lymphoma, and 83% in NHL. Derringer et al observed the 5-year survival rate as 100%, 78%, and 71% in patients with MALT lymphoma, mixed lymphoma, and DLBCL, respectively (Derringer,2000). Advanced age and advanced stage, DLBCL type, not performing RT or surgery, increased tumoral mass, thoracal involvement, existence of B symptoms, and difficulty in swallowing are factors that adversely affect the prognosis (Buyukasık,2011) (Graff-Baker,2009) (Table II).

Table II Summary of DLBCL and MALT Lymphoma

	DLBLC	MALT
Prevalence	>50%	10-23%
Clinical course	Very thrusting	Less aggressive
Microscopy	Huge lymphoid cells	Intermediate sized cells
Treatment choices	Radiotherapy + chemotherapy	For localized cases; radiotherapy For disseminated cases; radiotherapy+ chemotherapy
5 years survival	70-75%	96-100%

CONCLUSION

PTL is rare among thyroid malignant diseases. Especially in cases with Hashimoto disease, PTL should be suspected if there is an enlarging neck mass. Presence of increased posterior echoes on ultrasound imaging is in favor of PTL, but the definitive diagnosis is made by biopsy. With the development of immunophenotyping techniques, FNAB can be used as a first-step diagnostic test. If the diagnosis is equivocal, open surgical biopsy can be performed.

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CHAPTER 5

CASTLEMAN DISEASE; LYMPHOPROLIFERATIVE DISORDER

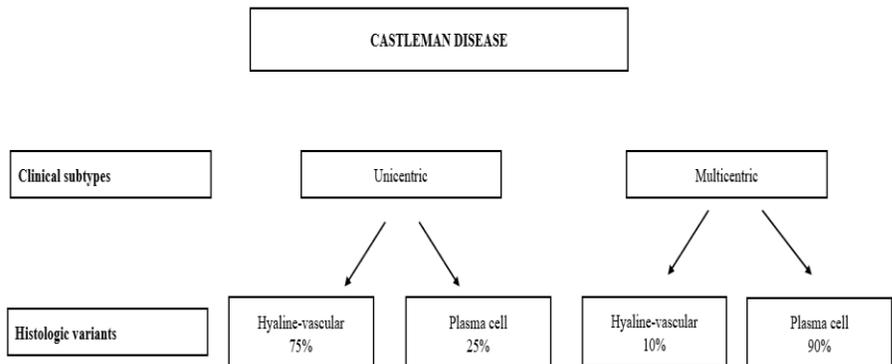
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INTRODUCTION

Castleman disease, or Castleman syndrome, is literally described as a rare lymphoproliferative disorder identified by the overgrowth of lymph nodes, which is extremely scarce, due the immune system regulation problems (Szalat, 2018). In 1956, Benjamin Castleman, American physician and pathologist, discovered a large non-cancerous mass without symptom containing lymph nodes in the thorax (Castleman, 1954). Afterwards, other localizations such as abdomen, pancreas, spleen, neck, pelvic peritoneum and peripheric lymph nodes were described. Localizations are seen in axilla (4%), abdomen (11%), neck (14%) and the most frequently in thorax (63%) (Anagnostou, 1972). Even if it is predominantly observed in adults regardless of gender, Castleman disease can be seen during the childhood (Keller, 1972). Although localized forms can be prognosed adequately, multifocal forms are still aggressive to be prognosed and etiologically obscure.

The diagnosis of Castleman disease is generally accomplished at the stage of the histologic evaluation of the surgical specimen containing two forms: unicentric, and multicentric. Also multicentric type divided into several subgroups; cases with Human Herpesvirus 8 (HHV-8) infection, cases with POEMS syndrome and idiopathic form associated with TAFRO syndrome (Table- I).

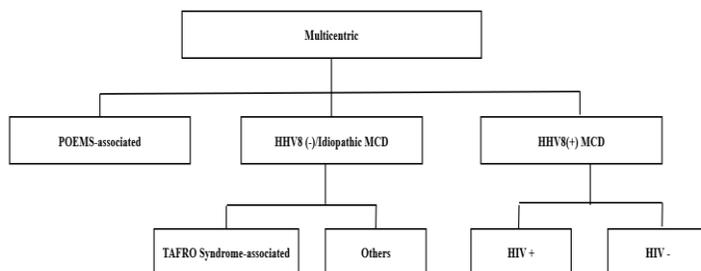


PRESENTATION

I. Unicentric Castleman Disease (UCD)

The presentation shows differences. It is usually clinically asymptomatic. Visible or palpable mass, abnormality in routine laboratory tests or any finding during unrelated examination can be an indicator of the disease. Although rare emergence of the disease can be with systemic symptoms or palpable enlarged lymph nodes.

Unicentric form which consists of one or more conglomerated lymph nodes constitutes approximately up to 80% of all cases of Castleman disease (Fajgenbaum, 2018) (Simpson, 2018) (Yu, 2017). Castleman disease has three morphological variants: Hyaline-vascular (75%), Plasma-cell (24%) and a rare combined type (Table-II).



Studies reveal that up to approximately 80% of unicentric Castleman disease patients show histologic features of HV variant (Simpson, 2018) (Yu, 2017) while the rest of patients show histologic features of PC variants. However, over 90% of patients with multicentric Castleman disease display morphological properties of Plasma-cell variant.

Since the symptoms of HV-CD cases are highly difficult to identify, a particular or unicentric pathological variation is observed as a secondary or accidental evidence. Although HV-CD frequently comprises lymph nodes in the thorax, lymph nodes in the abdomen may be detected in the minority of patients (Danon, 1993). The increase in the mass volume and compression of the adjacent tissues resulting in difficulty in breathing or compression on the vessels can induce oesophageal varices (Keller, 1972) (Wong, 2018) (Serin, 2002). In the minority of cases with Hyaline-vascular Castleman disease with thoracal involvement, myasthenia gravis was observed (Day, 2003).

In unicentric, Plasma-cell Castleman disease is seen in nearly all age groups and the existence of the mediastinum involvement is not as prevalent as in patients with HC-CD. In a major group of patients, lab abnormalities and frequently seen symptoms containing high body temperature, night sweating complaints, losing weight and weakness have been monitored (Fajgenbaum, 2018) (Yu, 2017) (Oksenhendler, 2018). According to the lab tests, anemia or thrombocytopenia is observed, the level of plasma Interleukin-6 is high, which is likely to serve a function in the aetiology of unicentric Plasma-cell Castleman disease in HIV negative patients (Fajgenbaum, 2018). Via the elimination of lymphatic channels impairing the circulation of lymphatic fluid and making it a closed system reduces the effects of cytokines.

II. Multicentric Castleman Disease (MCD)

It can be seen at any age (Oksenhendler, 2018). On physical and radiological examination the first sign is lymphadenopathy that can be peripheric or abdominal. Mediastinal lymph node involvement is less often in this form (Yu, 2017) (Oksenhendler, 2018) (Liu, 2003). In MCD splenomegaly (75%) and hepatomegaly (%50) can be detected. Other rare findings are neurological changes, skin rash and effusions in the body cavities (Yu, 2017) (Oksenhendler, 2018) (Liu, 2003). MCD is differentiated from the UCD by the presence of frequently seen symptoms such as high temperature, pleural fluid accumulation, fluid accumulation in the abdominal cavity, hepatosplenomegaly, lymph node involvement in multiple regions and biological clues of inflammation. High temperature, night sweating with or without

weight loss which called Type B symptoms are more common in MCD (Liu, 2003) (Fajgenbaum, 2017). In laboratory results decrease in thrombocyte and blood count, increase in sediment, Interleukin-6, Lactate Dehydrogenase, γ -interferon and CRP value and polyclonal hypergammaglobulinemia might be observed often (Yu, 2017) (Winter, 1996). According to this findings and symptoms it has a worse prognosis. MCD has two subgroups called as human herpesvirus 8-related MCD (Castleman, 1954) (Flendrig, 1969) and idiopathic MCD (iMCD) which has no known etiology (Menke,1992).

II. I. Human Herpes 8 Positive MCD

Nearly half of the patients of MCD occurs in the presence HHV-8 (Yu, 2017) (Oksenhendler, 2018) (Talat, 2012). The presence of immunodeficiency in these patients results in the reactivation of HHV-8. Such patients were also categorized as HIV positive and HIV negative. In the US HHV-8 positive MCD is more prevalent in cases with HIV infection so that epidemiologic features of these patients are similar. Usually this group of patients is older.

II.II. Idiopathic MCD

The prevalence of Idiopathic MCD ranges from 30% to 50% in all MCD cases. The clinical course is observed as acute or subacute. The disease is more severe when the patient with Idiopathic MCD also has TAFRO syndrome (Oksenhendler, 2018) (Fajgenbaum, 2017) (Igawa, 2018). TAFRO and non-TAFRO idiopathic multicentric CD can be differentiated by several factors such as the existence of low platelet value, Ig levels, serum fluid accumulation in body cavities and in-

creased capillary peripheral permeability (Igawa, 2018) (Iwaki, 2016). In cases with idiopathic MCD of non-TAFRO form, it is observed that lymphadenopathy is inclined to be more prominent (Igawa, 2018).

The result of MCD can be lethal on account of failure in many organs due to fatal infections and such cases are in danger due to potential development of non-Hodgkin (NHL) and Hodgkin (HL) lymphomas, Kaposi's sarcoma and POEMS syndrome, especially in the HHV-8 associated types (Peterson, 1993) (Maslovsky, 2000) (Frizzera, 1985). Up to 70% of HIV-positive MCD patients and 10% of the HIV-negative patients were presented with Kaposi's sarcoma during the disease process (Oksenhendler, 1996).

The clinical course is observed as unstable. Patients with HV-CD might be asymptomatic or only lymphadenopathy may be observed while those with MCD frequently exhibit symptoms such as high temperature, night sweating complaints, weight loss, involvement of common peripheric lymph nodes and/or general systemic lymph nodes and involvement of multiple organs (Keller, 1972) (Peterson, 1993). Reactions in acute stage and numerous autoimmune features can be observed in patients with MCD (Frizzera, 1985) (Frizzera, 2001). Although lymphadenopathy and autoantibodies are generally categorized in the group of systemic autoimmune diseases, identifying a sharp characteristic among different disease entities is difficult. In multicentric CD pathogenesis, the cytokine Interleukin-6 has been discovered to play the main role (Frizzera, 2001).

DIAGNOSIS

After physical examination, blood tests are requested. Blood tests reveal anemia and abnormalities in blood proteins which are specific for Castleman disease. For imaging ultrasonography, CT scan or MRI of the affected region is performed. Also PET-CT can be used for diagnosis and to evaluate treatment is effective or not. To differentiate Castleman disease from other lymphatic tissue diseases lymph node biopsy is performed.

TREATMENT

Treatment depends on type of the disease. In unicentric Castleman disease the recurrence rate of the surgical excision of the affected lymph node is low. According to studies, the rate of 5-years survival is observed between 90% and 100% (Talat, 2012) (Wang, 2015), and the rate of the 5-year disease-free condition has also been recorded over 80% (Talat, 2012). As the surgical excision of UCD is not always performed, partial excision comes after adjuvant radiotherapy is presented as effective in a small case series (Noh, 2013). If location of the node is difficult to reach, for example in the chest or in the retroperitoneum of the abdomen, major surgical intervention may be needed. If surgery is not possible medication can be used to downsize the node. Anti-interleukin 6 (IL-6) is also introduced as an alternative therapy for the cases unable to operate, which has been cited in the pathogenesis of CD (Fajgenbaum, 2018) (Blute, 2017). Due to the magnificent prognosis of UCD, the 10-year death rate lowers to 5% (Talat, 2012). Adjuvant radiotherapy also can be used.

Medications and other treatment regimens are generally used for multicentric Castleman disease. Treatment options depends on the extent of the disease and the presence of HIV or HHV-8. Immunotherapy, chemotherapy, corticosteroids and anti-viral drugs are the treatment options.

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CHAPTER 6

NONMICROSURGICAL EAR REPLANTATIONS

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INTRODUCTION

Ear amputations seem rarely. However, ear loss or deformity causes serious psychologic problems and aesthetic defects which are difficult to restore for the patient. Due to the complex anatomic structure, thin vascularization and symmetrical location, ear reconstruction is difficult. Therefore, studies including saving amputated part of the ear and increasing the survival rate have been an important issue for plastic surgeons.

Microsurgical replantation of the amputated ear part was first practiced by Pennington in 1980.¹ This method has the best aesthetic results when it is successful. Beside, it is important because of not harming peri auricular tissues and not taking away the chance of further reconstruction. Being an one stage operation is another advantage. Therefore, nowadays microsurgical replantation for ear replantation is recommended as a first treatment choice. However, it requires specialized microsurgery centers because it requires complex microsurgical techniques like, not founding the recipient vessel, reconstruction with venous graft, end to end anastomose. Beside, leech therapy, mechanical bleeding or heparin treatment might be required for venous congestion which can occur in almost every patient. In this situation anemia could occur and blood transfusion may be required. There is a case who takes 12 units blood transfusion in literature.² Operation time and hospitalization time is long. Therefore, although it is recommended as a first treatment option, microsurgical replantation can not find a wide application area.

Non microsurgical replantation was performed with various techniques until 17. Century. ³ Simple reattachment of amputated ear auricle was first presented by Brown in 1898. ⁴ Actually, until today, main purpose for non microsurgical replantation techniques was to increase the survival rate of the amputated part of ear as a composite graft.

Nowadays, because of low success ratio, simple reattachment is only performed for subtotal amputations and when the amputated part is smaller than 15 mm. However, there is a case in literature which is survived after total ear amputation, with simple reattachment used together with Hyperbaric Oxygen therapy and Platelet Rich Plasma as additional treatments.⁵ There is no definite information about using those additional treatments together with reattachment, but they can be tried for morbid patients who can not have progressive operations.

Burying amputated part of ear heterotopical abdominal ⁶, servical ⁷, or ortopically to post auricular region⁸ by dermabrading and saving cartilage for reconstruction technique is not used in nowadays. Ear cartilage loses its complex anatomical and elastic structure by heterotopic implantation. This situation is confirmed by histopathological studies that shows local ossification centers and increased fibrous tissue on the implanted cartilage ⁹. Orthotopical implantation was not in use because of composing amorph and adherent structure on the local tissues, not having an aesthetic reconstruction and taking off the choice of further reconstruction options. ¹⁰

Boudet's method, which was presented in 1972 is very successful due to preserving the unic structure of the ear and increasing the surviving rate as a composite graft. Therefore, nowadays it can be performed for ear amputations when there is no option for microsurgery. ^{11,12} According to this method, posterior skin of the amputated ear part is deepitelised and fenestrations are prepared. Anterior wound edge is sutured to the deficient. Skin flap which is prepared from postauricular region is sutured to the posterior edge of amputated ear. By this way, composite graft will be placed on a wide vascular bed. Cartilage fenestrations increases the contact with vascular bed and this increases the survival chance of the composite graft. ^{11,12} However this operation have two stages. Second stage is like separating amputated part of ear from vascular bed and grafting posterior side three months later. This method could be performed conveniently when the amputated part is bigger than 15 mm and not consisting ear lobule. Technically its easy. It is thought that deepitelisation of posterior skin of the amputated part and leaving some dermis over the cartilage helps preserving the anatomical shape of the cartilage. ¹¹

Another non microsurgical replantation method is suturing the dermabraded amputated ear part and covering it with temporoparietal fascia. At the same stage, skin cover can be supplied by putting the skin graft over temporoparietal fascia ¹³, or adapting amputated part's skin to the ear anatomically. ¹⁴ These methods have advantages due to presenting one stage reconstruction but some authorities criticize the use of temporoparietal fascia flaps as the appropriate "life boat" after failed microsurgical repair. ^{15,16}

In case of periauricular damage, ear cartilage can be implanted inside platysma and after providing neovascularisation, myocutaneous-cartilaginous flap can be transposed to its original position.¹⁷ Considering that cartilage which loses its original structure and transferred myocutaneous-cartilaginous flap can create bulkiness in the ear; seconder reconstruction with ric cartilage can be more perceptive for these cases.

In Staffen and friends study, which compared reattachment techniques for ear amputations¹⁰, it is emphasized that the first choice for ear amputations should be microsurgical replantation and engrossingly indicated that for the cases which microsurgical replantation can not be performed seconder reconstruction with rib cartilage should be planned. According to the study, pocket technique should be abandoned totally, because of the results that obtained by pocket methods are quite inconsistent functionally and aesthetically in comparison with seconder reconstruction with rib cartilage. The fact that cartilage loses it's original structure regardless the shape of banking and trauma to the periauricular tissue have negative effects for the patient's subsequent reconstruction choice. Planning primary wound closure and secondary reconstruction with rib cartilage is recommended for the situations when microsurgical replantation can not be performed. However, in literature, there are many functionally and aesthetically successful cases performed by Boudet method.^{11,12,18,19} Besides, in some studies Boudet method is presented as an option when microsurgical replantation can not be performed and indicated that the most important disadvantage is requiring two stage

surgery .^{11,12} Considering that reconstruction with rib cartilage is also two stage operation, using original tissue for minimizing donor site morbidity seems more advantageous. From the perspective of plastic surgery, it is not practical not using original tissue that has a chance as a composite graft. We consider that more prospective studies are needed for making an accurate algorithm.

CONCLUSION

As a result, microsurgical replantation is the primary option for ear amputations. Boudet method should be preferred when microsurgery can not be performed. Preserving temporoparietal fascia for further reconstruction methods, not creating distant donor site morbidity and high success ratio are the most important advantages. The most important disadvantage of the method is creating amorph and adherent tissue on postauricular region which decreases the success rate of second reconstruction with rib cartilage.

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Figure 1: Ear amputation by a human bite



Figure 2 : Fifth day after nonmicrosurgical replantation



Figure 3 : Fifteenth day of nonmicrosurgical replantation



Figure 4 : One month after nonmicrosurgical replantation

CHAPTER 8

DETECTION AND IMAGING OF CORONA VIRUSES UNDER THE ELECTRON MICROSCOPE

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INTRODUCTION

The World Health Organization (WHO) declared the outbreak of coronavirus 2 (SARS-CoV-2) disease (COVID-19), also called severe acute respiratory syndrome, which occurred in China, as a pandemic on March 11, 2020. Since SARS-CoV-2 caused a major pandemic epidemic and caused a global concern, multiple diagnostic tests were developed and results were presented in order to quickly and accurately identify patients with COVID-19.

Coronavirus (CoV) infection and more serious infections such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), which are common in the community such as the common cold, are self-limiting by presenting mild infections. It has been declared in studies and researches that it has a very large virus allele that can be observed (1,2).

There are many types of coronavirus that are especially found in humans and can be easily transmitted from person to person, which are HCoV-229E, HCoV-OC43, HCoV-NL63 and HKU1-CoV. These subspecies, which are constantly circulating among humans, appear as common viruses that usually cause the common cold. To clarify the subject further, it has been studied that virus can be detected in animals as many subtypes, and it has been examined that the virus pass from animals to humans and cause severe disease. As a result of research and studies, it has been suggested that SARS-CoV was transmitted from civet cats and MERS-CoV from dromedary camels to humans (1).

On December 31, 2019, the World Health Organization (WHO) China Office announced that there were cases of pneumonia with unknown etiology in the city of Wuhan, Hubei province of China. This virus, which was observed on January 7, 2020, has never been detected in humans before, defined as new coronavirus (2019-nCoV). Later, the name of the 2019-nCoV disease was named as COVID-19, and the virus was named SARS-CoV-2 because of its close resemblance to SARS CoV (1).

CoVs are genotypically and serologically divided into four subgroups: (α , β , γ , and δ -CoV). Human CoV infections are caused by α - and β -CoVs. SARS-CoV-2 is a new beta-coronavirus that causes coronavirus disease. (3,4).

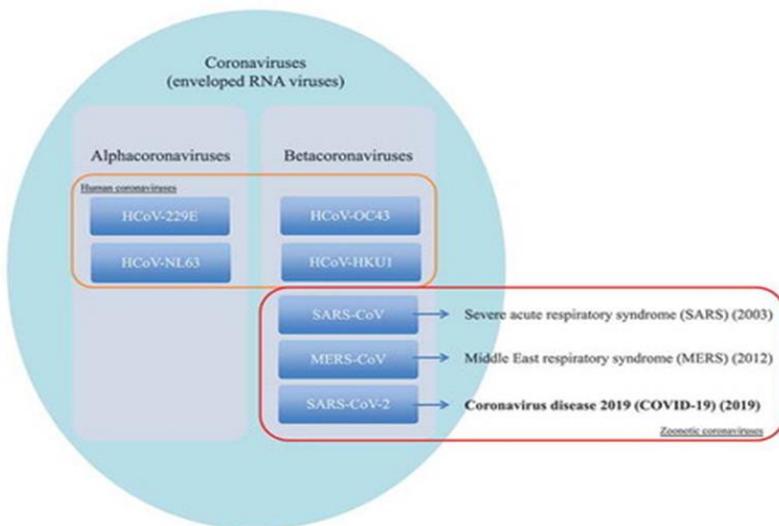


Figure 1. Classification of coronavirus that infect humans and the diseases they cause (3).

Patients with SARS-CoV-2 infection generally showed symptoms of fever, dry cough, upper respiratory tract obstruction, sputum production, shortness of breath, rarely headache, hemoptysis, and diarrhea (4,5). In addition, cases with loss of smell and taste have been reported (6).

Structural Feature of the Coronavirus

Coronavirus is a single-stranded, positively polarized, enveloped RNA virüs, 65-125 nm in diameter, 26 to 32 kb in length, belonging to the Coronaviridae family. Because they are positively polarized, they do not contain the RNA-dependent RNA polymerase enzyme, but they encode this enzyme in their genome. They have rod-like extensions on their surface. Based on the Latin meaning of these protrusions "corona", which means "crown", these viruses were named Coronavirus (crowned virus). (1,7).

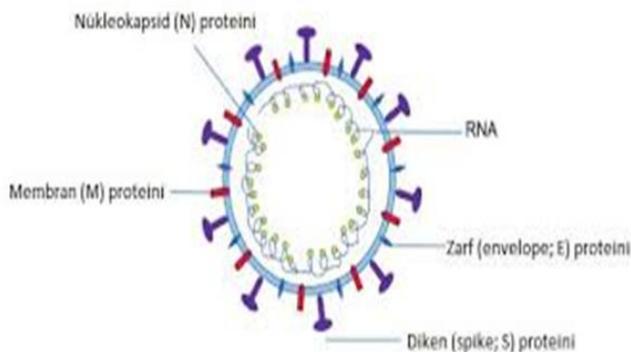


Figure 2. Schematic structure of coronavirus (1)

COVID-19 Sample Collection Method

The disease is mainly transmitted by droplets. Sample collection is usually in the form of Nasopharyngeal swab (NF), Oropharyngeal swab (OF) and combined swab (NF+OF), in which samples are taken from the lower respiratory tract. Wang et al reported that the oropharyngeal (OF) swab (n = 398) was used much more frequently than NF swabs (n = 8) during the COVID-19 outbreak in China; however, SARS-CoV-2 RNA was detected in only 32% of OF swabs, while this rate was significantly higher (63%) in NF swabs. (8).

Other samples, such as whole blood, urine, and autopsy from deceased patients may also be collected to detect the presence of the virus and monitor viral clearance, but further research is required to determine their efficacy and safety. It has been reported that SARS-CoV-2 RNA was detected in the stool of 48.1% of patients during the course of the disease and remained positive in the stool for more than 33 days even if respiratory tract samples were negative. (9).

Diagnostic Tests

- Nucleic acid amplification tests (NAAT),
- Sequencing,
- Serological tests,
- Electron microscopy (EM); It is a microscope that uses electrons rather than light to create images. Compared to EM, light microscopy (LM) appears to have many advantages. In EM, unlike LM, a beam of electrons accelerated in a vacuum is used instead of light as the

illumination source. In LM, usually stained preparations are examined by passing light through the sample and used in many fields such as medicine, science and engineering. However, they cannot give the high magnifications necessary for us to see very small particles such as atoms. EM produces high magnification. It has a large depth of field, meaning it creates high resolution images. The quality, clarity and detail richness of the image depend on the resolution, which is 0.5-1 micron in LM and 2-20 angstrom in EM. (10,11,12,13). There are two basic types of EM, Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM). It is known as the third type as Scanning Transmission Electron Microscopy (STEM), which has less usage area. (10,11,14). Electron microscopy (EM) has a very important place and presents very important information on COVID-19 lung tissue, including materials used in autopsy, as a great auxiliary technique. TEM, a variant of the electron microscope, is of great interest to observe and reveal the characteristics of SARS-CoV-2 in specific cells and its subcellular compartments. When we look at the study Almeyda and Tyrrell revealed in 1965, epithelium of the respiratory system made the unique structural morphology of coronavirus particles from organ cultures (15). In the first studies of CoV-2, the lung was considered as a province, and SARS- the first ultrastructural in vivo study was evaluated by considering the bronchoalveolar lavage fluid and the results were presented (16). Transmission Electron Microscopy (TEM) has been widely used in many studies and researches to investigate SARS-CoV's and MERS-CoV's morphology, properties or structure and good results have been

obtained (17,18). Scanning electron microscope (SEM), which is another type of electron microscope, is widely used for microbiological studies and research, as well as for the diagnosis of many infectious diseases. (19Philippe Colson et al. SEM was used to examine Vero cells infected with SARS-CoV-2 in a study conducted in 2020 (20).

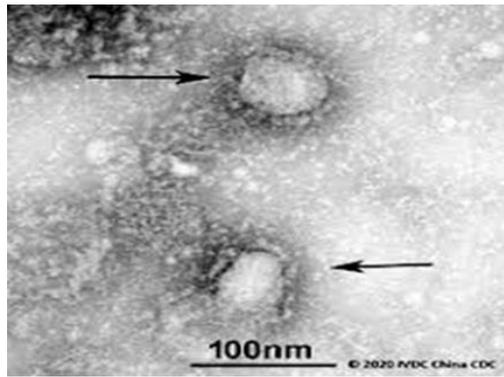


Figure 3. Electron microscope image of new **Coronavirus (betacoronavirus) (1).**

When We Examine the Examples of Studies Performed on Different Tissues Using Electron Microscopy in Coronavirus Infection

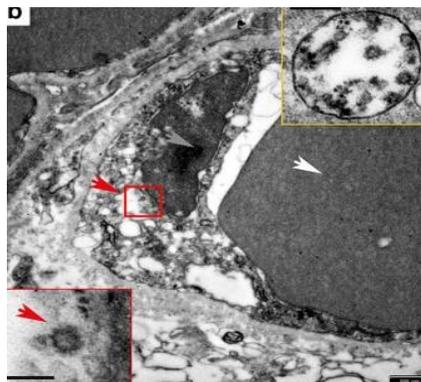


Figure 4. Virus particles (red arrowhead) are usually found in endothelial cells (white arrowhead, erythrocyte; gray arrowhead, endothelial cell nucleus);

In our study using Transmission Electron Microscope (TEM), our aim while examining liver tissues was to determine the result of ultrastructural changes in the tissue and the presence of SARS-CoV-2 viral particles, and the results were presented. The tissue is examined in detail under TEM, by taking biopsy samples from liver, the image samples obtained by passing through certain stages (22). When we look at the findings, typical coronavirus particles in the cytoplasm of hepatocytes in liver tissue were observed and most of them were belong to viral particles. Another finding was surface thickening of the corona peplomer structure. When we examined the hepatocytes infected with SARS-CoV-2, it was revealed that there were mitochondria with an indeterminate structure and a material with high electronic density and prominent swelling (Şekil 5A,B).

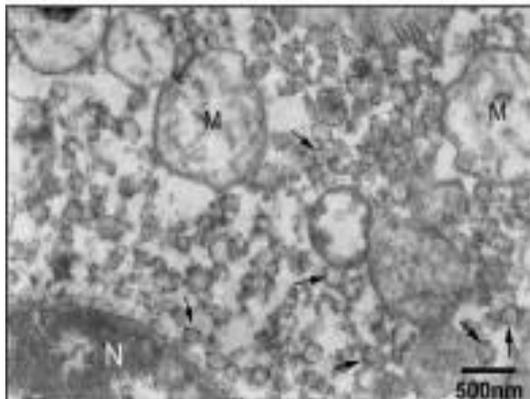


Fig. 5A. Mitochondria (marked as M) conspicuous with swelling and granular reduction showing ultrastructural defects at (original magnification $\times 15,000$) COVID-19, coronavirus disease 2019.

As another finding in images provided by TEM, hepatocytes were found to have a large proportion of coronavirus particles varying in size from 70-120 nm in the cytoplasm. In addition, no changes were observed in the structure of viral particles. It has been demonstrated that there are lipid droplets with high electronic density (Şekil 5B).

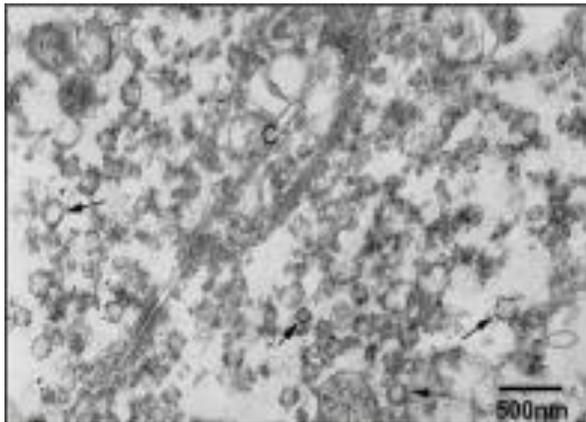


Figure 5B. Electron microscope showing numerous coronavirus particles (arrow) in the cytoplasm of hepatocytes.

If we evaluate the results of other studies; The tissue pieces taken from the placenta were passed through certain stages and examined by transmission electron microscopy and the results of the findings were evaluated (23). Considering the findings after this process, a single visible virion image invading a syncytiotrophoblast was obtained with TEM and the result was revealed (Figure 6).

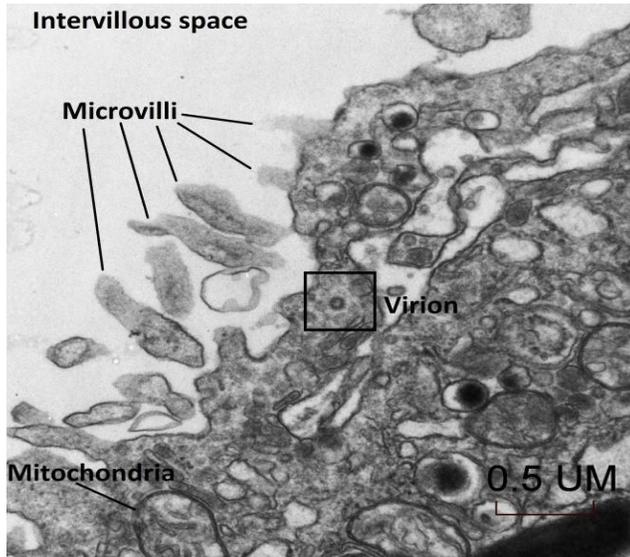


Figure 6. Transmission electron microscopy of a single visible virion occupying a syncytiotrophoblast

When we evaluated other studies, particles with a coronavirus-like structure were found in the cytoplasm of the epithelium of the renal proximal tubule, as well as in the podocytes and, to a much lesser extent, in the distal tubules (24). If we consider the diameter of the particles, which are similar to the virus structure, it ranges from 65 nm to 136 nm, and has a distinctly pointed tips, like appearance of a sun "corona", about 20 to 25 nm. It has been suggested that these coronavirus features we have examined include the adjacent double membrane with surface projection, the nucleocapsid conforming to the viral envelope, and the internal electron-clarity of the particles (Şekil 7a,b,c,d).

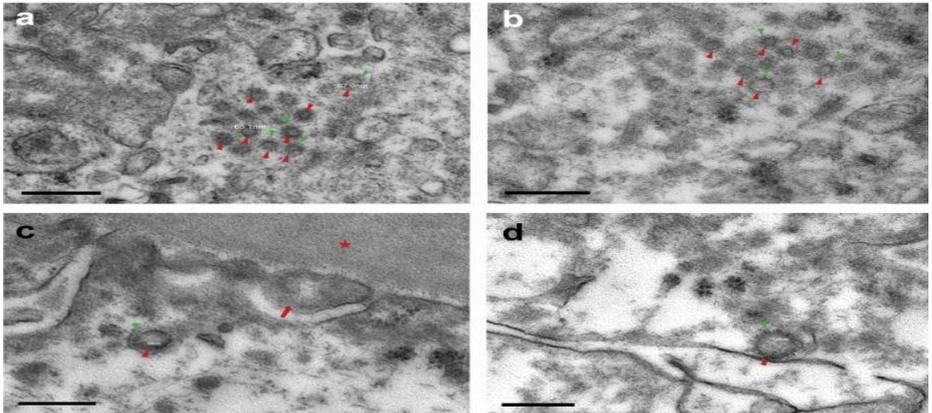
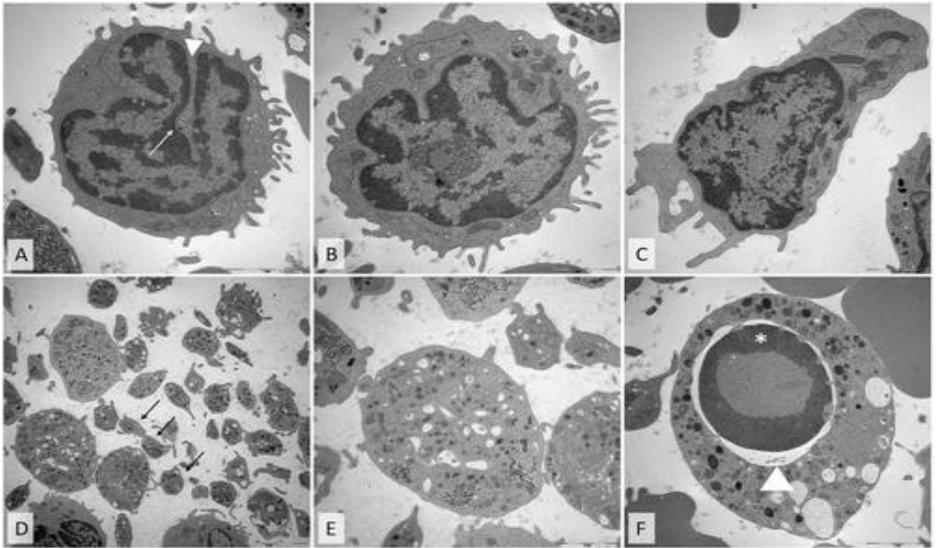


Figure (7a,b,c,d) Coronavirus-like particles (red arrowheads), (a) proximal, (b) distal, (c,d) prominent spike in podocytes (green arrowheads), glomerular basement membrane (star) .

When we examine the analysis of another study; leukocytes and mononuclear cells were isolated from blood samples and subjected to some process to be examined under the electron microscope (25).

Based on transmission electron microscopy data, large numbers of lymphocytes showed marked nuclear invasions, sometimes involving cell organelles such as mitochondria. In addition to these, highly lobulated nucleated lymphocytes were seen. Another finding was that granulocytes were seen in the early stages of apoptosis, exhibiting hypercondensed chromatin and at the onset of nuclear shrinkage (Fig. 8a,b,c,d).



(Fig. 8a,b,c,d,e,f) Representative ultrastructural changes of abnormal cells. A, Lymphocyte with invagination of the cytoplasm (arrowhead) containing a mitochondria (arrow). B, Lymphocytes with highly lobulated nuclei. C, Significantly elongated lymphocyte. D and E, Ultrastructural alteration of platelets and granulocytes: D, normal sized platelets (arrows) and (E) giant platelets, F, Granulocyte, shrinking (arrowhead) and chromatin condensation (*), showing apoptosis with nuclear pycnosis

In another study using TEM for detection; biopsy samples obtained from four deceased and one living testicular tissue obtained from six autopsy patients were examined under electrone microscope. Biopsy samples in the obtained testicular tissue were subjected to certain stages, then dyed and viewed in a JEM-1400 transmission electron microscope (JEOL, Tokyo, Japan) at 80 kV and the images were recorded by an AMT BioSprint digital camera (AMT, Woburn, MA, USA) (26).

As a result, when we examine the image of the testis tissue, many structural and various morphological changes are seen, as well as showing a great effect in malformatism. (Fig. 9A.B).

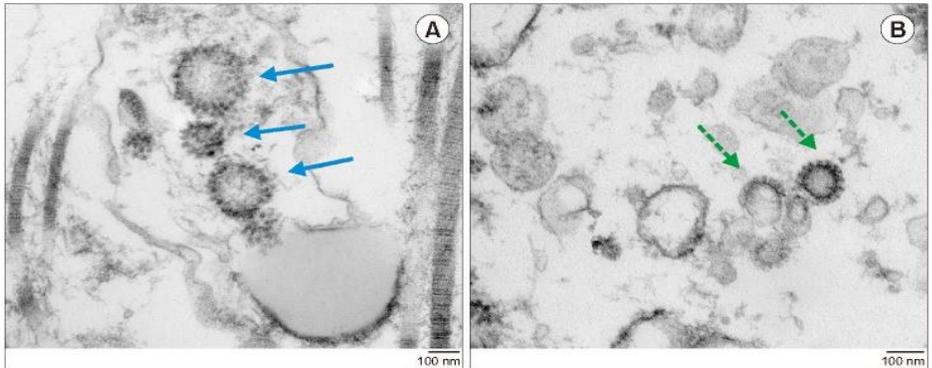


Figure-9A. Coronavirus-like sharp viral particles (blue arrows) in the seminiferous tubules of a live patient who has previously contracted the COVID-19 virus and subsequently seroconverted. 9B. Infected with COVID-19 virus in the seminiferous tubules after autopsy. Coronavirus-like pointed viral particles (green dotted arrows)

RESULT

In addition affecting the whole world negatively, corona virus causes serious socio-economic damage. With its emergence, coronavirus causes serious mortality and morbidity. In line with the information obtained as a result of studies, various treatment methods are being developed and it is leading the world to get rid of this common disease quickly and take various measures.

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CHAPTER 8

POSITIVE AND NEGATIVE EFFECTS OF USING CHEST COMPUTED TOMOGRAPHY IN COVID-19

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INTRODUCTION

The disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, which was spread from Wuhan city of Hubei province of China to the whole world after December 2019, was named the coronavirus disease 2019 (COVID-19) (Lu et al.,2020; Huang et al.,2020). According to the latest data from the World Health Organization (WHO), the COVID-19 pandemic caused approximately 152 million confirmed cases and 3.2 million deaths in 223 different countries (WHO, 2021). Studies have showed that the spread rate of COVID-19 has increased even more with the new variants that have emerged recently (Nikhra, 2021; V Oosterhout et al., 2021). Early diagnosis plays a vital role as COVID-19 is spreading rapidly from person to person. If the disease is diagnosed early, treatment can be done faster (a better prognosis), and the rate of spread of the disease can be reduced by patient isolation (Peck, 2020).

The gold standard in the diagnosis of COVID-19 is real-time reverse-transcription polymerase chain reaction (RT-PCR). The diagnosis of COVID-19 is made by laboratory testing through the identification of viral RNA in RT-PCR (Huang Et a.,2020; Corman et al.,2020; Shan et al.,2020). The vast majority of tests available on the market for early detection of COVID-19 are based on real-time RT-PCR tests (Afzal, 2020). RT-PCR has limitations such as insufficient kit numbers, false-negative results or false-positive results (insufficient sampling or procedural errors) and late results (Huang et al.,2020; Afzal, 2020; Green et al., 2021; Liu et al., 2020).

CT is an advanced imaging technique used to view the lung structures of patients with suspected or confirmed COVID-19. Many scientific studies conducted worldwide have indicated the importance of chest CT in the diagnosis of COVID-19 and follow-up of COVID-19 (Deng et al.,2020; Yang et al.,2020; Bernheim et al., 2020; Cinkooglu et al.,2020; Li et al., 2020). Chest CT scans, which increased in frequency during the COVID-19 outbreak, have some impact on patients, medical staff, and the economy. The purpose of this research is to determine the positive and negative effects of chest CT using in COVID-19.

1. POSITIVE EFFECTS OF USING CHEST CT IN COVID-19

1.1. The importance of chest CT in the diagnosis and follow-up of COVID-19

Health authorities say it is vital to identify symptomatic and asymptomatic suspects in COVID-19 outbreak, to tract contact tracing and quarantine processes. In this way, the transmission rate of the virus can be slowed down (Gostic et al., 2020). Chest CT is also widely used to aid early diagnosis of COVID-19 disease (Yang et al.,2020). Chest Computed tomography (CT) reveals the exact size, location, and other features of lesions in lungs. Therefore, chest CT is a reliable and indispensable technique used in lung diseases (Zhu, Yu and Huang,2004; Li, M., 2020). RT-PCR has found great use in other infectious diseases in the past and the diagnosis of COVID-19 today (Arya et al.,2005). However, the RT-PCR test may take time to result (up to 24 hours) (Sheridan, 2020; Ai et al.,2020; Coritti et al., 2020).

Chest CT imaging and the evaluation of the radiologist can be faster (Cinkooglu et al. 2020; Kim, 2020). Chest CT is used for the rapid diagnosis of patients with a negative initial RT-PCR test, but with high clinical suspicion (Cinkooglu et al., 2020). The world health organization (WHO) recommends the use of chest CT in symptomatic situations in the guide published in the COVID-19 outbreak (Diagram 1.) (WHO, 2020).

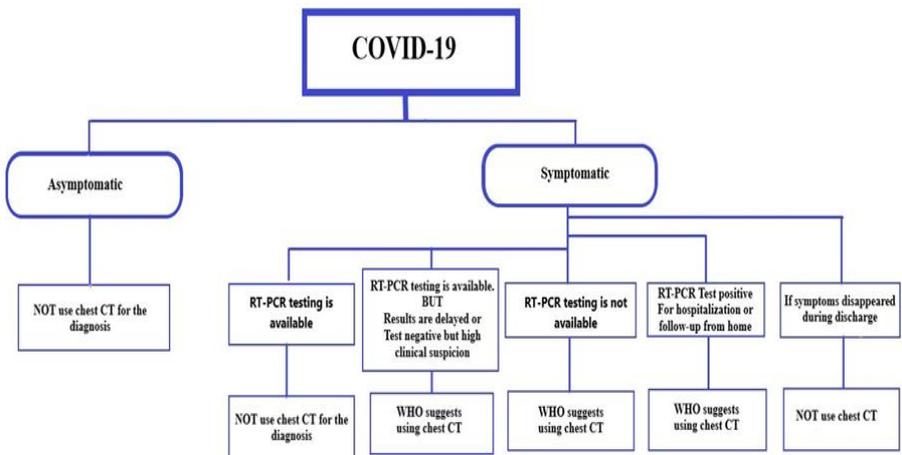


Diagram 1. Diagram illustrates the use of chest CT in COVID-19 (Compiled by the author).

Various studies have determined that chest CT has high sensitivity compared to the RT-PCR test (Long et al., 2020). In a study in which the results of chest CT and RT-PCR tests of 1004 patients were examined, it was found that chest CT had higher sensitivity than RT-

PCR (Ai et al., 2020). In another study reported that chest CT sensitivity (98%) was higher than RT-PCR (71%) (Fang et al., 2020). Other studies have also shown that chest CT has superior sensitivity (about 97%) (Caruso et al., 2020; Kanne et al.,2020). In addition, since the RT-PCR test cannot evaluate the severity and progression of COVID-19 disease, it increases the tendency to use chest CT (Kalra et al.,2020). Chest CT images are widely used in evaluation of the degree of pulmonary infection involvement, predict the prognosis, observing the course of the disease, and monitor treatment effectiveness (Yang et al.,2020, Guo et al.,2019). Chest CT is more sensitive in many diagnoses, including acute heart failure from COVID-19 myocardial injury (Driggin et al., 2020). Chest CT is used for the follow-up of cardiovascular findings that may occur in COVID-19 disease. Chest CT plays a key role in the diagnosis and management of COVID 19 (Rubin et al., 2020).

2. NEGATIVE EFFECTS OF USING CHEST CT IN COVID-19

2.1. Radiation exposure and Cancer risk due to chest CT in COVID-19

Patients are exposed to radiation during CT application because CT uses ionizing radiation to obtain images (Kavanagh et al., 2018). Ionizing radiation can seriously damage biological systems (Mojji and Moghimbeigi, 2011). It is difficult to express the amount of radiation dose that patients are exposed to during CT imaging with an exact number. A chest CT beam can reveal a radiation dose equivalent to 400 chest radiographs (Royall College of Radiologists, 1998). Patients

can receive a dose of approximately 4-7 mSv during chest CT imaging (Huda, Scalzetti and Roskopf, 2000; Wang et al., 2020). The radiation dose received by patients varies from patient to patient. Since this dose value is far below the threshold value where deterministic effects of radiation will occur, side effects such as erythema and epilation are not expected. But cancer and genetic effects from the late period stochastic effects of radiation are expected side effects (Revenel et al., 2001). Performing CT imaging can increase the risk of developing solid cancers and leukaemia in patients (Berrington de Gonzalez, 2009). Exposure to ionizing radiation has the potential to cause harm, no matter how small the radiation dose. Low-dose radiation exposure increases the amount of risk, especially in children and pregnant women (Li, 2020). Many studies have tried to determine the risk of radiation-induced cancer from CT (Kavanagh, 2018). Concerns about the increased risk of cancer due to the use of CT are constantly on the agenda (BEIR, 2006).

Institutes have reported incredible increases in the number of chest CT images during the COVID-19 outbreak (Ghetti et al., 2020). Physicians may request multiple CT scans from their COVID-19 patients in a short time during treatment (Niu et al., 2021). Patients with repeated CT scans are at higher risk of cancer due to greater exposure to radiation (risk can be > 2.7%) (Wang et al., 2020; Sodickson et al., 2009). Medical staff may be exposed to extra low-dose radiation during the COVID-19 pandemic due to the increased use in chest CT (Azadbakht et al., 2021).

2.2. Infection risk for medical staff and patients due to chest CT in the COVID-19

According to epidemiological research, COVID-19 disease is highly contagious and can spread rapidly among humans (Li, Q. et al., 2020). The method of transmission is by respiratory droplets as well as by physical contact (Huang et al., 2020). Medical staff, especially working in epidemic center, have faced an enormous risk of infection with COVID-19 (Xiong et al.,2020). Unfortunately, a large number of medical staff have contracted COVID-19 disease in their workplace. Medical staff in the CT department maintain physical contact with patients while preparing COVID-19 patients or suspects for chest CT (An et al., 2020). One of the risks for patients with suspected COVID-19 and medical staff is cross-infection during CT (Li, M. 2020). CT workers and patients can be infected in CT room. Additionally, multiple CT scans for COVID-19 patients' follow-up significantly increase the risk of infection (Li, j et al.,2020).

2.3. The psychological impact of COVID-19 on medical staff in CT department

Medical staff working in CT department are in constant contact with both colleagues and patients, so they are constantly at risk of getting COVID-19. While obtaining CT images of patients suspected of being infected or diagnosed with COVID-19, the medical staff's use of extra protective equipment and paying extra attention for hygiene rules results in extra fatigue. Having to work instead of colleagues who do not come to work due to lack of staff or infection increases the

pressure on healthcare workers (Verrier and Harvey 2010; Rutter and Lovegrove, 2006). They experience psychological problems such as anxiety, depression, and burnout due to their increasing workload and concerns about getting infected (An et al., 2020, Huang et al., 2021). Financial difficulties during the epidemic process in different countries, lack of access to protective equipment, job insecurity of medical staff, being exposed to more radiation due to the increase in the number of CT's are other problems. Psychological disturbances caused by the great difficulties experienced by medical staff are remarkable and should be considered (Kang et al., 2020; Shah et al., 2020).

2.4. Cost of chest CT in COVID-19

RT-PCR and chest CT are used continuously in the diagnosis of COVID-19. The number of RT-PCR and chest CT's has significantly increased since COVID-19 is transmitting to most people. The increase in the number of diagnostic methods to prevent further spread of the disease has also affected countries' budgets (Sriwijitalai and Wiwanitkit, 2020). In a study, the cost per service of RT-PCR and CT is examined and showed that chest CT was a more expensive method (Laupacis, Keller and Przybysz, 2020). Personal protection equipment, room, device cleaning supplies, device maintenance, device repair and spare parts replacement prices can be added to the cost of chest CT in COVID-19 (Rubin et al., 2020). Although developed countries such as China recommend the use of chest CT in conjunction with RT- PCR in the diagnosis of COVID-19 (WHO

Guide, 2020), RT-PCR still a good choice for early detection of COVID- 19 for developing countries with limited economic resources (An et al., 2020). If physicians request imaging only according to the needs of patients, healthcare costs can be saved. It is beneficial to use a cost-utility analyser for the use of CT in diagnosis and follow-up of COVID-19. Cost analysis is significant, but it is even more important to do what is necessary for the patient's health (Rehana et al., 2013).

3. RADIATION PROTECTION DURING CHEST CT IN COVID-19

The essence of radiation protection in healthcare is to protect the general public, patients, and healthcare workers from the harmful effects of radiation. Imaging devices such as CT used in the diagnosis of diseases contain ionizing radiation that is harmful to human health (Uddin et al., 2019). The ALARA (as low as reasonably attainable) principle is the guiding principle for CT examination (Zhu, Yu and Huang et al.,2004; Yu et al., 2009). Radiation dose is one of the most significant factors determining CT image quality and affects the diagnostic accuracy of a CT examination. Parameters such as the use of contrast, number of slices, slice length, patient anatomy, tube voltage, electrical current, pitch, and collimation determine the image quality and radiation dose during CT imaging (Ravenel et al., 2001; Niu et al., 2021). The new CT technology automatically adjusts parameters to the patient's anatomical characteristics, and the radiation dose can be significantly reduced (Rehani and Berry, 2000; Radpour et al., 2020). Given the increased risk of exposure to ionizing radiation

as a result of increased chest CT demand during the COVID-19 outbreak, it is necessary to use CT dose reduction protocols to reduce the amount of radiation (according to the ALARA principle). In the period when the COVID-19 pandemic was widespread, clinics tried to establish high-resolution low-dose protocols (Radpour et al., 2020; Kang et al., 2020; Liu H. et al., 2020; Kwee et al., 2020). There is no need to scan areas other than the lung area when taking a chest CT in COVID-19 patients. Studies suggest the use of single-phase, non-contrast and rapid scanning techniques achieve low doses in chest CTs during the epidemic (Kalra et al., 2020; Ghetti et al., 2020). Studies have indicated that with images obtained from the low-dose protocol, lung frosted glass nodules and exudative lesions caused by COVID-19 can be detected (Niu et al., 2021). Medical personnel working in CT department should reduce the radiation dose without compromising image quality to avoid incorrect diagnosing of COVID-19 patients (WHO Guide, 2020). An inadequate low dose protocol will produce the poor image quality and cause CT repeat. In this way, patients and healthcare workers will have to be exposed to radiation unnecessarily (Wong et al., 2012). For this reason, care should be taken when creating the low-dose protocol. Well-implemented low-dose protocols during the pandemic also reduce the risk of cancer induction (Ghetti et al., 2020).

The general public is unaware of the consequences of exposure to ionizing radiation. Medical staff are responsible for minimizing the radiation dose to reduce the risk of radiation exposure during CT (Niu et al., 2021). To protect from radiation during a CT scan, the exposure

time to radiation must be reduced. Working hours of medical personnel should be arranged in a way to shorten the duration of stay in the radiation environment. During the CT scan, the medical staff should be in a separate radiation-shielded room. Medical personnel's radiation monitoring equipment (such as a film badge and thermoluminescence dosimeter) is useful in determining the radiation dose they receive (Uddin et al., 2019; IAEA 2018; Goske et al., 2008). If radiation workers exceed the radiation dose limit, immediate medical check-ups are performed.

4. PROTECTION FROM INFECTION RISK IN CT ROOM

The unexpected and rapid spread of COVID-19 disease has led to changes and innovations in the health system. Authorities should take extra precautions to protect medical staff and patients during the CT scan of patients diagnosed with or suspected of having COVID-19. Given the high transmission rate of COVID-19, which is assumed to be related to the field of study in hospitals, clinics should prepare COVID-19 infection control protocols (Nakajima et al., 2020).

Medical staff who have to make physical contact with the patient during the CT scan should use the protection equipment at the highest level while in contact with a patient. Protective equipment includes protective clothing, gloves, protective cap, gown, eye protection, N95 respirator, face shield, face masks. Healthcare professionals should properly put on and take off protective equipment and ensure the use of rigorous surgical hand-washing techniques in the contaminated area (WHO 2020; An et al., 2020; Mossa-Basha et al., 2020).

Patients and their relatives must observe the distance rule in waiting areas (An et al., 2020). If possible, a separate route should be established for COVID-19 patients to travel to and from specialized CT (Mossa-Basha et al.,2020). Based on the fact that virus particles can spread throughout the room and live on surfaces, the CT device and room must be disinfected after each scanning. CT imaging rooms should be frequently ventilated (Huang et al.,2020; Lee et al., 2021; Hossein et al.,2020; Niu et al.,2020).

5. EDUCATION AND TRAINING OF MEDICAL STAFF IN CT DEPARTMENT

Due to the unexpected spread of the COVID-19 epidemic, changes in the workflow in health systems have had to occur. Healthcare professionals suddenly found themselves on a busy schedule and dealing with COVID-19 patients. Health institutions had to create new working procedures according to the new normal. Health authorities should provide training to all healthcare personnel on donning and removing personal protective equipment, hand hygiene, infection prevention, and control protocols (WHO 2020) ²⁸. Informing and training healthcare professionals about radiation and the health damage of radiation constitute the basis of radiation protection (Royal Collage of Radiologists 1998; Le Heron et al., 2010). With the high contagiousness of COVID-19, changes have been made in education and training activities. Online training has replaced face-to-face training (Robbins et al.2020). Online training should be done not only for technical issues but also for psychological support to healthcare

personnel. The negative impact on healthcare professionals can be reduced with technology and ongoing education (Akudjedu et al.,2020; Redmond et al.,2020). Clinical studies have revealed the importance of education of healthcare professionals in terms of both themselves and patients' protection (Uddin et al.,2019; Nakajima et al.2020).

CONCLUSION

As can be understood from the article, chest CT is frequently used in COVID-19 and this situation causes many positive and negative effects. Computed tomography is expensive, but it's superiority in imaging is indisputable. Unfortunately, the increase in chest CT scans appears as an increased radiation burden on patients and healthcare professionals. The risk of radiation-related cancer and genetic diseases in both patients and healthcare workers raises concerns. In addition, the risk of infection spread during CT scan increases. In the use of chest CT in the COVID-19 epidemic, the benefit-risk analysis should be done correctly. The medical staff working in the CT department have a great responsibility to protect both themselves and the patients. Low dose protocols to be created during CT imaging can significantly reduce the radiation dose. Guidelines and increased training frequency will help to reduce the increasing pressure on medical staff working in CT department.

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